Annual Report
2019-20

INDIAN COUNCIL OF MEDICAL RESEARCH
Serving the nation since 1911

Indian Council of Medical Research
New Delhi

Annual Report
2019-20

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Dr. Harsh Vardhan

माननीय केंद्रीय मंत्री
Hon'ble Union Minister

स्वास्थ्य एवं परिवार कल्याण मंत्रालय
Ministry of Health and Family Welfare

श्री अश्विनी कुमार चौबे
Shri Ashwini Kumar Choubey

माननीय राज्य मंत्री
Hon'ble Minister of State

स्वास्थ्य एवं परिवार कल्याण मंत्रालय
Ministry of Health and Family Welfare

PREFACE

It gives me immense pleasure to present the Annual Report of the Indian Council of Medical Research (ICMR) for the year 2019-20. ICMR scientists worked as a team to achieve the goals in sync with government policies and programmes in the field of biomedical research. There were several significant achievements of the year. The foremost being, as part of the SARS-CoV-2 pandemic response, ICMR-NIV, Pune optimized real-time RT-PCR assay (E gene) for screening and confirmation (RdRp, N and ORF 1b genes). It performed quality control for all the government and private laboratories performing COVID-19 testing in Maharashtra and supplied 3,57,626 reagents. The confirmation of the first 03 cases in India was reported on 30th Jan. 2020 as imported cases from Wuhan, China. Till 31st March 2020, 5045 samples were screened and 304 tested positive.

There was establishment of diagnostic assays, countrywide network of laboratories, quality control, trainings on biosafety practices, virus isolation and NGS of whole genomes, during the ongoing SARS-CoV-2 pandemic 2019. ICMR COVID-19 Data Portal was developed (https://cvstatus.icmr.gov.in) to manage COVID-19 testing and analysis. COVID-19 Testing Laboratories Location portal was also developed https://covid.icmr.org.in. It is a portal to navigate and find out nearest COVID-19 Testing Laboratory location across the country.

In an effort to screen Indian nationals stranded in Iran, NIV team comprising of two scientists and technical experts were deputed to screen them and enable their evacuation during March 5 to March 17, 2020. Throat swabs were collected from 2028 individuals on site, of which 308 tested positive for SARS-CoV-2.

Investigation of Nipah virus outbreak in Ernakulum district, Kerala in June 2019 was done. Infection was confirmed in a 21 year old male student in Ernakulum district, Kerala. RNA detection and antibody prevalence in fruit bats from the neighborhood of the index case confirmed the association of bats in virus transmission. On-site training of health care workers and on-site laboratory staff helped in dealing with the outbreak effectively. Indigenous anti-NiV IgM and IgG antibody ELISA were developed and optimized for future surveillance studies.

Also, a novel cost effective virus precipitation method was standardised for detection of polio and non-polio enteroviruses during environmental surveillance. A real-time multiplex RT-PCR for serotyping of dengue viruses was developed.

ICMR partnered with British Council UK for the Researcher Links Workshops under the Newton Bhabha Fund programme .These workshops are designed to provide financial support to bring together

a UK/Indian bilateral cohort of early career researchers to meet the overarching objectives. Under ICMR/AU-STRC Health Practitioners/Researchers Capacity Building Scheme, ninety-five African Health Practitioners/Researchers from 26 African countries were trained.

India Cancer Research Consortium https://icrc.icmr.org.in has been established to strengthen fight against cancer. It will bring together stakeholders with interests in basic sciences, clinical and translational research and public health policy related to cancer.

ICMR has also entered into an agreement with Federation of Indian Chambers of Commerce and Industry (FICCI) for both national and international commercialization of health technologies under HTAC program. HTAC program has three components viz. Commercialization component, training component and exposition component.

The WHO FCTC Global Knowledge Hub on Smokeless Tobacco at ICMR-NICPR, assisted country Myanmar to identify priorities and key recommendation for framing policies for tobacco control.

There was publication of White paper on *Electronic Nicotine Delivery System* (ENDS), describing its addictive potential and threat to the country's tobacco control laws and on-going tobacco control programmes. This led to the promulgation of the Prohibition of Electronic Cigarettes (production, manufacture, import, export, transport, sale, distribution, storage and advertisement) Ordinance, 2019 in India.

ICMR-NICPR drafted a document for comprehensive ban on SLT products (manufacture and sale) along with ban on their use and spitting in public places for containing COVID 19 pandemic. The Union Home Ministry also took cognizance of this issue and included in its consolidated revised guidelines issued on 15th April to contain COVID-19 pandemic by declaring the act of spitting in public places a punishable offence with a fine under Section 51 (b) of the Disaster Management Act 2005. The states of Jharkhand, Telangana, Uttar Pradesh, Uttarakhand, Maharashtra, Haryana, Nagaland, Bihar and Assam immediately issued orders on the ban of use of smokeless tobacco products and spitting in public places for containing COVID-19 pandemic.

ICMR participated in the Health Research Conclave at Kolkata with an aim to provide a platform where eminent health scientists and researchers can interact with each other as well as with media, policy makers and general public. The theme of the conclave was 'Translating Research into Action for Improving Health of the Population' where eminent health experts spoke on Tribal Health, Nutrition, Medical Innovations and Emerging Infections.

The first volume Standard Treatment Workflows (STWs) was released by Bill Gates, Co-chairman and co-founder of the Bill & Melinda Gates Foundation. It includes 50 diseases across 9 specialties. These will serve as uniform treatment guideline for doctors in primary and secondary healthcare settings.

A Special issue on "India & COVID-19"was published in IJMR in February & March 2020. Efforts were done to publish articles most relevant to COVID to ensure dissemination of most opportune information to readers and policymakers.

During this period, 11 patents (8 Indian and 3 international patents) had been granted and 2 design applications had been registered. A total of 24 patents (14 Indian patents, 6 foreign patent applications and 4 foreign patents) and 2 designs were maintained.

ICMR-NCDIR prepared National Guidelines for Ethics Committee for reviewing Biomedical & Health

Research during Covid-19 Pandemic to facilitate easy understanding for the Ethics Committees to conduct review in expedited manner in the current prevailing pandemic situation. It is expected that this guideline will be useful not only for ethics committees but for all stakeholders in research and public.

ICMR-NCDIR drafted a position paper on 'Do Not Attempt Resuscitation (DNAR)' to guide treating physicians to take decision when the patient's chances of survival are extremely low and to preserve the dignity in death by avoiding medically non-beneficial CPR while providing compassionate care.

Under Human Resource Development, ICMR selected 145 candidates for Junior Research Fellowship (JRF) through national level exam, 1085 medical undergraduates were selected for short term studentship (STS), Post-doctoral Research Fellowship (PDF) was granted to 15 candidates and financial assistance was given to a total of twelve clinical scientists through Nurturing Clinical Scientists Scheme. MD/ Ph.D Programme is continuing in three universities and eight students were selected. A total of 266 non-ICMR scientists were given financial assistance to attend conferences abroad. A total 17 Emeritus scientists were shortlisted. ICMR institutes continued to provide training to various State level health officials.

ICMR, through online system, received 2904 extramural adhoc proposals, and 2189 extramural SRF & RA fellowship proposals, out of which 773 extramural adhoc proposals and 815 SRF & RA fellowship proposals were technically approved after elaborative evaluation. Two specified 'Call for proposal' programmes pertaining to certain priority areas, were also launched during the year, which resulted in receipt of 334 proposals online. ICMR Scientists published over 800 research papers in national and international journals.

(Dr. Balram Bhargava)
Secretary, DHR & DG, ICMR
New Delhi

EDITOR'S DESK

The Indian Council of Medical Research (ICMR) is today the apex and premier medical research organization in the country which spearheads planning, formulation, coordination, implementation and promotion of biomedical research. It is one of the oldest medical research bodies in the world. In 1911, Government of India made a historic decision to establish Indian Research Fund Association (IRFA) with the specific objectives of sponsoring and coordinating medical research in the country. After Independence, in 1949, the IRFA was re-designated as the Indian Council of Medical Research (ICMR) with considerable expansion in its functions and activities.

To enhance national capacity for detection of COVID-19, existing virus research and diagnostic laboratories (VRDLs) in the country and NCDC labs were trained. Biosafety training was given to NDRF personnel as well. Twenty real time RT-PCR kits were evaluated while evaluation of 7 rapid diagnostic test kits was initiated. ICMR-NIV was involved in making of in-vitro transcripts as positive controls for SARS-CoV-2 testing in all VDRLs.

ICMR-NIV did external onsite validation of Nipah PoC and indigenously developed anti-Nipah human IgM and IgG ELISA assays with Institute of Epidemiology Disease Control and Research, Dhaka, Bangladesh and signing of MoU was done. Genetic diversity of dengue virus serotypes circulating in different regions of India was studied in collaboration with VRDL network. The institute found that Microcephaly was not detected among babies delivered by Zika positive women. Study also detected bat coronavirus in *Pteropus* and *Rousettus* species of bats in India. There was establishment of a network of Laboratories for epidemics and Natural Calamities at the Kerala Unit.

The following policy briefs were prepared by ICMR-NIRRH—a)Expanding Informed Contraceptive Choice for Indian Women: Will Nexplanon Matter; b)Enhancing Utilization of Adolescent Health Services; c) Involvement of Self Help Group (SHG) Women to improve health seeking behaviour of tribal women; d)Genetic testing (CFTR-mutations) in Indian men with congenital bilateral absence of vas deferens (CBAVD) before undergoing Intracytoplasmic Sperm Injection (ICSI); e) Genetic testing for non-obstructive azoospermia and oligozoospermia; f) A Model for Addressing Burden of Snakebites in Rural India through Health System Capacity Building.

First national evaluation of GOI's free-ART national-program impact in 396 ARTC was led by ICMR-NARI collaborating with 5 ICMR institutes.

ICMR-RMRC Dibrugarh helped in establishment of a regional depot for storage and supply of COVID-19 testing kits/ reagents to the designated real-time PCR laboratories in northeast India.

ICMR

INDIAN COUNCIL OF MEDICAL RESEARCH

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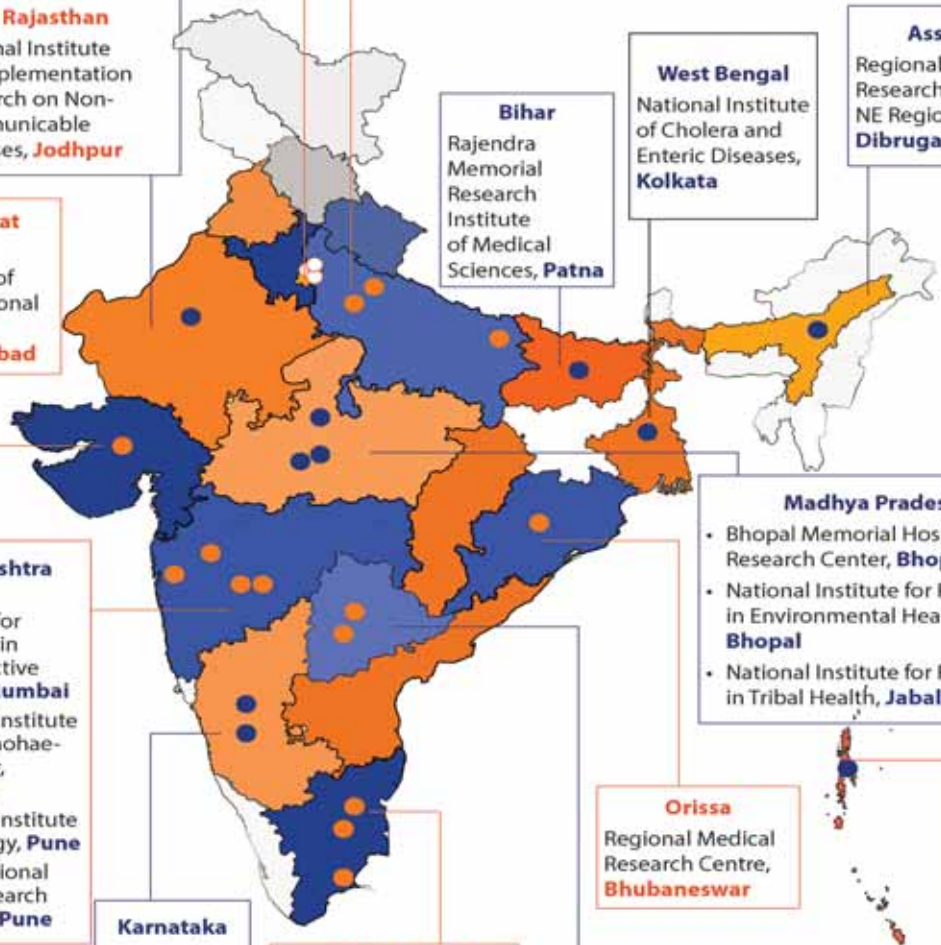
INSTITUTES/REGIONAL MEDICAL RESEARCH CENTRES



Uttar Pradesh

- National JALMA Institute for Leprosy & Other Mycobacterial Diseases, **Agra**
- National Institute of Cancer Prevention and Research, **Noida**
- Regional Medical Research Centre, **Gorakhpur**

New Delhi

- National Institute of Malaria Research, **New Delhi**
- National Institute of Pathology, **New Delhi**
- National Institute of Medical Statistics, **New Delhi**

Rajasthan

National Institute for Implementation Research on Non-Communicable Diseases, **Jodhpur**

Bihar

Rajendra Memorial Research Institute of Medical Sciences, **Patna**

West Bengal

National Institute of Cholera and Enteric Diseases, **Kolkata**

Assam

Regional Medical Research Centre, NE Region, **Dibrugarh**

Gujarat

National Institute of Occupational Health, **Ahmedabad**

Madhya Pradesh

- Bhopal Memorial Hospital & Research Center, **Bhopal**
- National Institute for Research in Environmental Health, **Bhopal**
- National Institute for Research in Tribal Health, **Jabalpur**

Maharashtra

- National Institute for Research in Reproductive Health, **Mumbai**
- National Institute of Immunohae-matology, **Mumbai**
- National Institute of Virology, **Pune**
- ICMR-National AIDS Research Institute, **Pune**

Orissa

Regional Medical Research Centre, **Bhubaneswar**

Karnataka

- National Centre for Disease Informatics and Research, **Bengaluru**
- National Institute of Traditional Medicine, **Belagavi**

Tamil Nadu

- National Institute of Epidemiology, **Chennai**
- National Institute for Research in Tuberculosis, **Chennai**
- Vector Control Research Centre, **Puducherry**

Telangana

- National Institute of Nutrition, **Hyderabad**
- National Animal Resource Facility for Biomedical Research, **Hyderabad**

Port Blair

Regional Medical Research Centre, **Port Blair**

ICMR-NICPR has been designated as nodal center for training Medical Officers of all States in cancer screening by MoHFW in May 2019. NICPR has trained 345 Medical Officers, 145 Gynecologists and 112 dentists from Govt sector in cancer screening.

ICMR-RMRC Gorakhpur did formulation and distribution of infographics (pamphlets) on SWACHCHHATA & HEALTH HYGENE as part of Swachchha Bharat Abhiyan in HDSS villages (>1200 families). Distribution of infographics on JE / AES awareness in 28 HDSS villages (> 3000 families) was also done.

ICMR-RMRC Bhubhneswar is the only centre in Odisha imparting the training programmes on health informatics which emphasize the digital India health prospects. Centre also supported preparation of 15-district convergent nutrition action plan as per guidelines of Poshan Abhiyaan.

The Malaria Elimination Research Alliance India (MERA India) was operationalised by ICMR-NIMR. It Evaluated new tools for malaria control like diagnostics (RDTs), antimalarials (alternative ACT) and vector control tools (combination LLIN).

ICMR-NCDIR did Implementation of NCDIR electronic Mortality software (NCDIR e-Mor) in hospitals of the National Cancer Registry Programme (NCRP) network. Also, team developed policy on Research Integrity and Publication Ethics (RIPE) The primary aim of the policy is to ensure highest professional and ethical standards for biomedical and health research at all stages.

Nutrition Surveillance System (NSS) was established by ICMR-NIN in 6 states to provide early warning signs of malnutrition among vulnerable population groups to take immediate actions. Team also developed and launched Nutrition and Health E-modules for common people education and grassroot level functionaries like Anganwadi Workers under Poshan Abhiyaan.

National Data Quality Forum has been established at ICMR-NIMS to create an ecosystem to ensure data quality. A National Consultation was conducted with stakeholders.

SBHSR Division concluded two national task force projects on Road Traffic Injuries and established an electronic-based comprehensive and integrated RTI surveillance system. Study also demonstrated the feasibility of establishing the system within the public health system.

Hon'ble Vice President Sh Venkaiah Naidu gave prize to ICMR Scientists for the most Informative Stall in the 107th Indian Science Congress which was inaugurated by the Hon'ble Prime Minister of India Shri Narendra Modi on 3rd Jan., 2020. The Pride of India Expo was inaugurated by Dr Harsh Vardhan, Hon'ble Union Minister of Science & Technology and Earth Sciences who visited ICMR pavilion and interacted with the ICMR Scientists. The Council also showcased its activities and achievements by displaying posters, live demonstrations, publications, films and distributing pamphlets.

ICMR-NIOH developed an ELISA based indigenous Kit for detection of serum CC-16 in collaboration with ICMR-NIV. It also developed a training module in association with Public Health Foundation of India, Delhi, on Basic Occupational Health & Safety involving WHO, ILO & other national occupational health experts of India.

Mission SHAKTTI (School-based Health Awareness, Knowledge Test and Training Initiative): A School-Based Dissemination Programme was initiated by ICMR in collaboration with Directorate of Education and National Gandhi Museum in 36 schools of Delhi to take forward Gandhiji message of Health and Hygiene adopting physical fitness, meditation, balance diet and cleanliness for Happy and

Healthy India. Around 2800 students participated in the event. This program was also replicated in Jabalpur (by ICMR-NIRTH) and Kolkata (during IISF 2019) where around 400 students participated. It is planned to be extended in other parts of the country in future.

ICMR media policy and ICMR Disaster Management Plan 2019 were developed and released by RMPPC Division. The rationale of the disaster management plan is to equip the department and its associated offices/labs to assess risk and manage disaster effectively. In this document, DHR-ICMR has provided detailed Disaster Management Plan (DMP) for national component as well as contingency plan for the Department and its attached bodies.

A total of 11 issues of IJMR, including two Special Issues on "India & COVID-19" were published. Five per cent more articles, contributed by foreign authors were published as compared to the previous year. Impact factor increased to 1.503 compared to the previous year (1.251).

A total of 46 Scientists and Young researchers were given the ICMR Awards in 31 different categories for the year 2017 and 2018. For the year 2019, a total of 165 workshop applications on Clinical Training/Translational Research were approved for funding support. Out of 525 MD/MS/DM/MCh/MDS thesis support proposals received, 100 proposals were awarded financial assistance for the year 2019-20.

Two 'Call for proposals' programmes were launched during the year which resulted in receipt of 334 proposals online. These included a). Call for proposal on Research areas in Leishmaniasis. b). Call for proposal under North East Seed Grant scheme.

(Dr Chanchal Goyal)
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CONTENTS

COMMUNICABLE DISEASES

Communicable and infectious diseases pose serious public health problems. ICMR's research efforts in the area of communicable diseases were made by 16 institutes/ centres including Regional Medical Research Centres (RMRCs) and their field stations located in different parts of the country as well as by granting adhoc projects in extramural mode in universities/ medical colleges and other organizations. The research activities carried out by different ICMR Institutes and their outcome for the year 2019-20 are detailed in this chapter.

INTRAMURAL RESEARCH

BRIEF UPDATE ON VARIOUS ACTIVITIES RELATED TO COVID-19 UNDERTAKEN BY ICMR/DHR

I. Testing for COVID-19

a. In January 2020, ICMR-NIV, Pune standardized the RT-PCR based diagnostic test and was the standalone lab for COVID testing, whereas today we have close to 2400 labs with testing capacity close to 14 lakh per day. 526/536 Medical Colleges are now testing for COVID-19 and 659/741 districts have a RTPCR testing facility whereas all 741 districts have RAT testing available. Proactive efforts are being made to establish facility in remaining districts through PM cares funds and other resources.

b. Resources in labs have been augmented by providing multiple RT-PCR machines, high throughput machines, automated RNA extraction platforms, increased manpower etc. This has led to a reduced turnaround time of testing wherein > 85% of the results are provided within 48 hours.

c. Immense efforts have been made to establish labs in difficult terrains like Ladakh, Sikkim, Arunachal Pradesh, Nagaland as well as other NER states, islands like Lakshwadeep and Andaman & Nicobar.

d. For remote and rural areas, TrueNat/CBNAAT platform, validated by WHO for TB, have been repurposed for COVID testing. Currently, close to 3000 TrueNat (indigenous platform) machines have been deployed.

e. High throughput machines (testing capacity of >1000 per day) were set up at 10 different locations in India and were inaugurated by Honb'le PM. Mobile testing labs were inaugurated by Hon'ble HM and deployed in collaboration with Spicehealth.

f. Rapid antigen testing was approved in last week of June. This point of care test has tremendously improved access and ease of testing. India became the first country to deploy COVID-19 RAT in program.

g. Strategy for pooled testing of samples was standardized and disseminated.

h. 24 validation centres have been set up for fast track validation of newer diagnostic

commodities. So far, more than 1150 different diagnostics have been validated of which 577 are approved. In line with the "Atmanirbhar Bharat" initiative of the Hon'ble PM, ICMR has approved 416 (72%) indigenous test kits. Indigenous manufacturers are also being hand-held to improvise their products. This led to ten-fold decrease in the pricing of diagnostics.

i. Un-interrupted supply of testing commodities to states through 20 ICMR depots has been ensured.

j. ICMR- NIV team travelled to Iran to help in the evacuation of Indian shia pilgrims (>6000) stranded in Iran in Feb. 2020. RTPCR lab was set-up in Tehran and 2028 samples were collected from 5 cities (Qom, Tehran, Shiraz, Mashhad, Isfahan). Special flights operated by Indian Air Force & Iranian Airlines for repatriation of Indian Nationals.

k. A quarterly Quality Control program has been implemented for more than 1250 RTPCR laboratories. With the help of WHO External Quality Assurance program has been also been implemented. This effort is envisaged to improve the quality of testing.

l. A uniform data entry portal is hosted by ICMR. This database carries India's COVID-19 testing data for more than 20 crores tests.

m. A common sample referral form (SRF) has been developed and deployed with the help of National Information Centre (NIC) through the RTPCR application.

II. Nationwide serosurvey to determine the seroprevalence of SARS-CoV-2

Blood samples from a total of 24000 samples from 71 districts were collected and tested for IgG antibodies against SARS-CoV-2. Three Nationwide serosurveys have been conducted from May 11 to June 4, 2020; August 17 to September 2 and December 17 to January 8. The nationwide adjusted sero-prevalence was found to be 0.73%; 7.1% and 21.5% respectively. The third serosurvey also included 7000 healthcare workers.

III. Isolation of SARS-CoV-2 virus by ICMR-NIV, Pune

a. Three different strains of SARS-CoV-2 have been isolated and cultured:
   - India became the 5th country to isolate the virus in March 2020.
   - UK variant strain was isolated in December 2020
   - Brazil variant strain was isolated in February 2021

b. Virus isolation paved the way for development of following technologies:
   - Indigenous ELISA IgG kit by NIV, Pune. Technology was transferred to 7 Indian companies.
   - Hyper-immune horse serum, which offers a promising tool for prophylaxis and treatment of SARS-CoV-2 exposed/ infected individuals. ICMR has provided the virus and is working closely with three companies for clinical development of this product.
   - Development of indigenous whole virion inactivated vaccine by Bharat Biotech International Ltd.
   - Laboratory assays like the gold standard Plaque Reduction Neutralization Test (PRNT) was established.
   - Animal challenge experiments were conducted to understand the efficacy of vaccines and therapeutics.

IV. Drug Trials

a. **World's largest Plasma Therapy Trial (PLACID):** The trial was conducted in a total of 464 participants across 39 hospitals. A set of clinical and laboratory parameters were monitored over 28-day period in patients enrolled in intervention (235) and control arms (229). The trial has revealed no significant benefit of plasma therapy in terms of reducing severity of disease and mortality.

b. **WHO Solidarity Trial:** India: ICMR-National AIDS Research Institute led the trial which was initiated trial in April 2020 across 26 hospitals

and 1048 adults randomized. The globa trial in >11000 individuals concluded that Remdesivir, Hydroxychloroquine, Lopinavir and Interferon - little or no effect on overall mortality, initiation of ventilation and duration of hospital stay in hospitalized.

V. COVID-19 Vaccine trials supported by ICMR/DHR

a. COVAXIN of Bharat Biotech International Ltd (BBIL):

- Provided virus strain
- Characterized vaccine strain
- Conducted preclinical studies in hamsters & monkeys
- Technical & Lab support for phase 1 & 2 trials.
- Technical & lab and financial support for phase 3 trials

b. COVID-19 vaccines manufactured by Serum Institute of India:

- Phase 2/3 studies of COVISHIELD (AstraZeneca)
- Phase 2/3 studies of COVOVAX (Novavax)
- Preclinical Hamster studies: indigenous candidates

c. ZyCoV-D of Zydus Healthcare:

- Preclinical studies in monkeys at ICMR-NIV, Pune

d. Proposals in pipeline:

- Preclinical studies in Monkeys of Biological Evans vaccine candidate
- Preclinical studies in rats and hamsters of vaccine candidates of Reliance Industries

VI. Other activities:

a) Vaccine portal of India was inaugurated recently by Hon'ble HFM in September 2020.

b) Laboratory studies for development of monoclonal antibodies for COVID-19 prophylaxis and treatment have been successfully completed. Clinical evaluation and next steps are being taken up.

c) COVID-19 clinical registry across 40 tertiary medical institutes of eminence have been established. Aim is to understand the demographic features, clinical outcome and design suitable treatment modalities for COVID-19 affected patients.

d) Ten COVID-19 biorepositories for helping industry/academia with appropriate samples of SARS-CoV-2 for developing indigenous diagnostics etc. have been established.

e) Sewage surveillance has been standardized to detect presence of SARS-CoV-2 as early warning signal to predict increase in disease prevalence in a particular zone.

f) ICMR has been issuing timely advisories, treatment modalities, discharge guidelines, testing advisories etc. through the National Task Force chaired by Member Niti Aayog.

g) More than 100 antiviral drugs/compounds have been screened for their antiviral potential.

h) Good quality research projects with high translational potential in areas of epidemiology & surveillance, laboratory diagnostics, clinical and operational research have been funded.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS, CHENNAI (ICMR-NIRT)

Department of Clinical Research

The department is involved in various international and national clinical trials to study the short course regimens for drug resistant TB, higher dose of rifampicin for pulmonary TB and extrapulmonary TB, role of adjuvants in TB management. Some of the studies include STREAM Study - multi-country trial to evaluate shortened drug regimens in Multi Drug Resistant Tuberculosis; TBM Kids Trial - multi-country trial to determine optimal regimen for tuberculous meningitis in children ; BEAT study –

multicentric study to evaluate the effectiveness and safety of a fully oral non-injectable short course regimen with newer drugs for XDR-Tb patients; METRIF Trial - multicentric study to evaluate the anti-bacterial activity, pharmacokinetics, safety and tolerability of Metformin when given along ATT in new smear positive TB patients; HICON-R Trial - multi-centric study to evaluate the safety, tolerability, pharmacokinetics and anti-bacterial activity of High dose rifampicin versus Conventional dose of Rifampicin in new smear positive patients, evaluation of VPM1002 and MIP vaccine in prevention of TB among household contacts. Other research activities including understanding the cause of death among TB patients by verbal autopsy, improving airborne infection control practices in health centres, prevalence of TB among household contacts of MDR TB patients, predictors of emergence of additional drug resistance among MDR-TB patients.

Department of Socio-Behavioral Research

Targeted Intervention to Expand and Strengthen TB Control in Tribal Populations under the RNTCP, India showed that the prevalence of bacteriologically positive PTB was 490 per 100000 population. The PTB prevalence per 1 lakh population was the highest 791 [95% CI: 676 – 906] in the central zone and least 99 [95% CI: 33 – 166] in the west zone. Among the 17 states that were covered in this study, Odisha recorded the highest prevalence of 1002 [95% CI: 740 – 1264] and Jammu and Kashmir the lowest 72 [95% CI: 0 – 170] per 100000 population. . The other major studies of the studies conducted by the department include Patients' perception on Quality of Care in TB Care Settings in Chennai and Fostering resilience to psychosocial and HIV risk in Indian MSM.

Health Economics

Department of Health Economics was established in ICMR-NIRT, Chennai in on 4th July 2018. Some of the key mandates of Department of Health Economics is to conduct research on economic aspects of diseases with special focus to tuberculosis and capacity building for health economic research and practice in the country through various training programmes and workshops. The various projects undertaken in the department include Establishing Regional Resource Centre for Health Technology Assessment in India (HTA-In), Health Technology Assessment for screening of Type 2 Diabetes & Hypertension in India, STREAM-II: The Evaluation of a Standardized Treatment Regimen of Anti-Tuberculosis Drugs for Patients with MDR-TB – Health Economics Component – India, Health Technology Assessment for screening of Hepatitis B and C at Primary Health centres in Tamil Nadu and Social network analysis as a tool to improve active case finding at community level in Chennai, south India.

Department of Epidemiology

Nationwide TB survey was never repeated after 1956. A Nationwide TB prevalence survey is conducted to closely monitor the progress towards TB control with the aim to 'End TB' as per Sustainable Development Goals (SDGs). Survey for the prevalence of TB among homeless person found that the prevalence of TB among respiratory symptomatic was 47/1000 (26-67) and among asymptomatic was 6/1000(4-9).

Department of Bacteriology

The department of bacteriology supports the clinical trials carried out at NIRT, including setting up drug susceptibility testing for newer anti-TB drugs like bedaquiline and delamanid. Other major studies include Validation of indigenous diagnostic kits (Truenat) for Tuberculosis, based on the outcome of the study, Multi-centric validation of indigenous kit 'TB-Detect' for the diagnosis of TB , Testing of newer molecules and compounds for anti-tubercular activity, Assess the added value of Whole Genome Sequencing in differentiating relapses from re-infection, Cambridge-Chennai Centre Partnership on Antimicrobial Resistance in Tuberculosis: Focus on Novel Diagnostics and Therapeutics: Host Directed Therapy through autophagy stimulation, Prediction of treatment failure among diabetes-TB patients by peripheral blood transcriptional signature and Prevalence of

non-resolving pneumonia in children suspected with TB.

NTEP (National Tuberculosis Elimination Program) activities

ICMR -NIRT is one of the National Reference Laboratory under NTEP - closely monitors five states (Andhra Pradesh, Gujarat, Kerala, Tamil Nadu, Telangana State) and five Union territories (Andaman & Nicobar, Puducherry, Lakshadweep, Daman & Diu and Dadra & Nagar Haveli) and provides technical support for the TB laboratory activities of NTEP**.**

Supranational National Reference Laboratory Activity (SNRL)

As part of SNRL NIRT conducts EQA for culture and DST (Drug susceptibility) for the laboratories under the NTEP. This is also extended to interested SEARO members courtiers namely Myanmar and Timor Leste. We have also provide support to conduct drug resistance surveillance during the present year.

Department of Clinical Pharmacology

NIRT is one of the very few institutes in India that has validated methods for the estimation of anti-TB, anti-retroviral and anti-diabetic drugs by HPLC method. Study to understand the pharmacokinetics of second line MDR –TB drugs, including newer drugs like Bedaquiline and Delamanid showed that drug doses used currently in the programme produced optimal drug concentrations in majority of patients. Ethionamide was a key determinant of end of intensive phase status. In another study to design and synthesize of novel Rifampicin based heterocycles and Au-Ag metal nano clusters as potential Antitubercular agents, novel Gold metal nano cluster was synthesized, characterized and studied by in-vitro method. Some of the promising studies are following. (i) Synthesis and in-vitro studies of novel RIF-CFZ hybrid drug; (ii) Synthesis and in-vitro studies of novel RIF-MET Hybrid drug; (iii) Synthesis and in-vitro studies of RIF-Imidazole scaffold.

Department of Biochemistry

The Department of Biochemistry is functioning independently from 2018 with the following major activities of public health importance. (i) Providing high quality data for the clinical trials conducted at ICMR-NIRT (ii) Estimating the active content of the ATT drugs and reporting the data to the Drug Procurement Committee of NIRT and (III) Conducting independent basic research projects.

Department of Biostatistics

The department supports all the clinical trials of the institute in data management and the conduct of the trial. Some of the major projects of the institute Models Formulation using Cox Regression: A rational investigation on variable selection for time-to-event randomized clinical trial data on tuberculosis and development of a database of clinical study X-rays at NIRT, Chennai.

Department of Immunology

The study titled CYP2R1 gene polymorphisms in pulmonary tuberculosis showed that rs10741657 "AG" and "AA" genotypes are associated with TB protection and with higher 25(OH)D levels. The other major studies are Whole Genome Sequencing and Transcriptome analysis of Mycobacterium tuberculosis clinical isolates from Bovine and Human Origin, CYP27b1 gene polymorphisms in pulmonary tuberculosis, Study on Mutations Associated with Pyrazinamide Resistance in Mycobacterium tuberculosis, Identification of the latent tuberculosis specific marker by the immunoproteomic analysis of the cell wall and membrane proteins of M. tuberculosis, Attenuated mycobacteria based vaccine with a novel strategy for t cell priming, Identification of tuberculosis specific biomarkers in children by the proteomic analysis of urine, Gene knockout characterization of Rv2159, a alkyl hydroperoxidase of M. tuberculosis, Molecular analysis of monocyte subsets from humans infected with M. tuberculosis Another major ongoing study is to building laboratory, Surveillance and workforce capacity

to detect, respond to and prevent drug resistant tuberculosis in India.

Department of HIV

The department supports the clinical trials in NIRT, NACO as well involved many basic science research studies. Deciphering the role of the mucosal immune responses and cervicovaginal microbiome in resistance to HIV infection in HIV-exposed seronegative individuals which showed that a combination of soluble factors, mucosal natural killer cells, T follicular cytotoxic and helper cells in the female genital tract and a highly diverse cervicovaginal microbiome could play an important role in protecting against HIV infection. Other studies include Transmitted HIV-1 drug resistance in a treatment-naive cohort of recently infected individuals from Chennai, Identifying the unique molecular and biological characteristics of transmitted/founder HIV-1 isolates and systemic inflammation and increased risk of inflamm-aging and age-associated diseases in people living with HIV on long term suppressive antiretroviral therapy.

International Centre for Excellence in Research

The department has been involved in studies to understand the immunology of TB and comorbidities such as malnutrition and diabetes Mellitus. Other major studies include Characterization of immune responses in TB lymphadenitis and characterization of immune changes of pregnancy on TB. Study to understand the effect of helminth infection on antigen-specific immune responses in latent tuberculosis in South India showed that there was modulation of TB antigen specific cytokine responses and alteration of Th1 and Th17 responses in coinfection.

Public Health Importance

- WHO endorsement of Truenat as a point-of-care platform that would help universal access to TB molecular diagnostics in countries with endemic TB.
- Established the whole genome sequencing facility and capabilities for the detection of DR-TB mutations by computational analysis from strains collected from various IRLs to have a nationwide representation.
- NIRT is part of multiple multi-country clinical trial involving drug-sensitive pulmonary TB, drug-resistant TB and Pediatric TB, TB prevention (Vaccine) trial
- Student ambassadors have been actively involved in conducting TB awareness programs in their respective schools for the other students
- Established a well characterized biorepository for TB research
- Developed and validated a simple but high-throughput next generation sequencing protocol for sequencing of HIV-1 near full-length genomes.

ICMR-NATIONAL JALMA INSTITUTE FOR LEPROSY & OTHER MYCOBACTERIAL DISEASES, AGRA (ICMR-NJIL&OMD)

Leprosy Elimination

- **Reconstructive Surgery**- Under "Multicentric trial to study the effect of early active mobilisation as compared to three weeks immobilisation following tendon transfer procedures for Claw Hand", surgery camps were organized. RCS surgeries have been performed in around 30 patients of leprosy deformity including claw hand, lagophthalmos and foot drop. The comprehensive service of RCS includes pre-operative mobilization under inpatient settings, post-operative care, physiotherapy and functional rehabilitation.

- Leprosy vaccine with MIP

  Under the project "Programmatic implementation and comparison of MIP vaccine immune-prophylaxis and rifampicin

chemoprophylaxis for contacts for leprosy patients" under the national leprosy eradication programme (NLEP) in high endemic settings, following actions were taken.

- **Gujarat-**1500 healthy contacts of Person Affected with Leprosy (PAL) were vaccinated. Booster dose completed for 80% of the contacts vaccinated.
- **Bihar-**State level training completed and District level training will be started soon for implementation of the Vaccine
- **Kerala-**STAGI meeting held on 23rd Oct 2019 and approved the implementation of vaccine in phased manner
- **Chhattisgarh-**Proposal accepted in principle and final approval awaited

NTM- A project for Prevalence of Microbiologically Positive Pulmonary Non-Tuberculosis Mycobacterium (NTM) Including Species Information under the Revised National Tuberculosis Control Programme (RNTCP) was initiated, covering 12 states and117 Districts of the Country. It included formulating guidelines for management of NTM under programmatic conditions to RNTCP.

Tuberculosis

- A project entitled, "Prevalence and Determinants for TB Disease among Contacts of TB Patients: Study was initiated covering 5 States; 5 Districts of the Country, results of which will pave the pathway for one of the most important decisions for END TB strategy 2025 & also further
- Another project entitled-Strengthening Mechanism for TB Death Reporting under the Revised National Tuberculosis Control Programme (RNTCP) and the Registrar General of India
- Comprehensive guidelines for TB mortality estimation under RNTCP developed for implementation
- Community based models for annual estimation of TB mortality will be established

♦ Significant *in vitro* efficacy of Transitmycin against both drug sensitive and drug resistant *M. tuberculosis* isolates encouraged to evaluate its efficacy in guinea pig model of tuberculosis. The result indicates that small reduction in bacterial proliferation at 0.01mg/kg dose but with high toxicity

♦ The molecule at the selected dose and schedule based on the toxicity studies at ICMR-NIN, Hyderabad showed promise but also has toxicity.

ICMR-NATIONAL INSTITUTE OF CHOLERA AND ENTERIC DISEASES, KOLKATA (ICMR-NICED)

A. COMMUNITY BASED STUDIES

Early initiation of breast feeding and exclusive breast feeding practices in rural West Bengal

This cohort study weekly followed 319 mother-new-born dyads for 42 days of post-partum period with a focus to generate evidence on how to improve the current breastfeeding practices through sustainable restructuring of the current counselling process for antenatal mothers under health care delivery system.

National Surveillance System for Enteric Fever in India (Tier-1)

The study was designed to estimate the burden of culture confirmed typhoid fever in the community and to describe the incidence of acute febrile illness among children 6 months – below five years and associated treatment practices in the community. The study had been initiated in urban/semi urban populations in four States at various regions of India (Tamil Nadu, Maharashtra, Delhi and West Bengal) and each site had enrolled minimum of 6000 children and following them up for 24 months (Table 1). This multi-centric study will yield

community-based disease burden estimates in India, which shall advise the process of implementation of typhoid vaccines (Fig.1).

Table 1: Subjects enrolled for National Surveillance System for Enteric Fever

Events	Numbers
Total enrolled subjects	6017
• Subjects enrolled between 6 months and 4 years 364 days	2017
• Subjects enrolled between 5 years and 9 years 364 days	2000
• Subjects enrolled between 10 years and 13 years 364 days	2000
Total number of Fever episodes identified	17751
Total number of Suspected Typhoid Fever (STF) cases identified	4286
Total number of blood culture reported	2290
Positive cases	93
• S. Typhi	80
• S. Paratyphi	13

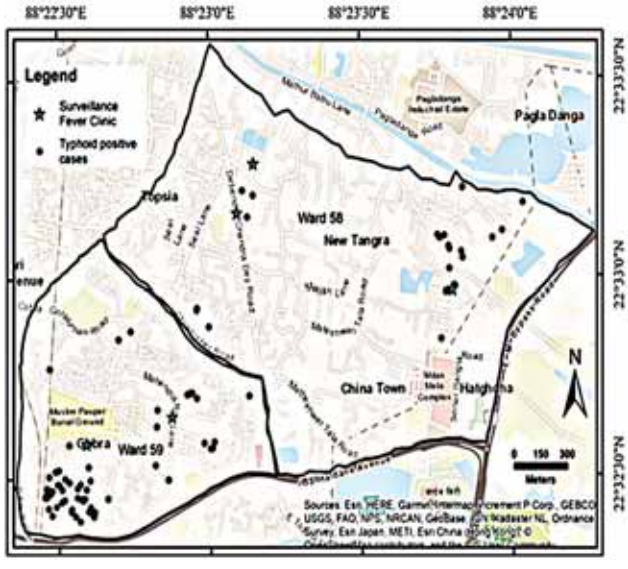


Fig. 1: Wards of Kolkata.

Immunogenicity and Safety of Rotavac® and Rotasiil® Administered in an Interchangeable Dosing Schedule among Healthy Indian Infants: A Multicentric, Phase IV, Open-Labeled, Randomized, Controlled Trial

Rotavac and Rotasiil are two India made rotavirus vaccines available through current public health care delivery system in India. This project was initiated upon request of the MoHFW, with the objectives of examining the immunogenicity and safety of delivering mixed dose regimens, comprising of both vaccines, compared to single vaccine doses (either Rotavac or Rotasiil). The study was carried out in urban/semi urban population in two states of India (West Bengal, Maharashtra). Each site enrolled 1980 healthy infants at 6-8 weeks and followed them till 28 days after third dose of vaccination aiming to inform the officials for scaling up of both the rotavirus vaccines through the national immunization program in India.

Strengthening/ Promoting evidence-based advocacy for influenza prevention and control in India

Under the Indian Network of population-based Surveillance Platforms for Influenza and other Respiratory viruses among Elderly (INSPIRE) multi-centric project, a total of 778 samples from the community were analyzed for the presence of influenza viruses. 56 (7.19%) samples were found influenza virus positive out of which 33 (4.24%) were influenza A and 23 (2.95%) were influenza B virus. H1N1, H3N2, influenza B Yamagata and influenza B Victoria subtypes were also found. 284 samples from hospitals were also analyzed of which 46 samples were positive for influenza viruses. 15 samples were influenza A H1N1, 29 samples were influenza A H3N2 Community study and 2 samples were for influenza B Victoria linage

SaniPath Typhoid- Assessment of Typhoid Exposure Pathways in Low-Income Urban Settings

Sanipath studies facilitated detection of S. Typhi (Typhoid bacilli) in the environment by molecular method. Various environment samples like drinking water, surface water, soil samples, open drains public latrine, flood water, bathing water, raw produce, street food, pumping station water/moore swab, on ground and off ground swab samples (child observation) floor swab, food preparation swab were collected (Fig 2).

Fig. 2: Sample collection from (a) Surface water; (b) Raw produce; (c) Pooled latrine case study.

Climate and non-climate factors in determining risks and predicting outbreaks of waterborne diseases

This study intends to decipher the impact of climate on diarrheal diseases, adjusted for effects of relevant non-climate factors, coupled with the role of local water quality as a link between climate change and diarrheal diseases. This may serve as a model that can be applied to similar geographical regions to gain an improved perspective of the climatic effects on waterborne diseases and design appropriate prevention measures.

B. LABORATORY-BASED STUDIES

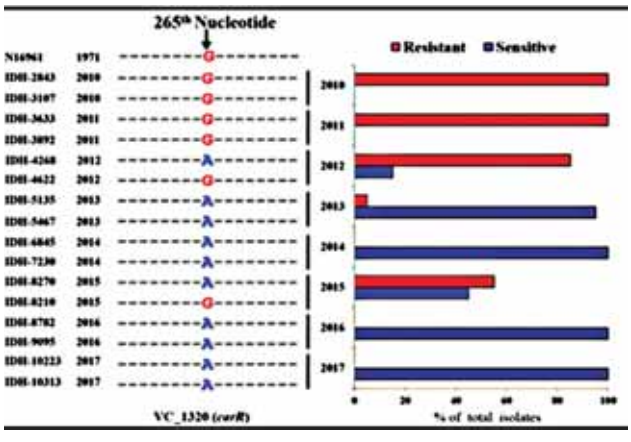


Fig. 3: A single base substitution at the 265th nucleotide position of *carR* gene of *V. cholerae* isolates in Kolkata. Strains containing "G" showed resistant phenotype against polymyxin B whereas the strains containing "A" showed sensitive phenotype.

A novel point mutation in carR triggered the emergence of polymyxin B-sensitive *Vibrio cholerae* O1

Vibrio cholerae O1 El Tor biotype is originally polymyxin-B resistant but recently they exhibit sensitive traits. We established that a novel single nucleotide polymorphism in carR gene has enabled them to become sensitive (Fig.3) and these CarR-variant strains down-regulate the expression of polymyxin-B resistance genes, almEFG. In-silico study showed that this particular mutation has pervasive positive/diversifying selection, which possibly has a selective advantage and environmental stability of currently emerged *V. cholerae* strains.

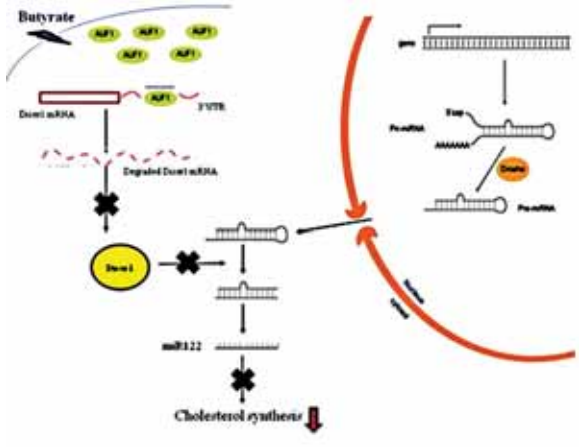


Fig. 4: Intake of multiple antibiotics decreased gut microbiota derived butyrate production leading to hypercholesterolemia in animals .

Emergence of OXA-232-producing hypervirulent Klebsiella pneumoniae ST23 causing neonatal sepsis

This is the first report of a carbapenem-resistant hypervirulent K. pneumoniae (CR-hvKP) causing neonatal sepsis. Whole genome analysis showed hypervirulent molecular markers along with bla OXA-232 gene responsible for carbapenem resistance located in a non-conjugative ColKP3-type plasmid.

Emergence of a 3rd generation cephalosporin resistant *S.* Typhi isolate in Kolkata

Recent emergence of 3rd generation cephalosporin resistant one *S.* Typhi isolate from hospital became the cause of concern. On WGS analysis of the strain, presence of bla_{SHV12} gene and IncX3 plasmid were found. It belonged to ST1 type and 4.3.1.2 lineage.

Purification and characterization of environmental microbial protease subtilisin and its role in apoptosis of cancer cells

A protease, similar to subtilisin, was purified from an environmental *Bacillus subtilis* strain that showed both dose and time dependent apoptosis on breast and colon cancer cells. The protease induced caspase independent pathway of apoptosis by protesomal mediated degradation of tubulin

Gut microbiome derived butyrate exploits miR122 biogenesis for cholesterol homeostasis

This study showed the critical link between butyrate and cholesterol biosynthesis in liver involving regulatory microRNA miR122 post transcriptional regulator AUF-1. Intake of multiple antibiotics decreased gut microbiota derived butyrate production leading to hypercholesterolemia in animals (Fig. 4).

Analysis of genetic diversity and evolution of Dengue virus using completely sequenced genomes

Envelope gene sequences of dengue virus formed two different clusters separately for each serotype based on amino acid usage. One cluster consists of genes from Asia and the other consists of genes from north and south America. Changes of evolutionary selective constraints have been noted between the two clusters.

C. STUDIES WITH TRANSLATION POTENTIAL

Selection of adjuvants to augment subunit vaccine-induced mucosal immune response against Typhoid causing Salmonella Typhi

Flagellar protein (FliC)- and cholera toxin B subunit (CT-B)-adjuvanted candidate Salmonella Typhi vaccine (T2544) augment intestinal mucosal immune response (IgG and secretory IgA, antibody secreting cells and CD4+ cells producing IL-17 and IFN-γ). This was associated with protection of the immunized mice against oral challenge of S. Typhi in an iron-overload model.

Nonmetabolizable arabinose inhibits *Vibrio cholerae* growth in M9 medium with gluconate as sole carbon source

Genes *edd* and *eda* constitute the Entner-Doudoroff (ED) pathway, which is obligatory for gluconate utilization in *Vibrio cholerae*. Arabinose, a pentose sugar nonmetabolizable by V. cholerae, can cause growth inhibition of *V. cholerae* in M9 media containing gluconate due to upregulation of *edd* over *eda* resulting intracellular accumulation of KDPG, a toxic intermediate.

Carvacrol is a potent inhibitor of *Vibrio cholerae* pathogenesis

The present study demonstrated Carvacrol, an essential bioactive oil fraction of Oregano, inhibited flagellar synthesis by downregulating the expression of class II and class III genes in *Vibrio cholerae*. This inhibited *V. cholerae* pathogenesis (Fig. 5) suggesting carvacrol to be a potent anti-virulence inhibitor, in *V. cholera.*

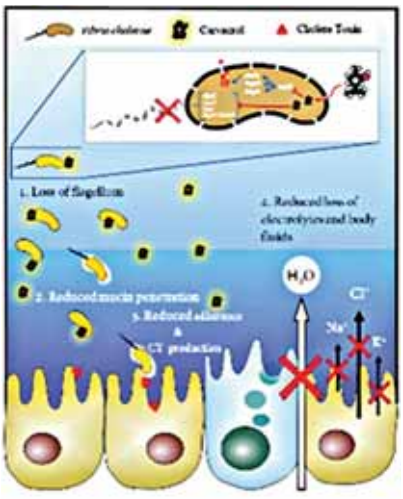


Fig. 5: Mechanism of inhibition of V.choleare pathogenesis by carvacrol.

Therapeutic intervention of *Shigella flexneri* host pathogen interaction by a small molecule herbal compound

In this study, a herbal compound capsaicin was found to reduce *Shigella flexneri* infection. Capsaicin during *S flexneri* infection induced autophagy by increasing nuclear translocation of transcription factor EB (TFEB) which played a major role in autophagosome biogenesis. This could be a novel approach in treating Shigellosis by with capsaicin by exploiting the mechanism of autophagy (Fig.6).

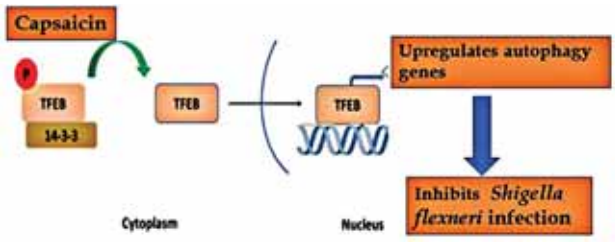


Fig. 6: Mechanism of Capsaisin induced autophagy during *S. flexneri* infection.

Studies on Immunogenicity and protective efficacy of multi-serotype OMV's of circulating *Salmonella* strains in Chicken model

Non-typhoidal *Salmonella* strains secreted Outer Membrane Vesicles (OMVs), which were found to be immunogenic in chicken. After three doses of oral immunization, OMVs induced increase in serum immunoglobulin levels in chicken. The serum IgY and IgA were found above the detection level till 180 days after oral immunization. OMV-immunized chicken when challenged orally showed 100% protective efficacy against homologous strains and 75-80% efficacy against heterologous strains.

D. HIV/AIDS RESEARCH

Piloting Audio Computer Assisted Self Interview (ACASI) in eliciting HIV related risks among Attendees at Integrated Counselling and Testing Centre (ICTC)

This pilot study evaluated the differences in reporting of HIV-related risk behaviours by ICTC attendees using ACASI and Face To Face (FTF) interactions in three different states of India: West Bengal, Meghalaya and Nagaland. Additionally, the study also compared the quality of captured information through ACASI versus FTF (Fig.7) aiming to benefit the population at risk of HIV infection through obtaining in-depth knowledge of HIV related risk behaviors.

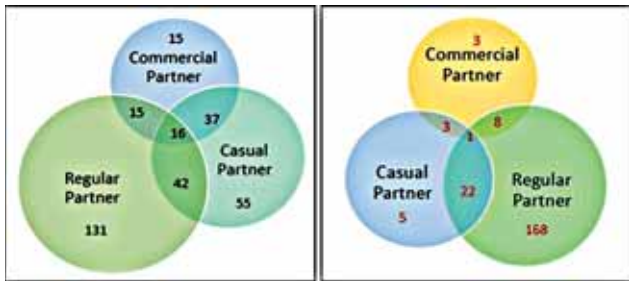


Fig. 7: Result of ACASI in eliciting HIV related risks among ICTC Attendees.

Behavioral Surveillance Survey – Lite (BSS-Lite)

BSS-Lite was implemented in 14 States among the population groups of Female Sex Workers, Men who have Sex with Men, Injecting drug Users and Hijras/Transgenders to estimate the prevalence of HIV related behaviors, knowledge, attitude and practices and service uptake among key population groups. Additionally, the survey findings hope to identify appropriate correction factors for the behavioral component of the HSS Plus (Fig. 8).

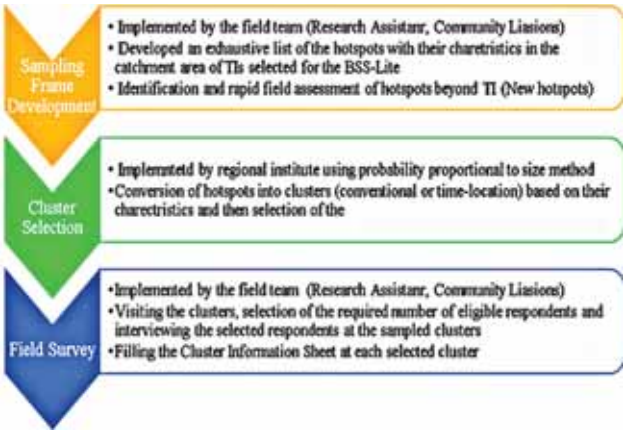


Fig. 8: Steps of Behavioral Surveillance Survey.

E. (A) STUDIES ON VIRAL DISEASES

Rotavirus activates the ATM-Chk2 branch of DNA damage response during infection to positively regulate viroplasm dynamics

The current study describes rotavirus-mediated activation of a non-canonical branch of DNA damage response (DDR) machinery involving a two-component system of sensor kinase ATM and its effector kinase Chk2 which favoured viroplasm fusion and productive viral perpetuation. Targeting ATM and Chk2 significantly inhibited rotaviral replication (Fig. 9).

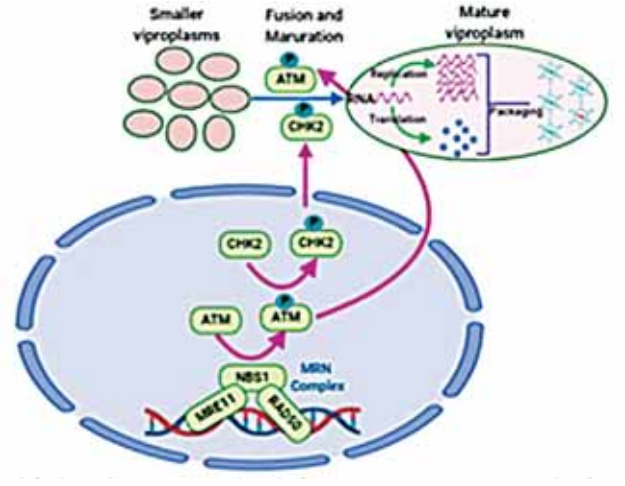


Fig. 9: Mechanism of activation of non-canonical DDR branch during rotavirus replication.

Studies on genomic variation of hepatitis C virus in high risk group population in Eastern part of India

WHO recommends elimination of viral hepatitis by 2030 and National Viral Hepatitis Control Programme in India is working towards. In India, direct acting antivirals (DAAs) are used for treatment of hepatitis C virus infection. This DAAs are new drugs and 5-6% HCV patients are already resistant to treatment, especially chronic liver disease patients infected with HCV genotype 3 (Fig. 10).

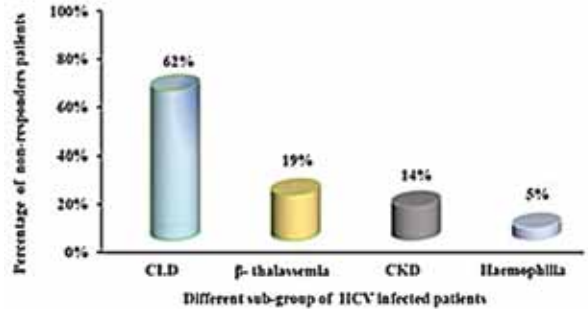


Fig. 10: Distribution of different group of DAAs non-responders patients (N=21).

Circulating Dengue Serotypes in 2019 Dengue outbreak in West Bengal

A total of 1259 dengue NS1 sero-reactive samples were received from all over West Bengal. Serotyping indicated co-circulation of all four dengue serotypes with DENV 2 (36.95%) being the major type, followed by DENV 3 (21.23%), DENV 1 (14.34%) and DENV 4 (4.78%). (Fig. 11).

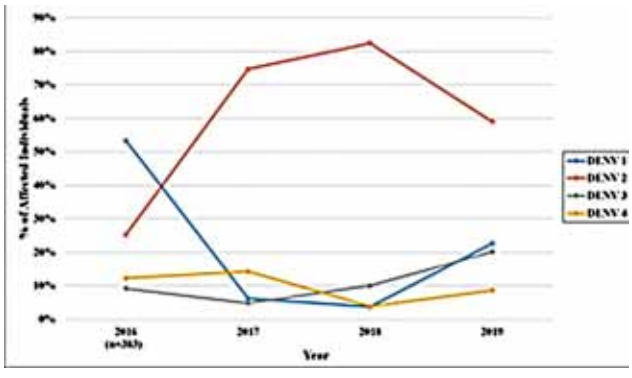


Fig. 11: Pattern of dengue serotypes prevalence in South Bengal in last four years during 2016-2019 (N=2621).

E. (B) VIRUS RESEARCH AND DIAGNOSTIC LABORATORY (VRDL)

Ongoing research involves diagnosis and research on common viruses and agents of public health importance. VRDL-NICED organizes regular hands-on trainings and workshops of healthcare professionals on epidemiology, molecular diagnosis

of emerging viral diseases and laboratory safety and quality assurance. The lab has been in the forefront of fighting the war against COVID-19 by providing RT-PCR based diagnostic support since 03 February 2020.

Table 2. Major Virus detected			
Dengue NS1 ELISA	778	108	13.88
Dengue IgM ELISA	845	132	15.62
Dengue IgG ELISA	33	12	36.36
Chikungunya IgM ELISA	59	23	38.98
Hepatitis A IgM ELISA	416	89	21.39
Hepatitis E IgM ELISA	656	57	8.68
Hepatitis E IgG ELISA	244	62	25.40
Hepatitis B Surface Ag ELISA	176	12	6.81
Hepatitis C Ab ELISA	225	9	4.00
Rotavirus Ag ELISA	386	83	21.50
Scrub typhus IgM ELISA	1987	613	30.85
Leptospira IgM ELISA	77	12	15.58
Rubella IgM ELISA	11	1	9.09
Measles IgM ELISA	13	1	7.69
Influenza A-H1N1 PCR	3614	147	4.06
Influenza A-H3N2 PCR	3614	286	7.91
Influenza B PCR	3614	126	3.48
Influenza B-Yamagata PCR	126	3	-
Influenza B-Victoria PCR	126	123	-
SARS-CoV-2	524	44	8.40

Chickungunya (n=437) and Zika (n=437) were not detected by PCR Japanese Encephalitis during this period. Japanese Encephalitis (n=40) was not detected by IgM ELISA during this period.

F. STUDIES ON PARASITIC DISEASES

State wise prevalence mapping of soil transmitted helminths in Indian children to support health impact evaluation

Primary survey and pre-deworming prevalence mapping have been completed in the states Uttar Pradesh, Telangana, Chhattisgarh, Tamil Nadu, West Bengal, Sikkim, Tripura, Assam, Meghalaya, Manipur, Mizoram, Arunachal Pradesh and data has been shared with Ministry of Health and Family Welfare.

Identification and Molecular Characterization of Common Enteric Parasites in Kolkata

This hospital based surveillance conducted among hospital admitted patient with diarrheal found the prevalence of E. moshkovskii to be 3.40%. This finding is of great importance as E histolytica prevalence rate are decreasing currently and possibly, E. moshkovskii is taking place.

G. CAPACITY BUILDING

- The institute invests heavily in building the healthcare capacity of the nation. During 2019-20. 57 PhD students (5 completed); 13 post-doctoral trainees; 60 Master's students got trained at the institution.
- ICMR-NICED was a participant in organizing the Health Research Conclave of the 5th India International Science Festival (IISF) held in Kolkata during 5-8 November 2019, where 600 participants took part. One hundred participants attended a Science Outreach Program at ICMR-NICED that was organized as a part of IISF.
- Eighty Homeopathy students were trained in the basics of research and laboratory practices.
- Divisions of Epidemiology and Biostatistics, Training and Extension, and Virology (through NACO/HIV, VRDL) undertake thirteen training programs targeting MD students, medical college faculty, program managers, and public health personnel, 640 participants attended the programs during 2019-20.

Public Health Importance

1. ICMR-NICED VRDL designated as the regional center for testing of COVID-19 in Eastern region of India; regional and central inventory/logistic centre; centre for validation of commercially available kits for COVID-19.
2. One national repository for antimicrobial resistant bacteria (NRAMRB) has been established at NICED to cater the researchers

of Govt. and Non Govt. organization in their research. One Antimicrobial resistance Hub(AMR Hub) was established to upscale the research related to AMR.

3. Designation of ICMR-NICED as WHO prequalification evaluation laboratory for cholera & HIV in vitro test kits

4. Identification of greater virulence in Haitian variant of *Vibrio cholerae O1* strains causing outbreaks compared to the canonical El Tor strains circulating earlier

5. Emergence of third generation resistant S. Typhi strains in eastern India

6. Development of a Salmonella protein-based subunit vaccine that is effective against both *S. Typhi* and *S. Paratyphi* infections.

7. Development of Fortified soy-yogurt composition for anti-hypercholestrolemic effect which can be used as a therapeutic agent in hypercholesteremic patients.

8. Reporting of a single formulated nonliving heat-killed combination immunogen from different diarrheagenic *E. coli* and *V. cholerae* that could protect against different bacteria in an animal model.

9. Reporting of the emergence of azithromycin resistance in *V. fluvialis* isolates from diarrheal patients in Kolkata, which has become a major public health problem.

10. Identification of overexpression of Argonaute 2 (AGO2) as an alternative method for suppressing rotavirus infection.

11. Surveillance for viral infections of public health importance – HIV, dengue, chikungunya, influenza, zika, hepatitis (A and E) – undertaken through the NICED Viral Research and Diagnostics Laboratory (VRDL).

12. Surveillance and molecular characterization of enteric viruses among children (<5y) reporting with acute gastroenteritis during 2019-20 reveals that rotavirus was the predominant cause of infection (14.41%), followed by Norovirus (8.88%), Adenovirus (7.46%), Astrovirus (3.43%) and mixed infections (8.88%) out of a total of 1339 screened samples.

ICMR-NATIONAL INSTITUTE OF MALARIA RESEARCH, NEW DELHI(ICMR-NIMR)

IMPROVING MALARIA DIAGNOSIS

Studies on the deletions in *P. falciparum* histidine rich protein 2 and 3 genes (*pfhrp2*/*pfhrp3*) – effect on the malaria rapid diagnostic assay

Malaria still remains one of the main public health problem through the worldwide despite the enormous advances made in different aspects of the fight against this disease *viz*. vector control, diagnostic and treatment. Rapid diagnostic tests (RDTs), especially those targeting histidine-rich protein 2 (PfHRP2) of *Plasmodium falciparum*, have become an important diagnostic tool in the malaria-endemic areas. The chances of RDT-oriented successful treatment are increasingly compromised by the appearance of mutants with deletions in *pfhrp2* and *pfhrp3* genes. To determine the prevalence of deletions in *pfhrp2*/*pfhrp3* genes from *P. falciparum* isolates PCR assay and further sequencing was undertaken. A review analysis was also undertaken to determine the prevalence of field *P. falciparum* isolates with deletion in *pfhrp2* and/or *pfhrp3* genes and their proportion among false-negative results in the PfHRP2-based RDTs in Sub Saharan Africa (SSA) and India. In areas where *P. falciparum* is highly prevalent, as in SSA and India, the circulation of mutants with deletions in *pfhrp2* gene might compromise the PfHRP2-based RDT management of patients attending health facilities. High rates of deletions present in *pfhrp2* gene in Africa and India among the cases of false negative PfHRP2-based RDT results were found.

The pooled prevalence of *pfhrp2* deletions was 8% and 5% while for *pfhrp3* deletions in Africa and India. Parasites lacking *pfhrp2* gene were found among 27% and 69% of false negative PfHRP2-based rapid diagnostic test results in Africa and India.

A new biomarker identified for diagnosis of *Plasmodium falciparum* malaria

In recent years, HRP2/3 gene deletions have been reported within and outside India. To overcome this challenge *P. falciparum* glutamate dehydrogenase is a suitable candidate biomarker. Molecular research confirmed that three genes of PfGDH are present on two different chromosome of parasite, which make GDH as a conserved target. ICMR-National Institute of Malaria Research, New Delhi has confirmed PfGDH as biomarker for diagnosis of falciparum malaria using polyclonal antibodies against recombinant PfGDH. The research showed antibodies are 96.30% sensitive and 100% specific for PfGDH antigen. Development of malaria rapid diagnostic test (RDT) kit using PfGDH as antigen is in progress.

WHO recognised Malaria RDT Lot Testing Laboratory

The WHO recognised Malaria RDT Lot Testing Laboratory at NIMR continued testing malaria RDT lots procured by the national programme and requested as a part of the regulatory requirement. Total of 58 RDT lots of different products were tested and passed the quality tests. The institute organized various refresher courses on malaria microscopy to build the capacity in the country.

Malaria Slide Bank

Malaria Slide Bank has been established at NIMR. Blood smears are prepared from malaria patients following the SOPs, stained, examined, validated and stored. They can be issued for quality assurance and training purpose. Till date over 5000 slides have been collected.

IMPROVING MALARIA TREATMENT

Monitoring efficacy of antimalarials

NIMR carried out therapeutic efficacy studies to guide the policies at 7 sentinel sites during the reporting period: Dhalai (Tripura), Lawngtlai, (Mizoram), Udalguri (Assam) and West Garo hills, (Meghalaya), Mangalore (Karnataka), Surendranagar (Gujarat) and Raipur (Chhattisgarh). Total of 269 patients were enrolled. They were followed up for 28 / 42 days according to WHO protocol. The current antimalarial treatments i.e. artemether lumefantrine in north eastern states and artesunate + sulfadoxine pyrimethamine in rest of the country for P. falciparum malaria and chloroquine for P. vivax malaria continue to be efficacious.

Surveillance for artemisinin resistance in West Bengal

This surveillance study is a one-arm prospective evaluation of clinical and parasitological responses to partial directly observed artesunate followed by sulfadoxine pyrimethamine treatment for uncomplicated malaria. It is aimed to study the efficacy of the artesunate in West Bengal.

Malaria surveillance is being carried out at site for patient enrolment. Of over 1200 fever patients reporting to CSTM during the study period, six were found to be eligible for the study. One patient was screen failure. Thus, five patients have been enrolled till date. The first patient was enrolled in the study on 05/12/2019. All the five patients responded to treatment.

There was one serious adverse event recorded in one patient.

Comparative study of dihydrofolate-reductase gene sequences from different regions of India

Drug resistance genes in *Plasmodium falciparum* parasite can be used for monitoring/surveillance of resistance in endemic malaria areas. Molecular

analysis of resistant and sensitive parasite isolates has revealed a rise at codons 16, 50, 51, 59, 108 and 164 of dihydrofolate reductase (*dhfr)* gene associated with resistance to pyrimethamine, the most widely used antifolate partner drug in the combination therapy. The present study provides a glimpse of *P. falciparum dhfr* genotypes compared from eight different geographical regions of Indian field isolates from northeastern regions (Assam, Arunachal Pradesh and Tripura), central region (Madhya Pradesh), eastern regions (Jharkhand, Chhattisgarh and Orissa) and northern region (Delhi) with 3D7 (ID 9221804) using the alignment tool in MEGA X. We found prevalent mutants in *P. falciparum* infections at N51I, C59R, 108N and I164L (Fig. 12). Molecular surveillance can serve as a useful tool to monitor the prevalence/ emergence of resistant genotypes within endemic populations and can serve for determining the efficacy of antimalarial drugs.

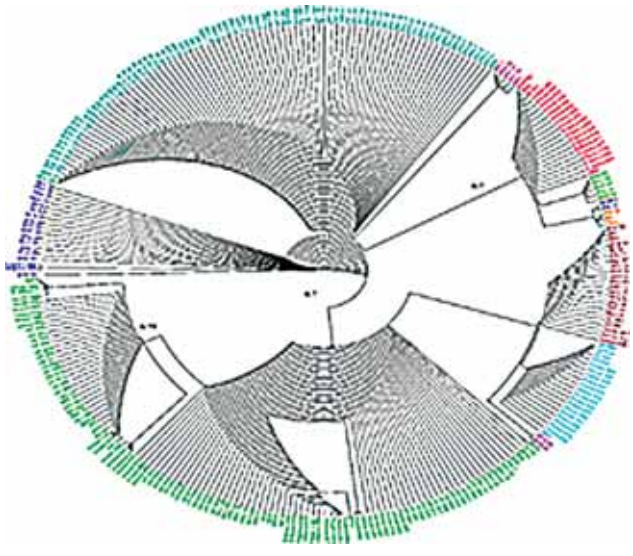


Fig. 12: Radial cladogram depicts the distribution of *P. falciparum* dihydrofolate-reductase genotypes from different geographical isolates in India. The colour represents the mutation codon combination distribution with their bootstrap values in bracket: wild type (30), 108 (30) codons, 51,59,108 (20) codons, 51, 59 (30) codons, 51, 108 (34) codons, 51 (31) codon, 59, 108, 164 (27) codons, 51, 59, 108, 164 (20) codons, 59, 164 (42) codons, 59, 108 (20) codons, 59 (65) codons.

P. falciparum Metacasapases; Unusual proteases as a new drug target

Metacaspases are novel cysteine proteases found in apicomplexan whose function is poorly understood. Our earlier studies on Plasmodium falciparum metacaspase-2(PfMCA-2) revealed that the caspase inhibitor, Z-FA-FMK, efficiently inhibited PfMCA-2activity and, expression, and significantly blocked in vitro progression of the parasite developmental cycle via apoptosis-like parasite death. Building on these findings, we synthesized a set of novel inhibitors based on structural modification of Z-FA-FMK with the amides of piperic acid and investigated their effect on PfMCA-2. One of these analogs, SS-5, specifically inhibited the activity and expression of PfMCA-2. The activities of some other known malarial proteases (falcipains, plasmepsins and vivapain), and human cathepsins-B, D and L, and caspase-3 and -7, were not inhibited by SS-5. SS-5blocked the development of P. falciparum in vitro (IC50 1mM) and caused prominent morphological distortions. Incubation with SS-5 led to persistent parasite oxidative stress accompanied by depolarization of mitochondrial potential and accumulation of intracellular Ca2+. SS-5 also inhibited the development of P. berghei in a murine model. Our results suggest that the inhibition of PfMCA-2 results in oxidative stress, leading to apoptosis-like parasite death. Thus, SS-5 offers a starting point for the optimization of new antimalarials, and PfMCA-2 could be a novel target for antimalarial drug discovery (Fig. 12).

Clinical Trials

Based on the clinical trials carried out by NIMR, the antimalarial combination Dihydroartemisinin Piperaquine was registered in India. NIMR is carrying out clinical trial to study the efficacy and safety of biocurcumax as an adjunct therapy to standad of care in falciparum malaria.

SERVICES

Fever Clinic

NIMR has fever clinics at Delhi and its field units.

At fever clinic at Delhi, a total of 3700 fever cases were screened for malaria from January 2019 to December 2019. 98 malaria cases were diagnosed, out of which 94 were *P. vivax* and 4 *P. falciparum*.

Peak of the malaria cases was seen in the month of August and September. All the confirmed malaria cases were given treatment as per the national treatment guidelines.

NIMR is one of the sentinel surveillance sites for diagnosis of dengue and chikungunya. A total of 783 dengue cases were diagnosed in 2019. Maximum number of cases reported in the month of September. All the confirmed dengue cases were advised regarding intake of plenty fluids, use of antipyretics and to avoid antiinflammatory drugs and were referred to hospital for further investigations and management.

VECTOR STUDIES

Epidemiology of Malaria Evolution in South Asia: Vector Abundance, Geographical Distribution, Molecular Characterization and Vector Parasite interaction in the Goa State

This study was carried out in 9 UHCs / PHCs with variable malaria endemicity based on the malaria incidence reported during the years 2017-18 (Source: DHS, Goa data). Three PHC's in each category based on incidence were selected high incidence (i.e. > 300 Cases), Moderate incidence PHCs between (100 to 300 cases/annum) followed by Low incidence PHCs (cases/annum <100). CDC light traps were used for collection of mosquitoes. A total number of 324 traps were deployed to capture the mosquitoes in the seasonal representative months i.e. winter season (in January), summer (April) and monsoon (July). A total of 687 *Anopheles* females of 14 species were captured in winter season, 544 of 15 species in summer season and 787 of 10 species in monsoon season. In all the seasons, a total of 2018 mosquitoes belonging to 16 species having mainly *An. stephensi* (233), *An. subpictus* (180), *An. annularis* (2), *An. fluviatilis* (2), and *An. sundaicus* (2). *Anopheles* mosquitoes were captured more in winter and monsoon than in summer season, however least species richness was observed in monsoon. Number of *Anopheles stephensi* showed a distinct rise in monsoon season, while *Anopheles subpictus* captured remained almost constant throughout the seasons.

Hemocyte specific FREP13 abrogates exogenous bacteria in hemolymph, but promotes midgut endosymbionts

The mosquito's immune blood cells, 'hemocytes' imparts a highly selective immune response against various micro-organisms/pathogens. Among several immune effectors, FREPs (Fibrinogen related proteins) have been recognized as a key modulator of cellular immune responses, however, their physiological relevance has not been investigated in detail. Transcriptional profiling of selected seven FREP transcripts showed distinct responses against different pathophysiological conditions, where an exclusive induction of FREP12 ($P<0.0001$) after 10 days of *P. vivax* infection, suggested its possible role against free circulating sporozoites for future exploration. We not only observed a higher affinity of FREP13 and FREP65 towards gram-negative and gram-positive bacteria, in the mosquito hemocytes, respectively, but also an increased bacterial survival and proliferation, in FREP13 mRNA depleted mosquitoes hemolymph. On the contrary, we also noticed post-blood-feeding, a significant delay of 24hrs in the enrichment of gut endosymbionts in the FREP13 silenced mosquitoes. Taken together, we conclude that hemocyte specific FREP13, carries the unique ability of tissue-specific regulation, having an antagonistic antibacterial role in the hemolymph, and agonistic role against gut endosymbionts .

Pilot-scale bio-ecological studies on *Aedes aegypti* in Chennai, Tamil Nadu to develop alternate Dengue/Chikungunya control strategy

The study showed diverse breeding habitats of Aedes aegypti such as natural, water storage and discarded containers with high house, container, breteau, and pupal indices (Fig 13). *Aedes aegypti*breeding was high during November/December corresponding to the Northeast monsoon. The species was susceptible to Temephos (larvicide) and deltamethrin(adult

bioassay using bottle assay). The key potential containers of *Aedes aegypti* breeding was plastic containers.

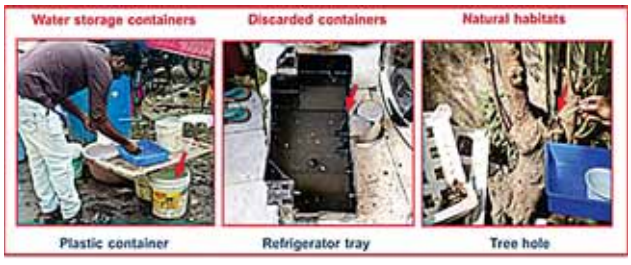


Fig. 13: Potential breeding habitats of *Aedes aegypti.*

Good Laboratory Practice (GLP) Certification - WHO Collaborating Centre for Phase – I testing and evaluation of public health pesticides products

NIMR laboratory has been designated as the WHO Collaborating Centre for Phase – I testing and evaluation of public health pesticides products up to Dec 2020. It was proposed for certification for GLP with financial resources and technical support. An application is made to NGCMA (Govt. of India) for certification of the lab at Delhi and Bengaluru in October 2019 and presently is under consideration with NGCMA.

Determining discriminating concentrations in bottle assays for insecticide compounds that are unstable on filter papers, and for some selected compounds suitable for filter paper impregnation

NIMR is part of this WHO funded multicentric study. Total of 11 insecticides from 7 insecticide classes were tested against malaria and arboviral disease vectors at NIMR using bottle assays and filter papers. Revised dosages are awaited.

Fig. 14: Bottle Assay.

PCR-based diagnostic assay for the differentiation of all members of the Fluviatilis Complex

Anopheles fluviatilis is a major malaria vector in India which is comprised of four cryptic species provisionally designated as species S, T, U and V. Earlier, a 28S-rDNA based allele-specific polymerase chain reaction (ASPCR) assay was developed for the differentiation of the then known three members of the *An. fluviatilis* complex, i.e., species S, T, and U. In consequence of the discovery of a new cryptic member, species V, in the Fluviatilis Complex, a modified PCR-based assay was developed to include identification of new species. In the modified procedure, the ASPCR assay was performed first, followed by restriction digestion of PCR product with an enzyme BamH I, which cleaves specifically PCR amplicon of species V and the resultant PCR–RFLP products can differentiate all the four cryptic members of the complex. Morphologically identified *An. fluviatilis* samples were subjected to sibling species identification by modified PCR-based assay and standard cytotaxonomy. The result of PCR-based assay was validated through cytotaxonomy as well as DNA sequencing of some representative samples. The modified PCR-based assay differentiates all four sibling species (Fig 4). The result of modified PCR-based assay tested on field samples was in agreement with results of cytotaxonomy as well as DNA sequencing of representative samples.

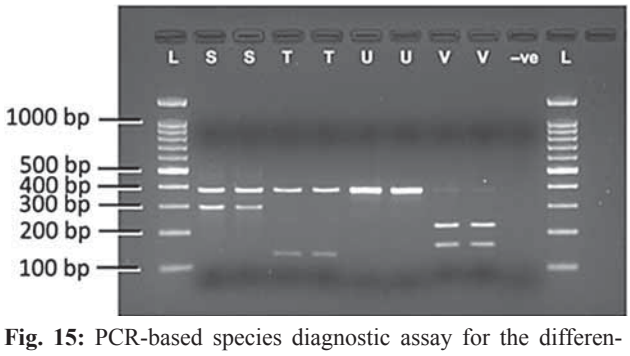


Fig. 15: PCR-based species diagnostic assay for the differentiation of members of An. fluviatilis complex. L: 100 bp DNA ladder, S: species S, T: species T, U: species U, V: species V; –ve: negative control, without DNA.

EPIDEMIOLOGY

Disasters and Vector borne Diseases

In different parts of the country, various disasters like flood, drought, heatwave, earthquake, landslide, tsunami, and cyclone etc. occur, posing a threat to vector-borne diseases like malaria and dengue. So far, there is no consolidated information about the particular type of disaster resulting in upsurge/ outbreak of which type of vector-borne diseases. The analysis of recent floods indicates that on the one hand, the floods in Kerala in 2018 did not result in any upsurge of vector-borne disease while heavy rainfall in Patna (Bihar), resulted in an outbreak of dengue in 2019. It was found that in Kerala, the flooded water receded within 4-5 days while in Patna, stagnant water in residential areas paralysed movement of inhabitants as well as public health services. However, heavy breeding of *Aedes* mosquitoes was witnessed in scrap, containers on the rooftop, and in containers left out after receding of groundwater. A toolkit for linking various disasters and vector-borne diseases is being developed.

Health Adaptation Plan on Climate change and Vector Borne Diseases

Climate change is an emerging issue affecting the spatial and temporal distribution of vector borne diseases. In order to address the adverse impacts, an Health Adaptation Plan detailing the vulnerable areas and the action to be taken by state nodal officers has been developed with emphasis on malaria.

Health Impact Assessment of Narmada Basin Dams and Resettlement & Rehabilitation Colonies in MP: Phase III

Three field laboratories have been established under the project three field units one each at Indore (6 Dams), Sanawad (7 Dams) and Bhopal (7 Dams) to carry out Health Impact Assessment with the objectives - a) to assess the adverse health impact of reservoirs, down streams, canals and command areas on incidence of malaria and other vector borne diseases b) To assess risk factors related to malaria and other vector borne diseases and water borne diseases in Resettlement and Rehabilitation colonies; c) To assess the quality of drinking water in terms of toxic minerals in the existing water sources (if any) and microbial contamination in the canal drinking water sources and d) To make recommendations of mitigation measures for each component in dam for control of malaria and other vector borne and water borne diseases.

Entomological and epidemiological surveillance are being carried out each month and IEC activities like health camps, demonstrations, school orientation, and pamphlet distribution are also being done regularly in selected villages under each dam site and Resettlement and Rehabilitation colonies. ASHAs are being educated to control vector borne diseases in projects areas. Microbiological survey are being done in villages for the presence of harmful bacteria in drinking water out of which samples were found positive for *Salmonella typhimurium, S. enteritidis, Citrobacter fraundii, Vibrio cholerae or V. parahaemolyticus*.

On the basis of work done, mitigation measures are being suggested to NVDA on monthly basis for taking actions. The data regarding entomological and epidemiological surveys with the current situation of vector borne diseases and water testing is being communicated to the State Health Department and mitigation measures for identified problems are also being suggested to stake holders.

Malaria Elimination Research Alliance-India (MERA-India)

In order to identify, plan and scale up research efforts to eliminate malaria from India by 2030, a program called Malaria Elimination Research Alliance (MERA)-India was launched by the ICMR on the 'World Malaria Day' in 2019. MERA-India is a conglomeration of National and International partners like World Health Organization (WHO) and National Vector Borne Diseases Control Program

(NVBDCP) working towards malaria control and elimination. The mandate of the alliance is to bring together researchers working in the field of malaria in the ICMR and non-ICMR Research Institutions, Universities and National Programme.

MERA-India fosters multicentric studies in thematic areas so as to provide a platform for pan-India data. The alliance, spearheaded by ICMR-National Institute of Malaria Research (ICMR-NIMR), launched a call for proposals focused on priority research areas and received an overwhelming response from researchers globally. Out of which, 6 proposals were recommended for the funding after a Peer Review. Rest of the proposals, submitted by different investigators but on common thematic areas, had been brought under an umbrella. MERA India also organized a 'Brainstorming Meeting' of potential investigators to develop multi-centric projects in thematic groups at ICMR Headquarters, New Delhi. These proposals are in the process of funding.

PUBLIC HEALTH IMPORTANCE

- The Malaria Elimination Research Alliance India (MERA India) was operationalised.
- Evaluated new tools for malaria control like diagnostics (RDTs), antimalarials (alternative ACT) and vector control tools (combination LLIN)
- Developed LAMP for identifying Sulphadoxine-Pyrimethamine resistance in *P. falciparum.*
- Developed a new diagnostic test for detection of *P. falciparum* glutamate dehydrogenase.
- Zika virus was isolated and sequenced from *Aedes aegypti* mosquitoes from Jaipur (Rajasthan).
- Capacity building of state officials
- For supporting malaria elimination in Punjab, disease burden studies were carried out, and technical support provided to the state.

ICMR-VECTOR CONTROL RESEARCH CENTRE, PUDUCHERRY(ICMR-VCRC)

LYMPHATIC FILARIASIS

Development of monitoring and evaluation protocol for accelerated MDA with IDA for lymphatic filariasis elimination programme

Following the recommendations of WHO and Technical Advisory Committee (TAC), the Ministry of Health, Govt. of India approved the triple drug regimen (Ivermectin, Diethylcarbamazine and Albendazole, IDA) for accelerating LF-elimination in India. The National Vector-Borne Diseases Control Programme (NVBDCP) implemented the accelerated strategy in five hard-core LF endemic districts. As the existing monitoring and evaluation (M&E) guidelines (for MDA with DA) may not be appropriate as the new strategy requires only 2-3 rounds of MDA (with coverage ≥65%) to achieve the thresholds for LF elimination. Hence this study was proposed to develop appropriate M&E protocol by generating evidence base to identify appropriate infection indicator(s) and target population that can be used to decide on stopping MDA with IDA. Two study areas (Yadgir sub-district, Karnataka, undergone 16 rounds of MDA with DA and Simdega district, Jharkhand, naïve to MDA) were selected. This study has three phases: (i) baseline survey prior to MDA, (ii) post-MDA survey 1 and (iii) post-MDA-survey-2. In each phase, filarial infections are assessed in humans and vectors. In both the study areas the baseline blood surveys have been completed (Fig.16). The prevalence of CFA in random and sentinel sites were comparable (Random sites: 9.3% in 5-9 years old and 18.8% in those aged ≥10; Sentinel sites: 8.2 and 19.8% respectively). Corresponding Mf prevalence were 0.4 and 2.7%, and 0.2% and 1.4% for the two classes, in random and sentinel sites. Similarly, in Yadgir, the baseline prevalence of CFA in random and sentinel sites were 8.6 and 18.7% among 5-9 years old and those aged ≥10 years and corresponding prevalence of Mf were 0.5 and 2.2 % respectively. In the sentinel sites, Ag prevalence were 7.4 and 20.3% with Mf prevalence

at 0.2 and 3.9% in the children and those aged 10 and above. The vector infection was estimated to be 4.5% (95% CI: 3.6-5.5%). The coverage surveys conducted post 1st round of MDA-IDA in Simdega and Yadgir estimated a coverage of 84% and 65.5% respectively.

Fig.16: Baseline blood survey at Yadgir.

Adaptation, validation and application of LYMFASIM model to predict the risk of resurgence following stopping MDA based on transmission assessment survey (TAS)

Optimising evaluation unit (EU) size for TAS: Model predictions were used to assess the feasibility of downsizing EU size from district to a sub-district level for TAS. The results showed that the cost of the programme reduced by 14% (from 10,64,219 USD to 9,16,628 USD), if TAS were to be conducted at sub-district level M&E strategies for MDA-IDA. In parallel with the above-mentioned operational research study, the LYMFASIM simulation model is being applied to identify the appropriate indicators and target population for developing the monitoring and evaluation protocol for the IDA-based MDA programme. LYMFASIM was used to simulate impact of 10 MDA-scenarios (1000 simulations for each) representing different rounds of MDA-IDA (1, 2, … ,9,10) with a constant MDA coverage of 65% by randomly varying the monthly mosquito biting rates from 1200-3600 per person that results in the demographic and epidemiological data for ~2 million populations representing a district with 1000 villages. Preliminary results showed that for MDA naïve district with baseline community Mf- and CFA-prevalence of 9% and 25%, at least 6 annual rounds of MDA-IDA with 65% coverage is required to achieve >99% probability of elimination (i.e. zero Mf-or Ag prev.) of LF 45 years after the last round of MDA (Fig. 16). Children aged 5-9 years or individuals aged 10+ years could be the target population for making decision to stopping MDA-IDA. Further, the results showed that with the WHO recommended threshold for stopping MDA (Mf-prevalence <1%, blue dotted line, Fig.17), though would require only 3 rounds, a decision to stop MDA with 3 rounds is likely to result in 20% risk of resurgence compared to <1% risk corresponding to 6 annual rounds of MDA (Figs. 17 & 18).

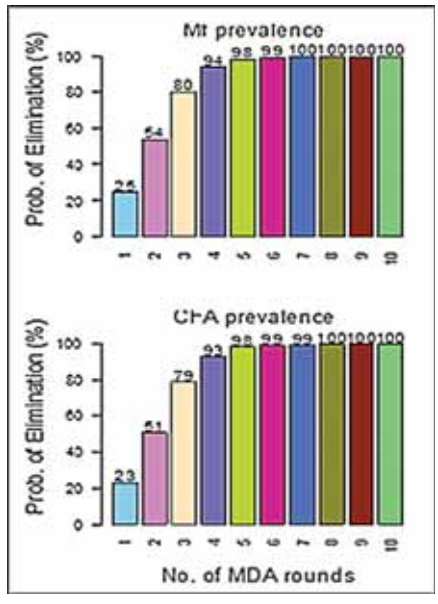


Fig. 17: Probability of elimination in relation to number of rounds of MDA with IDA. Elimination is defined as 'zero Mf or CFA prevalence' 45 years after last round of each MDA.

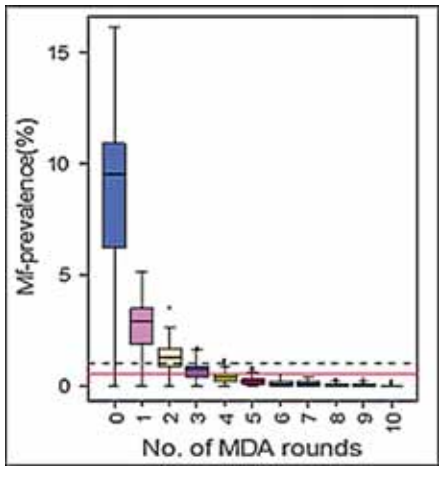


Fig. 18: Community Mf-prevalence prior to and 1-year after each round of MDA with IDA. Blue dotted line indicates the WHO recommended 1% Mf threshold for stopping MDA and the solid redline is a provisional Mf-threshold of 0.5%. The horizontal line inside the box shows the median, the whiskers are 25th and 75th percentiles and the error bars are 5th and 95th percentiles based on 1000 repeat simulations with 65% MDA-IDA coverage.

Our simulations results indicate that the Mf-prevalence should be below 0.5%, which corresponds to 6 annual rounds of MDA-IDA with 65% coverage to achieve the 99% probability of elimination (Figure 2, solid red line). The results of this modelling study will be validated with field data generated through the ICMR-VCRC operational research study for developing guidelines for M&E of accelerated LF elimination programme in India and in other endemic countries.

Development of a Xenomonitoring protocol for monitoring and evaluation of *Brugia malayi* transmission

A study was undertaken for the development of a xenomonitoring protocol for monitoring and evaluation of *Brugia malayi* transmission. The preliminary study on the vector infection showed that out of 83 pools from 1670 Mansonia mosquitoes collected in Balasore district, 2 pools were found to be positive for *Brugia*, indicating its prevalence in the district covered under Mass drug administration (MDA). Molecular Xenomonitoring (MX) protocol developed at VCRC, validated in three districts with varying epidemiological settings, is a potential surveillance strategy to evaluate MDA in LF elimination programme at different stages of monitoring and evaluation.

Evaluation of the degenerative effects of filarial lymphoedema on contra lateral knee joint in lymphatic filariasis patients in Puducherry and Tamilnadu - A Prospective case control study

A collaborative project with JIPMER, Puducherry on the degenerative effects of filarial lymphoedema on contra-lateral knee joint was completed in which 303 participants (133 lymphoedema patients and 170 controls) were recruited. Tamil version of Lower Extremity Functional Scale (LEFS) and Filarial Lymphoedema Quality of Life (LE-QoL) tool were developed and evaluated. These tools can be used in any future studies that measure lower extremity function. Sub-analysis on the risk factors for osteoarthritis of the knee by ordinal logistic regression showed that medial tibio-femoral tenderness and Crepitus in knee Joints are the two major signs that indicate knee osteoarthritis changes and BMI is the major risk factor for knee osteoarthritis. Non-parametric Wilcoxon Signed Rank Test showed that eversion of the ankle joint movement was significantly reduced ($z=3.033$, $p=0.002$) with knee osteoarthritis. This indicated the importance of the measurement of range of motion of adjacent joints in knee osteoarthritis.

Repurposed drugs for antifilarial activity

In a study to develop antifilarial agents by drug repositioning strategy or repurposing, identified three drug candidates with *in vitro* macrofilaricidal activity in comparison with the currently used drugs DEC, Ivermectin and Albendazole. Further studies are underway.

MALARIA

Studies on behavioural change in anopheline vectors in areas of insecticidal nets (ITNs/ LLINs) used in Odisha, a possible challenge to malaria elimination programme

The study site was Koraput and Malkangiri districts of Odisha State. After distribution of LLINs, the overall abundance of *Anopheles fluviatilis* was very low in two districts. In Koraput district, there has been a shift in the indoor resting site of *An. fluviatilis* from human dwellings to cattle sheds. In Malkangiri district, the density of this vector species was almost nil in human dwellings and greatly reduced in cattle sheds and outdoors. *An. culicifacies* comprised of B, C & E in both Koraput and Malkangiri districts, and E was found to be predominant. Of the total *An. fluviatilis* samples analysed, only species T was found in both the districts. The HBI of *An. fluviatilis* and *An. culicifacies* was 0.004 and 0.013, respectively in Koraput district and Malkangiri districts; both the vector species was highly zoophagic. The malaria incidence in the study villages of both the districts was zero during the study period. The infection rate of *An. culicifacies* in Koraput and Malkangiri

districts was 1.4% and 0.9%, respectively. The infection rate of *An. fluviatilis* in Koraput and Malkangiri districts was zero throughout the study period. *An. culicifacies* was found to be resistant to DDT, malathion and deltamethrin in Koraput and Malkangiri districts. Further bioassays with 5x and 10x concentration of deltamethrin indicated that the resistance development in *An. culicifacies* to this synthetic pyrethroid was at 'moderate level'. The use rate of LLINs in the study villages of Koraput district varied from 73.3% to 100% and in Malkangiri district from 76.6% to 100%. There was a shift in resting behaviour of both *An. fluviatilis* and *An. culicifacies* from human dwellings to cattle sheds, zero density in human landing collections and low human feeding in both the vector species. These findings are attributed to the impact of LLINs. Therefore, LLINs should be replenished in time to sustain the gain achieved so far.

Reappearance and disappearance of *Anopheles minimus* Theobald (Diptera: Culicidae) in West Singhbhum hills in India

An entomological survey was carried out to investigate the reappearance and disappearance of *Anopheles minimus* Theobald (Diptera: Culicidae) in West Singhbhum hills in India and found 16 species of *Anopheles*, but failed to locate three of the 19 species of *Anopheles* previously reported from the area. The disappearance of *An. minimus* and low prevalence of *An. fluviatilis* is corroborating with the declining trend of malaria incidences (37, 998 cases (API: 19.51) in 2016 to 453 cases (API: 0.22) in 2019) in Keonjhar district and (30,508 cases (API: 13.82) in 2016 to 1,755 cases (API: 0.72) in 2019) in Sundargarh district. Since, *An. minimus* is considered as one of the primary malaria vectors in India and the presence of this vector has been reported earlier in different areas of Singhbhum hills.

Evaluation of bio-efficacy and durability of long-lasting insecticidal nets distributed by malaria elimination programme in India

An evaluation of bio-efficacy and durability of long-lasting insecticidal nets distributed by malaria elimination programme in Odisha State was carried out in Koraput district, highly endemic for *falciparum* malaria. 74.8% of the LLINs were physically present after 30 months of distribution. The numbers (%) of LLINs used previous night varied from 30% to 61% between study villages. 74% respondents were using the LLINs throughout the year and 26% only seasonally. Of the total, 85% of the nets were reported to be washed and 95% nets were dried under shade as recommended. Altogether, 58% of the surveyed nets were found torn with holes. Of these, 74 (57%) nets were in good condition, 10 (8%) nets were in serviceable and 45 (35%) nets were badly torn and needed replacement. A total of 45 (93.75%), 68 (80%) and 71 (63.8%) LLINs were physically present in hilltop, foothill and plain villages, respectively. The LLINs did meet the efficacy criteria, given the 100% mortality to the exposed *An. jeyporiensis* mosquitoes post 30 months distribution. The findings of this study were communicated to the programme officials of the state and LLINs were replenished soon after 31st month post-distribution of LLINs.

LEISHMANIASIS

Entomological and epidemiological investigations on leishmaniasis among the tribal populations in the Western Ghats, Kerala

The study areas were the foothills of Western Ghats, in Thrissur and Malappuram districts of Kerala. Entomological surveys resulted in the collection of a total of 718 sandfly specimens comprising 15 species. *Phlebotomus argentipes* (62.26%) is the predominant species belonging to indoor resting habitat. 12 species of *Sergentomyia* were also identified from the study areas. 2 groups of sandfly species are yet to be identified. 244 semi-gravid/gravid sandflies were processed for natural infection and none of them was positive. Blood meal analysis of 20 specimens are also being processed. 9 *P. argentipes* COI gene sequences and 7 *P. argentipes* EF-1α gene sequences have been

submitted to NCBI GenBank. For epidemiological investigation a total of 113 tribal families from different tribal communities (Ulladan, Malayan, Mannan and Kadar) comprising a population of 650, were surveyed for visceral and cutaneous leishmaniasis. Among the surveyed population one visceral leishmaniasis case was identified and treated in Thrissur medical college. 12 individuals were suspected for cutaneous leishmaniasis, out of which one was diagnosed as positive for CL is being treated in Thrissur medical college.

Molecular and genetic analysis of dermatropy/ viscerotropy of *Leishmania donovani*

During this study one visceral and one cutaneous leishmaniasis with typical symptoms caused by *Leishmania donovani* were recorded which is a non-endemic region in India. ICMR-VCRC has characterized the parasite species involved in this VL infections to be "MON37" zymodeme. The VL case exhibited typical clinical symptoms like hepatosplenomegaly, fever, malaise, pancytopenia, anaemia, emaciation and anorexia. The diagnosed patients were treated with intravenous infusion of single dose of Liposomal Amphotericin B (10 mg/ kg). The molecular diagnosis was performed on bone marrow and trephine biopsy samples from the patient by PCR amplification of mini-circle kDNA gene, RFLP analysis of 3′ UTR Hsp70 and DNA sequencing of Hsp70 gene amplicons (GenBank accession no. **MT010559**), characterizing the parasite species involved in the infections to be *Leishmania donovani*. Further genetic analysis of 6-phosphogluconate dehydrogenase gene sequences (A976G) indicated the parasite to be belonging to the zymodeme "MON37" (GenBank accession no. **MT010560**). CL patient was also diagnosed by PCR amplification of mini-circle kDNA and Hsp70 gene amplicons. Genetic profiling of *Leishmania donovani* from CL patient samples is under process and the patient is under treatment from Govt. Medical College Thrissur.

Mathematical modelling: understanding and controlling the patterns of visceral leishmaniasis (VL) and transmission

This study aims to extend the models of Visceral leishmaniasis (VL) within the NTD Modelling Consortium to (i) generate models of transmission dynamics that can be used to support the move towards zero transmission, and (ii) provide a short-term prediction framework that can be used to support the maintenance of elimination (close to) real time. To capture the evidence base for the above, a systematic review entitled "Mathematical modelling of the population dynamics, spatial distribution and abundance of sandfly populations in relation to eco-environmental factors" was carried out by searching articles published on mathematical modelling of the above aspects in various eco-epidemiological settings up to February, 2020. Thirty-three studies, 5 describing the population dynamics of sand flies and 28 on application of models to identify the eco-environmental factors associated with sandfly distribution and abundance, were included in this review. The findings of the review indicate that the existing VL transmission models, though included transmission components, none of them have explicitly modelled both the sandfly population dynamics and transmission dynamics of VL due to paucity of data from field or experiments.

DENGUE/ ZIKA/ CHIKUNGUNIYA

Laboratory studies on *Wolbachia*-based vector control strategy for control of dengue/ chikungunya transmitted by *Aedes aegypti*

ICMR-VCRC has been conducting laboratory studies on *Wolbachia* based control of dengue and chikungunya. *Wolbachia* carrying *Aedes aegypti* eggs were received from Monash University, Australia and cyclic colonies have been raised up to 24th generation. ICMR-VCRC has generated two new Indian *Ae. aegypti* colonies by backcrossing *Ae. aegypti* females infected with *w*Mel and *w*AlbB *Wolbachia* (Aus) strains with wild type *Ae. aegypti* (Pud) males and the newly generated *w*Mel and *w*AlbB infected *Ae. aegypti* (Pud) release lines are being maintained over 12 generations. The *w*Mel (Pud) and *w*AlbB (Pud) release lines must have

comparable fitness characteristics to that of wild type *Ae. aegypti* (Pud) strain. Hence, the fitness of the release lines was tested by assessing wing length, fecundity, hatchability, feeding rate, adult survival, induced cytoplasmic incompatibility and maternal transmission efficiency. The study results showed that the *w*Mel and *w*AlbB trans-infections in the two newly generated *Ae. aegypti* release lines produced strong cytoplasmic incompatibility, perfect maternal transmission and biological/reproductive fitness benefits indicating the suitability of the two release lines for testing under field release trials.

A pilot scale bio-ecological studies on *Aedes aegypti* population for developing alternate dengue control strategy

The study generated information on spatio-temporal distribution of *Ae. aegypti*, *Stegomyia* infestation, estimates of relative proportions of *Ae. aegypti* and *Ae. albopictus*, types and location of breeding sites prevalent in the area, variations in larval and pupal indices during different seasons in the breeding sites with special reference to key breeding sites/ containers, minimum infection rates of dengue and chikungunya infections and susceptibility of *Aedes* species to different insecticides. A pre-requisite for any novel strategy to be used that targets adult population control /suppression/replacement is the real time estimation of the adult female *Aedes* populations. The information generated will serve as a baseline data prior to the implementation of such novel strategies.

Entomological investigation of unusual outbreak of Dengue fever in summer season in Odisha, India

A severe outbreak of dengue fever occurred in Tikarapada village of Rayagada district during April 2020. A total of 117 people suffered from fever and out of which 49 were found positive for dengue NS1 (non-structural protein 1) antigen. A study was conducted to find out entomological factors contributing to the dengue outbreak. The house index (HI), container index (CI), pupal index (PI) and Breteau Index (BI) were 24.8, 11.6, 32.7 and 40.6, respectively in the dengue outbreak village. A total of 171 *Aedes* mosquitoes of two known dengue vector species; *Aedes aegypti* (79%) and *Ae. albopictus* (21%) emerged from pupae. The entomological survey confirmed the presence of dengue vectors in Tikarapada village. A good number of *Aedes* breeding sources were available in the outbreak village. A report was shared with the district as well as State health authorities recommending for implementing integrated vector control measures to contain the vector-borne diseases.

Role of immune cells in the pathogenesis of dengue virus disease

Investigated the monocytes and eosinophils associated matrix-metalloproteinases expressions in dengue viral disease. Exposed the THP-1 monocytes cells with purified dengue NS1 protein (Non-structural protein-1) of type-2 serotype at a concentration of 20 µg/ml for 24 hours. Measured the expression profiles of MMP-2, MMP-9 and MMP-14 genes in control and dengue exposed human THP-1 monocytes cells. Exposure of NS-1 protein (20µg/ml) significantly up-regulated the expression profile of matrix-metalloproteinases (MMPs) in monocytes. Specifically, the mRNA expression profiles of MMP-2, MMP-9 and MMP-14 were increased after the exposure of NS-1 protein. The increased expression patterns of these proteins may suggest their role in the tissue dysfunctions of endothelium and thus development of plasma leakage in the severe cases of dengue pathogenesis like DHF and DSS. Also measured the expression profile of meprin-alpha (a MMPs) gene, in response to dengue NS-1 protein. NS-1 protein down-regulated the expression of meprin-alpha gene. Paracetamol is the most commonly used drug against dengue fever however, its exact role associated to MMPs expression was not known. Therefore, assessed the effect of paracetamol on NS-1 induced expression patterns of MMP-2, MMP-9 and MMP-14 genes in monocytes cells and found that paracetamol decreased the expression profile of MMP-2 and MMP-14 genes during the

24 hours' exposure period. This data suggests that paracetamol exerts its effect via down regulating the expressions of matrix-metalloproteinases. Collectively, it can be said that innate immune cells especially monocytes and eosinophils are involved in the pathogenesis of dengue viral disease and over expressions of matrix metalloproteases mediates the dengue pathogenesis.

Clinical, Epidemiological, Entomological and Virological Features of Dengue fever outbreak in Thiruvananthapuram District- A cross sectional study

Altogether, 284 samples were collected by Thiruvananthapuram Medical College team and among these, 155 were processed for DENV/ ZIKV infection by ICMR-VCRC, Kottayam FS. 60 (38.7%) samples were found positive for DENV infection. All 4 serotypes were recorded. Kollam District was found much more affected than Thiruvananthapuram District during 2019. The DENV positivity in Kollam District (n=66) was found to be 78.78% compared only 8.9% recorded in Thiruvananthapuram (n=89). Also, DENV2 (46.15%) and mixed infections (38.46%) contributed the major share of DENV positives in Kollam. The studies showed an increase in the prevalence of mixed infections during 2019 compared to the previous years. The studies showed an increase in the prevalence of mixed infections during 2019 compared to the previous years.

Exploring potential application of Dengue NS1 antigen kits for detection of Dengue virus in Aedes mosquito samples

Current methods of detecting DENV in field-caught mosquitoes require specialized equipment and trained personnel. Alternatively, commercially available NS1- antigen based ELISA kits may be used for the detection of DENV. This study is designed to explore the diagnostic potential of NS1- antigen as an alternative method for detection of Dengue virus in *Aedes* mosquito samples. In the preliminary experiments we have tested the InBios Company's enzyme linked immunosorbent assay (ELISA) kit (*InBios* DENV *Detect*™NS1). The NS1 antigen detection limit of the kit was determined by testing recombinant viral dengue virus 2 NS1 protein antigen (R & D Systems) at different concentrations as per the manufacturer's instructions (Fig. 19).

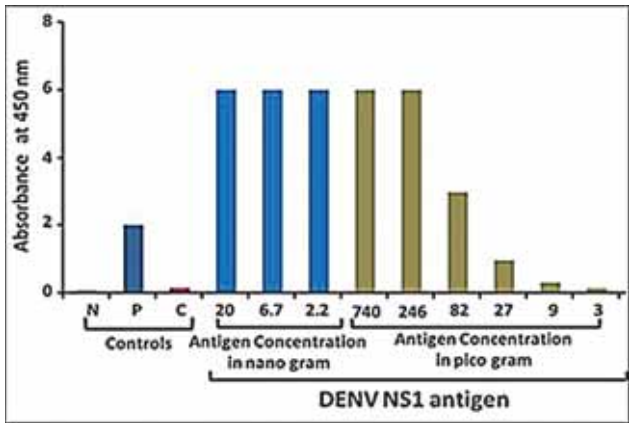


Fig. 19: Determination of sensitivity of DENV-NS1 ELISA Kit.

In the next experiment, the NS1 antigen in blood fed mosquitoes of pool size 5, 10 and 25 were tested. The kit was sensitive to detect the NS1 antigen in all the pools (Fig. 20).

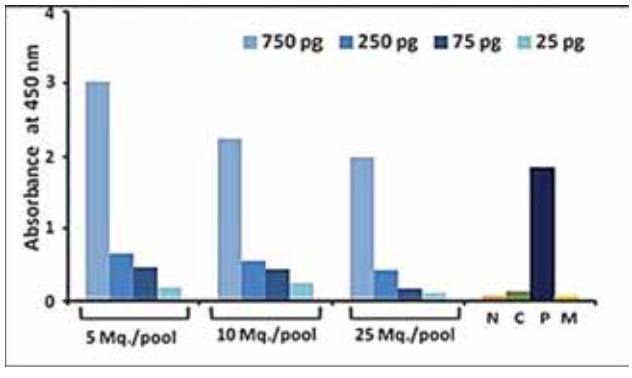


Fig. 20: Determination of sensitivity of DENV-NS1 ELISA Kit in blood fed mosquito pools (Mq- mosquitoes; N-negative control; P- Positive control; C-Cutoff; M-mosquito homogenate only)

Prevalence of *Wolbachia*, an endosymbiotic bacterium, in different mosquito species of Tamil Nadu, India

A study was performed to find the presence of *Wolbachia* and to estimate the prevalence of *Wolbachia* in four different mosquito species of Tamil Nadu, India. The study was conducted in four villages (Manjakuppam, Periyakattupalayam, Kandamangalam and Villupuram) from two districts (Cuddalore and Villupuram) of Tamil Nadu.

Natural occurrence of *Wolbachia* was found in all the 131 pools (n=1153) of *Cx. quinquefasciatus* and 21 pools (n=77) of *Ae. albopictus* tested using wsp gene specific primers. Of the 16 pools (n=86) of *Ae. aegypti* tested, *Wolbachia* was detected in 6 pools, while 6 of the 22 pools (n=) of *An. subpictus* were positive for *Wolbachia*. In order to find the lineage of Wolbachia, supergroups were identified in positive pools by targeting *Wolbachia* surface protein genes (Wsp gene) by semi-nested PCR assay. *Wolbachia* belonging to supergroup B was found in all the three species of mosquitoes and while supergroup A as well as B was detected in 82.4% of the pools tested in *Ae. albopictus*.

SCRUB TYPHUS & KFD

A study on the profile of rickettsial pathogens causing typhus fever in humans from Puducherry and Tamil Nadu State

In India, in the recent years outbreaks of typhus fever mostly scrub typhus have been reported both in northern and southern states and the southern states include Tamil Nadu, Karnataka, Kerala, Andhra Pradesh and Puducherry. In collaboration with a tertiary care hospital in Puducherry, a study was undertaken to find out the profile of typhus pathogen in patients visiting the hospital with typhus fever like symptoms. Samples collected from patients with scrub typhus like symptoms showed that 24% of the suspected cases were tested positive by nested PCR (Fig. 21). The results indicate the risk of transmission of infection from rodent reservoirs to human through the vector mite and tick.

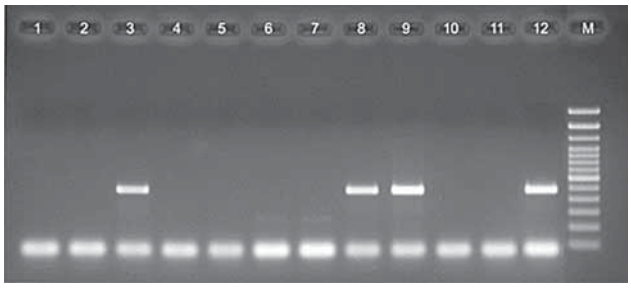


Fig. 21: Electrophoretic analysis of DNAs amplified by PCR on 1.5% agarose gel. Lane 3,8,9 shows amplification of 483 bp gene of scrub typhus pathogen Orientia tsutsugamushi; Lane 1,2,4,5,6,7,10 shows no amplification; Lane 11 is negative control; Lane 12 is positive control; Lane M is marker DNA.

Prevalence and abundance of ectoparasitic vectors of rickettsial pathogens and their animal hosts in areas reporting acute encephalitis syndrome (AES) in Gorakhpur district, Uttar Pradesh

Survey of ectoparasitic vectors of rickettsial pathogens in AES reported villages of Gorakhpur showed *Rhipicephalus sanguinensis*, the established vector of Indian tick typhus was the predominant ectoparasite species (88.0%). The flea, *Xenophsylla cheopis* and the louse, *Polyplax spinulosa* constituted 2.4% and 1.2% of the total ectoparasites collected respectively. Multi Locus Sequence Typing (MLST) analysis of the ectoparasites samples revealed the prevalence of natural infection of *Rickettsia conorii*, in ticks indicates the potential risk of transmission of Indian tick typhus in AES reported villages of Gorakhpur, Uttar Pradesh. The study provided evidence for risk of transmission of *Rickettsia conorii* (aetiological agent of Indian tick typhus) which in turn will be useful for formulating appropriate strategies for the prevention and control of rickettsial infections in this region.

In-silico prediction and *in-vitro* evaluation of diagnostic epitopes of outer membrane protein B (ompB) of *Orientia tsutsugamushi*

Screening of *Orientia tsutsugamushi* in rodent blood and vector mite samples was carried out by PCR. From the PCR positive local isolates, the amino acid sequence of the complete *omp*B was deduced. Five potentially immunogenic epitopes were identified by *in silico* evaluation. The antibodies developed against two out of three epitopes showed diagnostic potential for the detection of *O. tsutsugamushi* by dot-ELISA.

Study on the risk factors for acquiring Scrub Typhus, in Trivandrum district, in the endemic foci of Kerala - an initial report of the field work

Probable Environmental risk factors identified were presence of forest fringe area, bushes, shrubs

and grass, presence of river ('Killiyar'), streams supporting growth of thick vegetation, heavy rainfall supporting growth of grass and vegetation, presence of rodents, and moles. Behavioural risk factors were frequent movement through, grass and vegetation, cutting and carrying grass for cattle, storing firewood near houses, carrying firewood, keeping domestic animals close to houses, keeping pet animals within /close to houses, drying clothes on the grass, fences, ground and on rocks, careless disposal of domestic waste, attracting rodents sitting, lying down on the grass or ground, exposure to mud and grass as part of occupation and lack of awareness about scrub typhus fever and its prevention.

Mapping and risk assessment on KFD expansion in Western Ghats, India

Kyasanur Forest Disease (KFD) is an arbovirus infection found initially in Kyasanur forest area in southwest peninsular of India. KFD virus has been detected in tick parasites or the genera *Haemaphysalis* and *Ixodes*. Exposure to the bite of tick larvae in the forest causes the infection. Despite extensive vaccination efforts, an increasing number of KFD cases have been detected in Karnataka and the disease is expanding to newer areas, now new cases confirmed in Kerala, Goa, Maharashtra and suspected cases in Gujarat. In most occasions, KFD disease associated with deforestation. Forest areas in Western Ghats at decadal interval were mapped and land use land cover (LULC) pattern was classified. Deforestation and Human induced activities were identified and changes in LULC area calculated and mapped at decadal interval (Fig.22).

Table 3: Shimoga vs Western Ghats

	Shimoga					Western Ghats				
	1975	Area (in %)	2015	Area (in %)	% change	1975	Area (in %)	2015	Area (in %)	% change
Evergreen	478.5	11.86%	398.73	10.54%	-16.67%	20083	22.98%	18821	19.49%	-6.28%
Semi EG	827.3	20.51%	729.43	19.28%	-11.83%	22199	25.40%	20678	21.42%	-6.85%
Moist Dec	1262.5	31.30%	1051.15	27.78%	-16.74%	15641	17.89%	15235	15.78%	-2.60%
Dry Dec	735.6	18.24%	624.42	16.50%	-15.11%	5374	6.15%	5002	5.18%	-6.92%
Scrub	275.4	6.83%	209.7	5.54%	-23.86%	12231	13.99%	11140	11.54%	-8.92%
Grassland	189.6	4.70%	158.46	4.19%	-16.42%	1952	2.23%	1816	1.88%	-6.97%
Plantations	264.2	6.55%	612.32	16.18%	131.76%	9927	11.36%	23857	24.71%	140.32%
	4033.1	100.00%	3784.21	100.00%		87407	100.00%	96549	100.00%	

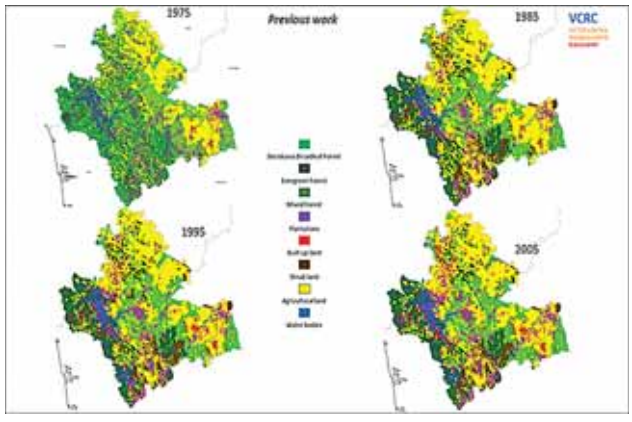


Fig. 22: Land use land cover pattern and forest classification in Shimoga district in Karnataka, for different decades.

A total number of 48 grids each covering 75 sq. km have been created for entire Western Ghats (Fig. 23). Using random grid sampling method 7 grids were selected randomly from the forest fringe, WLS and plantations in forest areas in Kerala (Wayanad WLS, Idukki WLS, Periyar WLS & NP and Neyyar WLS). The Villages falling near centroid of the grid were selected. So far, all the factors layers have been created, decadal forest differentiation maps generated, forest areas calculated, changes in land use land cover patterns and percentage of changes have been calculated. Ticks and required information (Land use land cover type and changes, temperature, humidity and rainfall) are being planned to collect from these villages. Tick collection details and Information about the collection sites will be recorded using the standard pro-forma.

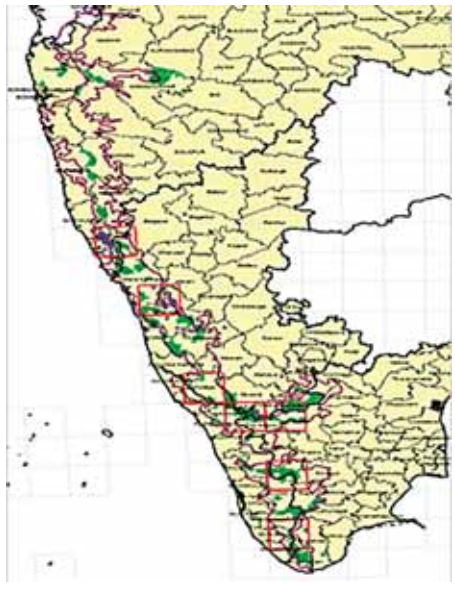


Fig. 23: Entire Western Ghats.

MICROBIAL / CHEMICAL AGENTS FOR VECTOR CONTROL

Development of an effective formulation for DPE-28 (*Indian Pat. No. 191820*), an insect growth regulator developed at VCRC for use in the field conditions for *Culex quinquefasciatus* control

Out of these eight alginate formulations of DPE-28, GR3, GR5 and GR7 were selected based on their release kinetics and prepared in two different batches to find out the batch consistency. Field collected *Culex* egg-rafts were introduced in the field collected water (10L) stored in tubs were treated with DPE-28 formulations at 0.001% (w/v). Every week fresh egg-rafts were introduced and observed for pupal mortality. All the three alginate granular formulations of DPE-28 were effective in controlling the immature population of the filarial vector *Cx. quinquefasciatus* by causing the pupal mortality up to 3-4 weeks when it was applied at 0.001% (w/v) level in the simulated field. There was no batch variation observed in the DPE-28 release from the formulation in all the three formulations in the case of percent content and active ingredient release. The granular formulations of DPE-28 may be taken up for a small-scale field evaluation.

Identification and characterization of specific mosquito toxin(s) from newly isolated bacterial strains *Bacillus subtilis* VCRC B-622, *Bacillus* sp. VCRC B-633 for mosquito control

Two bacterial strains with potential mosquitocidal activity were isolated from the environmental sources such as vermicompost and desiccated apple. The isolates were identified as *Bacillus subtilis* VCRC-B622 and *Bacillus* sp. VCRC-633. These bacterial strains are effective against the mosquito larvae of *Culex quinquefasciatus, Anopheles stephensi* and *Aedes aegypti*. Further studies are in progress.

Identification and characterization of mosquito larvicidal bacterium *Lysinibacillus* sp. VCRC B531

The bacterial isolate, *Lysinibacillus* sp. VCRC B531 was isolated from sand fly breeding habitats of Rajasthan showed mosquito larvicidal activity against the filariasis vector *Culex quinquefasciatus*. Morphologically and biochemically different from *Lysinibacillus sphaericus*, but binary toxin genes were found to be present in *Lysinibacillus* sp. VCRC B531. The nucleotide sequences of insecticidal toxin genes (41.9 kDa and 51 kDa) of VCRC B531 was found to be 100% identical with toxin genes of *L. sphaericus* standard strain VCRC B42 as well with *L. sphaericus* strains from the Genbank database.

New cost saving technology developed for the production of *Bacillus thuringiensis* var. *israelensis* VCRC B-17 and self-floating slow release formulations

Four different types of formulations such as aqueous suspension, Water dispersible powder, tablet and slow release formulations were developed by using *Bacillus thuringiensis* var. *israelensis* VCRC B17 produced by a new technology. This technology is cost wise cheaper than the existing submerged fermentation technique. Another advantage is initial investment cost is very less compared to submerged fermentation.

VECTOR STUDIES

Determining discriminating concentrations in bottle assays for insecticide compounds that are unstable in filter papers and for some selected compounds suitable for filter paper impregnation

ICMR-VCRC, being one of the institutes in the global network formed by WHO, determined and validated discriminating concentration for four new insecticide compounds (that are not stable on filter paper) *viz.,* Pyriproxyfen, Flupyradifurone, Clothianidin and Transfluthrin and two old compounds (that are stable on filter paper) *viz.,* Alpha-cypermethrin and Pirimiphos-methyl against susceptible VCRC-laboratory strain of *Anopheles stephensi*.

GLP FACILITY

Establishing quality management system for GLP Accreditation for Evaluation of vector control products

Good Laboratory Practice (GLP) is a managerial concept covering the organizational process and the conditions under which laboratory studies are planned, performed, monitored, recorded and reported. In this context the WHO has identified six institutes including ICMR-Vector Control Research Centre, Puducherry for establishing Quality Assurance Management systems for GLP accreditation for evaluation of vector control products. Facilities such as insectary, net washing and drying facility, insecticide Testing Facility (ITF), insecticide/LLIN storage facility, Field Site-Experimental Huts, Molecular Laboratory for Insecticide resistance, Data Management Unit, and archive have been created/updated to conduct Phase II evaluation of long-lasting insecticide net on GLP mode. The Centre has uploaded application online, using NGCMA portal for pre-inspection for accreditation of the GLP facility.

HUMAN RESOURCE DEVELOPMENT

M.Sc. Public Health Entomology (PHE) course

There is a growing need for entomologists in the field of Public Health in view of emerging and re-emerging vector-borne diseases in India and other tropical countries. In view of this felt need, a two years M.Sc. Public Health Entomology (PHE) course is being conducted at this Institute under affiliation to Pondicherry University. Twelve candidates have been admitted to the ninth batch of M.Sc. PHE course for the year 2019-21, with a stipend of Rs. 6000/- and Rs. 3000/- per month respectively for Category I and II. From the M.Sc. PHE batch of 2017-19, seven students have successfully completed, among them four students have been selected for internship based on the inter-se merit list obtained from Pondicherry University. As a part of study tour program (Fig. 24) of the course curriculum, M.Sc., students visited National Institutes such as NCDC, NVBDCP, NIMR New Delhi and RMRI Patna.

Fig. 24: Study tour program for MSc PHE Students.

They acquired good knowledge on Dengue vectors, insecticide resistance, strategies in controlling major vector borne diseases, Sandflies identification, collection and its control methods and rodent surveillance during the above visits. Also, they were taken to VCRC field stations at Koraput for Malaria study and Kottayam for Dengue and Chikungunya study, Chennai Sea Port to study formalized surveillance and reporting system of sea port.

Ph.D. Programmes: Six candidates (Microbiology Full time – 2 and Zoology Full time – 4) were awarded with Ph.D. degree. Five full time (Chemistry – 1; Zoology – 4) and one part time (Zoology) candidates continue to pursue their Ph.D. programme.

Student's Visit & Training: 453 visitors from different National Institutes visited ICMR-VCRC for orientation and exposure to various ongoing programmes/research of the Centre March 2019 to Feb 2020). Research scholars and PG students (37) from various Colleges/National Institutes were offered training at the Centre. Four Health Officers from Anti-Malaria Campaign, Sri Lanka had also undergone 12 days training on "Malaria Entomology and Vector Control" at ICMR-VCRC. Two MPH students from Central University of Kerala had undergone 6 weeks internship on the topic "A case study on chikungunya fever in adult/children during the re-emergent outbreak in 2018-19, Puducherry".

Public Health Importance

- The findings of the ICMR-VCRC community-based trial on safety, efficacy, effectiveness and acceptability of IDA, and the modelling study were the major evidence base for the LF elimination programme in India to adopt the new WHO recommended IDA strategy to accelerate LF elimination. Expansion of this strategy to cover all the districts with persistent infection will lend the programme to accelerate LF elimination.
- ICMR-VCRC teams evaluated the coverage and compliance MDA-IDA following the introduction of MDA-IDA in Simdega, Nagpur and Varanasi districts. Suggestions were given to the respective states and NVBDCP to improve the drug coverage and compliance in the subsequent rounds of MDA.
- Molecular Xenomonitoring (MX) protocol developed at VCRC, validated in three districts with varying epidemiological settings, is a potential surveillance strategy to evaluate Mass drug administration in LF elimination programme at different stages of monitoring and evaluation.
- Identified three drug candidates using drug repositioning strategy with *in vitro* macrofilaricidal activity in comparison with the currently used drugs DEC, Ivermectin and Albendazole.
- After distribution of long-lasting insecticidal nets in Odisha State, there was a shift in resting behaviour of both *An. fluviatilis* and *An. culicifacies* from human dwellings to cattle sheds. Zero density in human landing collections and low human feeding in both the vector species were observed. These findings are attributed to the impact of LLINs. Therefore, LLINs should be replenished in time to sustain the gain achieved so far.
- A severe outbreak of dengue fever occurred in Tikarapada village of Rayagada district during April 2020. The house index (HI), container index (CI), pupal index (PI) and Breteau Index (BI) were 24.8, 11.6, 32.7 and 40.6, respectively in the dengue outbreak village. A total of 171 *Aedes* mosquitoes of two known dengue vector species; *Ae. aegypti* (79%) and *Ae. albopictus* (21%) emerged from pupae. Based on the entomological survey findings, integrated vector control measures were adopted and contained the dengue outbreak within a week.
- Visceral and cutaneous leishmaniasis cases were recorded from the foot hills of Western Ghats belt of Kerala.
- Records of Visceral and cutaneous leishmaniasis caused by *Leishmania donovani* MON-37 strain along the foot hills of Western Ghats, Kerala.
- A progressive increase in mixed infection with different serotypes of dengue in Kerala was recorded.
- Increasing prevalence of chikungunya in Thiruvananthpuram and Kollam (Southern districts of Kerala) were recorded.
- wMel and wAlbB transinfected Indian strains of *Aedes aegypti* have been developed for field testing for control of Dengue and Chikungunya.
- Estimates of population density of *Ae. aegypti*, the vector of Dengue to be used as a baseline to implement and assess the impact of alternate novel dengue control strategy that target the adult population.
- Innate immune cells especially monocytes and eosinophils are involved in the pathogenesis of dengue viral disease and over expressions of matrix metalloproteases mediates the dengue pathogenesis.
- Generated evidence for the risk of transmission of Indian tick typhus in areas reporting Acute Encephalitis Syndrome (AES), Gorakhpur, Uttar Pradesh.
- Isolated a potent bio-larvicide, *Bacillus* sp. VCRC-B633 from desiccated apple which has

high impact on vector control compared to standard strains of *Bti*.

- A new bacterium namely *Bacillus thuringiensis israelensis* VCRC-642 was isolated for the first time from marine biofilm of boat's hull which is highly potent against *Cx. quinquefasciatus*, *Ae. aegypti* and *An. stephensi.*
- A new bacterium namely *Bacillus cereus* VCRC 641 was isolated for the first time from the fresh water fish named *Clarias batrachus* for the control of mosquito larvae.
- A new bacterium namely *Bacillus thuringiensis* serovar *israelensis* VCRC-638 was isolated for the first time from marine oil spill over soil for the control of mosquito larvae, the bacteria has the unique capacity to degrade the hydrocarbons (oil), utilizing it as a source for its growth. These bacteria would be useful for management of environmental waste.
- Developed a process for the production of *Bacillus thuringiensis* var. *israelensis* (VCRC B-17) by a cost saving technology and a self-floating slow release formulation.
- Developed alginate granular formulations for the indigenous insect growth regulator DPE-28.
- Developed a novel equipment for generating germ free and gnotobiotic mosquitoes and an eco-friendly and cost effective Ovitrap for vector surveillance.
- Established a quality assurance system and testing facilities towards GLP accreditation for evaluation of long-lasting insecticidal nets (Phase II).

ICMR-NATIONAL AIDS RESEARCH INSTITUTE, PUNE (ICMR-NARI)

CLINICAL EPIDEMIOLOGY

- HIV outbreak in the district of Unnao, Uttar Pradesh (UP) was investigated by the Scientists of ICMR-NARI. Subsequently a consultation meeting was held with the Project Director and Assistant Project Director, UP State AIDS Control Society (UPSACS) along with Independent experts and officials from ICMR-NARI and NACO at Lok Bhavan, Lucknow on 13th May 2019. The findings of the outbreak investigation highlighting stealthy spread of HCV and HIV due to exposure to unsafe injecting while seeking treatment were disseminated in this meeting. Future courses of action were discussed so that necessary intervention could be planned by the State health authority for the district of Unnao. This study was supported by ICMR Extramural and ICMR-NARI intramural grant.
- A qualitative study on acceptability of an indigenous oral mucosal transudate based HIV self-screening test was completed in 2019. This investigation involved men-having sex with men, transgender population, truckers, young adults (18 to 24 years) and clinic attendees. The national target that 90% of people living with HIV (PLHIV) in India would know about their HIV status, would be able to draw upon this study findings by informing the National AIDS Control Program (NACP) about people's voices and views. Grant was received from WHO.
- NACO supported Viral suppression studies among two cohorts of HIV infected persons on ART with 6.5 and 2.5 years of ART exposure were undertaken. This project demonstrated 9% virologic failure - well within the limit of India's 90-90-90 goals.
- 'Impact Evaluation of Government of India's (GOI's) free Antiretroviral Treatment Program' with an assessment of 396 ART centres across India demonstrated significant gains in survival / reduction in mortality among PLHIV receiving ART particularly at lower CD4 cell counts, older ages and among HIV-TB co-infected patients. First national evaluation of GOI's free-ART national-program impact in 396 ARTC; led by ICMR-NARI collaborating

with 5 ICMR institutes. Documented 3-fold reduction in death due to ART, detrimental independent effect of TB on survival, impact of ART on quality of life, advantageous cost-effectiveness ratio, identified gaps in services, provided future directions to focus on ageing HIV population and co-morbidities, immediate linkage to ART, retention, immunologic and viral monitoring. This project was supported by NACO - GOI.

- Feasibility of operationalization of early or immediate ART to HIV-infected partner as a combination intervention among HIV-serodiscordant couples. The study identified training needs and counselling gaps at Integrated Counselling and Testing Centres (ICTC) in 4 districts in two states and developed tools for counselling and patient education. 'Treat All' and "ART for Prevention' messages need to be disseminated at the time of testing itself (ICTC) and spouses of ART centre attendees should be tested at ARTC. New program initiatives to be inculcated in counselling immediately. Rotation of ART and ICTC counsellors recommended.
- HIV Sentinel Surveillance –Central Prisons. First bio-behavioural surveillance among Indian prisoners, prevalence and risk factors for HIV and Syphilis among inmates identified (NACO-GOI supported project).
- Behavioral Sentinel Surveillance. ICMR-NARI, supervised Behavioral Sentinel Surveillance –Lite (BSS-Lite) in Rajasthan, Maharashtra and Gujarat among Female Sex Workers (FSWs), Men who have sex with men (MSM), Hijra/Transgender People (H/TG) and Injecting drugs users (IDUs). Sample Frame Development identified many new hotspots hitherto unreached, but survey could not be completed due to pandemic. Overall exposure to program services was very high. While condom use among FSW and Transgender was high with clients, it remained low with regular male-partners. (NACO-GOI supported project)
- India Tuberculosis Research Consortium (ITRC) ICMR Extramural supported project - A Phase III, randomized, double-blind, placebo controlled study to evaluate the efficacy and safety of VPM1002 and Immunovac in preventing Tuberculosis (TB) in healthy household contacts of newly diagnosed sputum positive pulmonary TB (PTB) patients-Initiated at two facilities in ICMR-NARI.
- A multi-centric, non-randomized, non-controlled, open-label Phase IV trial to evaluate the safety, tolerability and effectiveness of Dolutegravir 50 mg tablet along with other antiretrovirals among HIV-1 infected subjects has been initiated in 2019 in collaboration with the YRG Care Chennai and VHS Hospital Chennai.
- Ocular manifestations among People Living with HIV (PLWH) attending ART centre at Pune, India: a cross-sectional study. Data on ocular manifestations among ART centre attendees generated will be useful for the national programme. This study was supported from ICMR-NARI Intramural grant.
- Guidelines were developed in consultation with stakeholders and experts to assist in mapping, size estimation and risk behaviour among key population in virtual space. WHO supported project.
- The interim analysis of the data generated from the Metformin trial revealed that Tab Metformin does not reduce the time required for sputum culture conversion, however it plays an important role in preventing lung tissue fibrosis. This can improve the post-treatment quality of life of the TB patients. This project is supported by India Tuberculosis Research Consortium (ITRC) ICMR Extramural and Open Source Pharma Foundation (OSPH).
- Estimating Incremental cost of treating antimicrobial resistant infections in India (EIC AMR Project) a multicentric observational study initiated in the month of February 2020 at

eight hospitals across the country participating in AMRSM. Supported by ICMR Extramural grant.

- Initiation of two phase III clinical trials for MDR TB patients- end TB trials involving new drugs (oral regimens) – Medicines Science Frontiers (MSF) supported trial.

SOCIAL AND BEHAVIORAL RESEARCH

- Subsequent to the ICMR's task force intervention study on 'Adolescent Reproductive and Sexual Health Education', a comprehensive book on adolescent health was published in September 2019.
- Demonstration study of Pre-Exposure Prophylaxis (PrEP) for MSM and Transgender women aims to understand implementation of provision of daily oral-TDF containing PrEP among MSM and TGW through both community and clinic based delivery models in India. This study is supported by ICMR.
- NACO supported study on 'Exploring Hard to Reach MSM (HRMSM) network structure and dynamics in India, a multi-centric study' was completed in 2019.

LABORATORY SCIENCES

- In the study titled 'Characterization of intratype genomic variants of Human papillomavirus type 16', we determined the variant based molecular signature as per cervical lesion grade that might serve as potential translational leads for genetic diagnostic probe development. We also identified variants that might impact the efficacy of prophylactic vaccines and have implications for future vaccine design. Supported by DST-SERB.
- Centre validated laboratory assays for detection of HBsAg and anti-HCV antibody (HCVAb) using dried blood spots (DBS). ELISA and chemiluminescene (CLIA) based assays for detection of HBsAg and anti-HCV using DBS were tested. We demonstrated that CLIA on Architect platform performed best for HBsAg detection while Ortho HCV ELISA performed best for HCV Antibody detection with DBS samples and could be used for DBS collected in future as part of the National Family health Survey (Four round; NFHS-4). The grant was received from WHO Country office.
- ICMR Extramural supported study of genital Human papillomavirus infection in men: type-specific distribution, risk determinants and natural history. Preliminary data shows HPV prevalence of ~20% among men from within India, which is almost equivalent to cervical infection in women.
- Diagnostic utility of self-collected buccal swab specimen as an alternative to sputum for molecular detection of pulmonary tuberculosis was initiated – Supported by Central TB Division.
- Estimation of seroprevalence for Hepatitis B and C among adults in India: National Family Health Survey-4 Supported by MoHFW, NCDC.
- ICMR-NARI Intramural supported project Identification of HPV T cell epitopes recognized by Indian population. : till now, Seven epitopes recognized by HPV infected Indian women were identified.
- ICMR-DBT funded National HIV Cohort Program Cohorts of HIV Resistance and Progression in Indian Children and Adults (CoHRPICA).
- Consortium of kit quality to support NACP. Quality control in CD4 and HIV serology labs under NACP: 100 kits diagnosing HIV/ HBVHCV were evaluated, six batches of HIV kits did not show the expected sensitivity hence not used in the programme. Sustainable through its own income
- ICMR Extramural supported study; Demonstrated Plasma Galectin-9 levels as a cheaper surrogate marker of HIV viremia.
- Demonstrated role of IL-5 in contributing to HIV viremia in viremic non responders under

NHFS-5. This study was supported by ICMR Extramural budget.

- Validation of 25-hydroxyvitamin D assessment from dried blood spots within the Longitudinal Aging Study in India. This study was supported by Harvard School of Public Health, USA.
- Government of India funded project Longitudinal Aging Study in India. Validated hsCRP, HbA1C &CMV antibody estimation on DBS samples, completed training by LASI partners
- MicroRNA profiling and deciphering their role in HIV-driven inflammatory responses at the female genital mucosa – DBT
- Phenotypic and functional characterization of CD4+Th17 cells during long term non-progression of HIV – ICMR Extramural
- Role of Toll-like Receptors (TLRs) on HIV Latency: An approach to 'Reactivate and Kill' the latently infected cells – ICMR under Indo-US RFA
- ICMR-NARI Intramural supported Role of transforming growth factor- β (TGF-β) on HIV shedding at the cervico-vaginal mucosa during HIV infection. TGF-β neutralization increased HIV shedding in the cervical epithelial cells
- National HIV drug resistance survey initiated. Successfully supported the HIVDR genotyping to Myanmar and Sri Lanka. This study was supported by WHO and UNOPS.
- ICMR Extramural supported project Development of diagnostic kit for rapid and early detection of *Orientia tsutsugamushi* based on isothermal recombinase polymerase amplification and lateral flow analysis - Four standard strains of *Orientia* have been grown successfully. Adequate quantity of DNA has been extracted and is ready for standardization of the assay- Development of a rapid PCR based kit for detection of *Orientia tsutsugamushi* will help in management of the disease.
- RAMANUJAN fellowship project entitled "MicroRNAs and Exosomes: The Key Players in Rotavirus Infection. Identification of several miRNAs as therapeutics against multiple viruses.
- Understanding the type and emergence of drug resistant mutations by sequencing the complete genomes of MDR and XDR *M. tuberculosis* strains by longitudinal follow-up supported by DHR.
- In collaboration with National Institute of Naturopathy and Nisargopchar Ashram, Pune a pilot study on Effects of Yoga and Naturopathy interventions in inflammatory status of obese patients was initiated.
- ICMR Extramural supported project Comparative analysis of genetic variation and expression of Apo family of lipoprotein, lipid metabolizing enzyme and transporter genes between HIV-associated lipodystrophy patients taking PIs with and without the history of receiving stavudine or zidovudine based regimen.
- Contributions to HIV-1 Viral Load Testing in India-
  i. ICMR-NARI developed 'National Guidelines for HIV-1 viral load laboratory testing' to be used across India.
  ii. Through a successful technology transfer from CDC, Atlanta, we undertook 'dried tube specimen for HIV-1 viral load proficiency testing panel preparation'. This led to establishment of a robust, cost effective HIV-1 viral load proficiency testing programme.
  iii. Validation and verification of DBS as a sample type for HIV-1 viral load estimation carried out and a robust, cost effective, sustainable assay for HIV-1 viral load estimation that will obviate the cold chain transportation has been delivered to the programme successfully.

RESEARCH CARRIED OUT UNDER PH.D PROGRAM

i. Determination of ADCC responses at the various stages of HIV-1 infection disease progression in Indian patients

ii. Non progressive HIV infection shows presence of functional NKG2D expressing Natural Killer T cells, but the function did not improve after antiretroviral treatment

iii. Polymorphisms in Toll-like receptors (TLRs) -7 and 9 genes in Indian population with progressive and non-progressive HIV-1 infection

iv. Non-progressive HIV-1 infection is associated with expansion of IL-21R expressing class-switched memory B cells

v. Genetic and neutralization properties of the envelope gene in HIV-1 and HIV-2 monotypic and dual infections

vi. Role of HSV-2 in HIV-1 / HSV-2 Co-infection and

vii. Antiretroviral drug resistance among HIV-1 infected adults attending ART clinics of a Metropolitan City of Western India, following targeted virological monitoring, versus those detected by conventional immunological monitoring

IMPLEMENTATION SCIENCE

Two Technical briefs were prepared by ICMR-NARI and shared with the National AIDS Control Organization (NACO); a) Assessment of Early infant Diagnosis of HIV infection in India and b) In search of a cheaper alternative to viral load testing for HIV treatment monitoring. Findings of two NACO funded studies were used to develop these technical briefs.

Public Health Importance

- Study findings on inclusion of counselling related to ocular manifestations among PLHIV were generated
- First evaluation of GOI's free-ART program impact in 396 ARTC, created dataset >1.6 lakh PLHIV, documented cost-effectiveness, impact on survival/mortality, quality of life, gaps in delivery, reasons for lost to follow-up
- Counselling did not much improve HIV knowledge in ICTC clients, more knowledge of HIV transmission may deter disclosure to spouse, but directed counselling helps disclosure
- Identified ways to reach out Hard to Reach population for the purpose of intervention, highlighted the paucity of health care TI in rural India
- 60 MSMs/TGs have started using additional HIV prevention method through PrEP
- First bio-behavioural surveillance among Indian prisoners, prevalence and risk factors for HIV and Syphilis among inmates identified
- Specific HPV16 substitutions with translational potential to serve as molecular markers of high-grade cervical disease and for HPV vaccine design identified.
- Assays that can be used optimally for viral hepatitis testing using Dried blood spots identified for National Chronic Viral Hepatitis Surveillance.
- Preliminary data shows HPV prevalence of ~20% among men from within India, which is almost equivalent to cervical infection in women.
- Demonstrated Plasma Galectin-9 levels as a cheaper surrogate marker of HIV viremia
- Demonstrated role of IL-5 in contributing to HIV viremia in viremic non responders
- Understanding the prevalence of ART drug resistance in Indian population
- National HIV drug resistance survey initiated

ICMR-NATIONAL INSTITUTE OF RESEARCH IN TRIBAL HEALTH, JABALPUR (ICMR-NIRTH)

Presence of additional Plasmodium vivax malaria in Duffy negative individuals from Southwestern Nigeria (Indo-African Collaboration)

Malaria in sub-Saharan Africa (sSA) is mostly caused by *Plasmodium falciparum* and, *Plasmodium vivax* was historically thought to be absent in sSA due to high prevalence of the Duffy negativity in individuals residing in this sub-continent. However, use of PCR for diagnosis has revealed extra burden of vivax malaria in samples collected from Oredo and Kosofe regions of Nigeria. Interestingly, four *P. vivax* isolates (out of 145 positive samples) were identified either as single (3) or mixed (one *P. falciparum/P. vivax*) infections (Fig. 25). Sequencing results confirmed all vivax isolates as truly vivax malaria and patient as Duffy-negative genotype. Identification of additional vivax isolates among Duffy-negative individuals from Nigeria, substantiate the expanding body of evidence on the ability of *P. vivax* to infect RBCs that do not express the DARC gene.

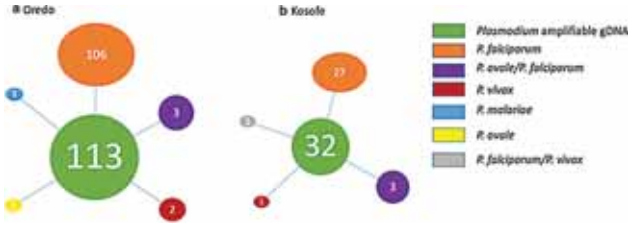


Fig. 25: Proportional dynamics of Plasmodium species at two study locations of Nigeria, Africa.

Intensified TB control among Saharia PVTG in Madhya Pradesh

Saharia PVTG is known to have very high prevalence of Tuberculosis, hence a project is being undertaken in collaboration with State Government to control TB among them. Active case detection, treatment and monitoring are the main components of the study. This year more than 3,00,000 individuals were screened for symptoms of Tuberculosis and 32543 presumptive TB cases were tested this year. Total 4539 cases were detected and put on treatment. Total of 191 MDR and 10 XDR have been detected and put on treatment. The success rate of TB treatment is over 90%.

Fig. 26: Field activities to screen individuals for active TB cases.

Field activities A disease survey for prevalence of TB was also carried out in all the districts. Total of 20851 individuals were screened of which 2868 were found to be symptomatic. Total of 259 cases were detected. The overall prevalence was found to be 1357 per 1,00,000 population.

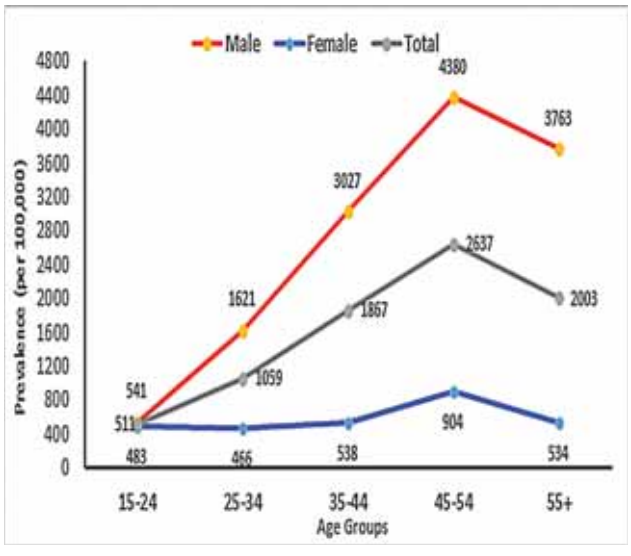


Fig. 27: TB prevalence by age and gender in Saharias.

Mandla-Malaria Elimination and Demonstration Project (MEDP)

Malaria Elimination Demonstration Project (MEDP) is a first-of-its-kind public-private-partnership between the Indian Council of Medical Research (ICMR) through National Institute of Research in Tribal Health, Government of Madhya Pradesh (GoMP), and the Foundation for Disease Elimination and Control of India (FDEC-India). The goal of MEDP is to demonstrate successful elimination of

malaria from 1233 villages of Mandla district and use the lessons learnt for eliminating malaria from rest of Madhya Pradesh and the country. The project enrolled the entire population (11,43,126) of the district for fever surveillance followed by testing of febrile cases and treatment of positive subjects using T4 strategy, which is Track (by fever), Test (by RDTs), Treat (by ACT) and Track (for completion of treatment). The study also used conventional vector control measures and information, education and communication (IEC) to increase demand in community for treatment for malaria.

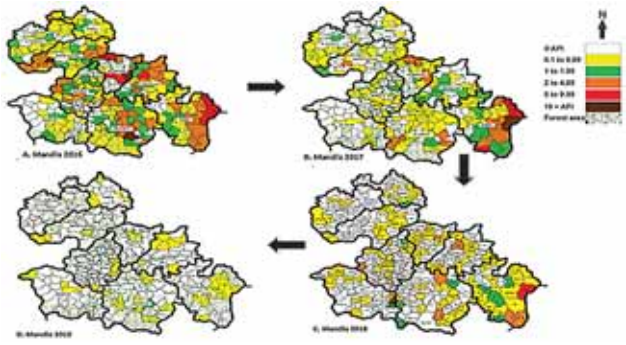


Fig. 28: Progressive decrease in malaria incidence in Mandla district of Madhya Pradesh.

The project demonstrated 83% reduction of indigenous cases of malaria during the period of June 2017 to March 2020, through case management and conventional vector control strategies. A total 357,143 febrile cases were screened, out of which 0.19% were found positive for the presence of malaria parasites. These results indicate that malaria elimination can be achievable in India in a stipulated time frame.

Understanding tribal culture, lifestyle, animal husbandry activities and cause of death in five tribes of India through establishment of tribal habitats in ICMR- NIRTH Jabalpur

The study is being carrying out in five different tribal communities in India. Accordingly, three ideal Hut Models of primitive tribes Baiga, Saharia and Bharia resided in Madhya Pradesh was established in the premises of NIRTH. Data collection of Baiga, Bharia, Saharia of Madhya Pradesh and Bhil tribes of Rajasthan has been completed. Now centre is planning to conduct survey among Bhil tribe of Sarguja district in Chhattisgarh.

Fig. 29: Field Survey for collecting demographic and zoonotic information to understand tribal culture

Prevalence of Fluorosis in the community of selected districts of India and Development of an appropriate intervention model for prevention and control of Fluorosis. (Multicentric ICMR Task Force Study)

This is a multicentric ICMR Task Force study. Chhindwara district of Madhya Pradesh is one of the site under this project. A total of 33 selected villages were surveyed with a total of 7187 households. We screened 644 water samples and 703 urine samples for fluoride. All these urine samples were also screened for Iodine. Apart from these, diet survey was also done in 533 households. A total of 70 locally grown food stuff were sent to NIN, Hyderabad for fluoride estimation. A total of 2390 children were found with dental fluorosis. Knock knee is the most common skeletal change in patients less than 15-year-old. Patients greater than 15-year-old have more problem in sit ups.

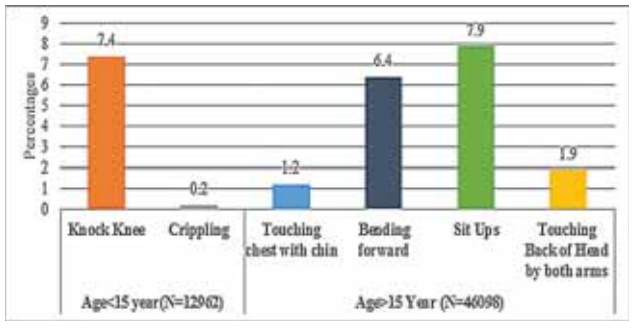


Fig. 30: Clinical Manifestation of Fluorosis in different age groups.

Centre also analysed 3084 water samples and 4677 urine samples for fluoride from other six sites i.e. RMRC Bhubaneswar, AIIMS Patna, NIN

Hyderabad, GMC Assam, AIIMS Jodhpur and PGIMER Chandigarh located in different states.

India Hypertension Management Initiative

The project has been initiated with the objective is to reduce cardiovascular disease morbidity and mortality in India. The India Hypertension Control Initiative (IHCI) is a multicentric study being initiated in 5 states in initial phase. This was launched in the State in April 2018, is a multi-partner initiative with the Ministry of Health & Family Welfare, Indian Council of Medical Research, State Government, WHO India and Vital Strategies. The project aims to reduce premature cardiovascular deaths by strengthening hypertension management and control using evidence-based strategies. A total of 77398 cases have been registered (Till February 2020) in Chhindwara, Bhopal and Ratlam. In the second phase of the study, three more districts have been included *i.e.* Ujjain, Sehore and Seoni. In these three districts another 15668 cases have been registered in the program.

1.7. Health Assessment of Villagers of Tamnar Block, District Raigarh, Chhattisgarh

At the request of Ministry of Environment and Forest and Climate Change, on the directives of National ST Commission "Health Assessment and Projection of Health of People living in Tamnar Block, Raigarh, Chhattisgarh" were studied. In this study, an attempt was made to find out the morbidity, mortality and nutritional status of the population residing in Tamnar Block of Raigarh District. The study was carried in 33 sampled villages of Tamnar Block.

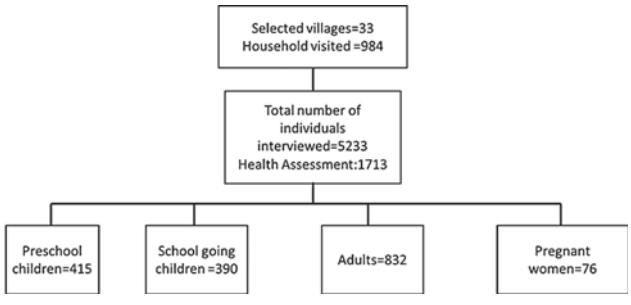


Fig. 31: Schematic representation of health assessment protocol in Tamnar Block, Raigarh, CG.

ARI were the major morbidities among villagers of Tamnar Block. Anaemia prevalence was about 64.8% among non-pregnant non-lactating women. Prevalence of hypertension was about 21.8%. Fungal infection (4.0%) was a common problem among > 15 years of age. Sputum positive Tuberculosis was higher than the National average in Tamnar Block. Non-communicable diseases accounted for 53.9% of the deaths. Infectious and parasitic diseases caused 13.9% of deaths whereas injuries and suicides accounted for 12.1% deaths. Among non-communicable diseases cardiovascular diseases (34.3%) were the leading cause of death. Neoplasm caused 4.7% of deaths. Digestive diseases accounted for 6.5% of deaths, Diabetes and kidney diseases caused 2.6% of deaths.

Public Health Importance

- Under the project Intensified TB control among Saharia PVTG in M.P. This year more than 3,00,000 individuals were screened; 32543 presumptive cases were tested. Of these 4539 cases were diagnosed and put on treatment. Total of 191 MDR and 10 XDR have been detected and put on treatment. The success rate of TB treatment is over 90%. A disease survey for prevalence of TB was also carried out in all the districts. The overall prevalence was found to be 1357 per 1,00,000 population.

- Centre achieved 83% reduction of indigenous cases of malaria in Mandla district during June 2017 to March 2020 through case management and conventional vector control strategies in malaria elimination demonstration project.

- Health Assessment of people of Tamnar Block has been done. Tamnar Block have difficult terrains and remote areas in Chhattisgarh. Non-communicable diseases accounted for 53.9% of the deaths. The findings of this health assessment may be useful in planning the health programmes for the area.

ICMR-NATIONAL INSTITUTE OF VIROLOGY, PUNE (ICMR-NIV)

EMERGING INFECTIONS

SARS-COV-2

Diagnostics, isolation and characterization of SARS-CoV-2: As part of the SARS-CoV-2 pandemic response, ICMR-NIV, Pune optimized real-time RT-PCR assay (E gene) for screening and confirmation (RdRp, N and ORF 1b genes). It performed quality control for all the government and private laboratories performing COVID-19 testing in Maharashtra and supplied 3,57,626 reagents. The confirmation of the first 03 cases in India was reported on 30th Jan. 2020 as imported cases from Wuhan, China. Till 31st March, 5045 samples have been screened and 304 tested positive. Samples were sequenced using NGS and complete genomic sequences were retrieved for two of the first 3 samples, followed by imported cases of SARS-CoV-2 via Italian tourists, and the suspected contacts in India. The sequences of the Indian SARS-CoV-2 strains clustered in different clades. Samples from Italian tourists and Indian contacts were cultured in Vero CCL-81 and nine isolates were obtained and confirmed by electron microscopy (EM) and molecular tools. All the sequences had ~99.98% identity with the Wuhan reference strain.

Training: To enhance national capacity for detection of COVID-19, existing virus research and diagnostic laboratories (VRDLs) in the country and NCDC labs were trained. Biosafety training given to NDRF personnel as well.

Iran mission: In an effort to screen Indian nationals stranded in Iran, an NIV team comprising two scientists and technical experts were deputed to screen them and enable their evacuation during March 5 to March 17, 2020. Throat swabs were collected from 2028 individuals on site of which 308 tested positive for SARS-CoV-2.

Drug repurposing studies for the SARS-CoV-2: Towards drug *repurposing for SARS-CoV-2, the* binding potential of HIV-1 protease inhibitors, lopinavir and ritanovir against the main protease (3CLpro) was investigated using computational docking studies.

SARS-CoV-2 Antiviral testing study: Anti-viral testing studies of a number of drugs, received from various institutes and companies were initiated. Inactivated SARS-CoV-2 was provided to CSIR-CCMB and IGIB for molecular studies on SARS-CoV-2 infection and development of antiviral compounds and candidate vaccines.

Validation of COVID-19 test kits: Twenty real time RT-PCR kits were evaluated while evaluation of 7 rapid diagnostic test kits has been initiated.

NIPAH VIRUS

Countrywide survey of Nipah virus (NiV) in *Pteropus* bats: Anti-Nipah virus antibodies were detected in *Pteropus* bats collected from Tamil Nadu, Kerala, Karnataka and Pondicherry. Nipah virus antibody and viral RNA was also detected in *Pipistrellus* and *Rousettus* bats from Maharashtra for the first time.

A follow up study was conducted to determine the persistence of Nipah virus antibodies in fruit bats one year after the 2018 outbreak in Kozhikode. No viral RNA or antibody positivity could be detected in 74 fruit bats screened.

Investigation of Nipah virus outbreak in Ernakulum district, Kerala (June 2019): Infection was confirmed in a 21 year old male student in Ernakulum district, Kerala. RNA detection and antibody prevalence in fruit bats from the neighborhood of the index case confirmed the association of bats in virus transmission. On-site training of health care workers and on-site laboratory staff helped in dealing with the outbreak effectively.

Development of sero-diagnostic assays for Nipah virus: Indigenous anti-NiV IgM and IgG antibody ELISA were developed and optimized for future surveillance studies.

ZIKA VIRUS

Cohorts for Zika Epidemiology in India (COZEI) Study: Microcephaly was not detected among babies delivered by Zika positive women (n=25) in outbreak areas in Rajasthan. However, preterm birth and low birth weight was recorded in few babies.

Emerging zoonotic infections

BAT CORONAVIRUS

Detection of bat coronavirus in Pteropus and Rousettus species: Bat coronavirus was detected in retrospective samples from *P. medius* (08) and *Rousettus* (03) species. RDRP gene sequences showed clustering in Lineage-D of the betacoronavirus genus. Subsequent studies with *Rousettus* bats from Maharashtra did not yield the coronavirus, but showed Nipah virus activity.

KYASANUR FOREST DISEASE

Standardization and Validation of KFDV Point of Care (PoC) assay: KFDV Point of Care (PoC) real time RT-PCR assay was standardized in collaboration with Molbio Diagnostics for clinical evaluation of human, monkey and tick specimens.

CRIMEAN CONGO HEMORRHAGIC FEVER

Crimean Congo hemorrhagic fever virus outbreak in Gujarat and Rajasthan: Investigated CCHF outbreaks in Rajasthan and Gujarat and confirmed 40 cases. Follow up studies in 353 and 291 close contacts in Gujarat and Rajasthan respectively showed six symptomatic and one asymptomatic case positive for IgM/IgG antibodies in Gujarat suggestive of human to human transmission.

Identification and characterization of novel viral isolates using Next-generation sequencing platform: A new insect specific virus, Phasi Charoen-Like Phasivirus was identified in *Aedes* aegypti mosquitoes collected from Karnataka state and characterization is in progress.

Next-generation analysis on the Acute Encephalitis samples from Muzaffarpur, Bihar: A total of 23 samples (CSF 5; serum 15; Urine 3) of AES cases from Muzaffarpur, Bihar were analyzed using NGS platform and no virus specific sequences were found.

NGS analysis of non-human primate samples from Nandan Kanan Zoo, Orissa: Organ samples of an Orangutan and one Nilgiri Langur were processed for virus detection using NGS and detected Mason-Pfizer monkey virus in Nilgiri langur and could not find any evidence of virus/ bacterium in the orangutan samples.

Identification of referred samples from an outbreak area in Udhampur district in Jammu and Kashmir: Samples (n=13) from children with respiratory and renal complications (URTI/ LRTI) with fatality were tested using NGS and shown the presence of virus contigs of human coronavirus OC43 virus, Human rhinovirus B35, Human Respiro virus 3, Rhinovirus A and Human respiratory syncytial virus A. However, cause of death was suspected to be of non-infectious origin.

AVIAN INFLUENZA VIRUS

Diagnosis of avian influenza (AI) for referred human samples: Referred human samples from poultry workers during an outbreak of Influenza (AI) H5N1 in Ambikapur, Chattisgarh, during December 2019 were tested and found negative.

Gene pool analysis of H5N1 and H9N2 avian influenza viruses: Full genome sequencing of eight H9N2 viruses isolated from birds and poultry drinking water samples from Pune have been completed.

INFLUENZA AND OTHER RESPIRATORY INFECTIONS

Sentinel surveillance for influenza in India: Of 2499 SARI patients tested for different respiratory viruses by real time PCR, Influenza virus was detected in 100 (4%) samples, of which Influenza A

pdm09(H1N1), Influenza A(H3N2) and Influenza B represented with 19 (0.8%), 07(0.3%) and 74(3%) samples respectively.

Respiratory syncytial virus (RSV) in tribal children in Melghat, Maharashtra: Nine of 1160 samples from children below2 years of age showed RSV RNA while 94 samples tested positive for influenza viruses.

Strengthening evidence-based advocacy for influenza prevention and control in India: Surveillance of 1093 cases in elderly people revealed incidence rate of ARI (1.8) and ALRI (0.07) and AURI (1.79) episodes per elderly per year. Among 468 samples screened, influenza and RSV positivity was detected in 21 [4.48%] and 4 samples respectively.

VIRAL HEPATITIS

Study of involvement of Host/Virus factors in Hepatitis E virus infection during pregnancy: SNP studies conducted in HEV infected non-pregnant women and males revealed genotypes 1/1 and 1/2 as well as allele 1 in the cytokine gene IL1RN VNTRs are susceptible while genotype 2/2 and allele 2 are protective to HEV infection. Assessment of the role of B regulatory cells (Bregs) in HEV pathogenesis revealed higher IL-10 expression on B cells in acute hepatitis E patients suggesting that Bregs are functional in Hepatitis E and they express HEV-rORF2p specific IL-10 only, not TGF-β.

Computational drug repurposing approach for the development of therapeutics against Hepatitis E virus (HEV): Analysis of transcriptomics, proteomics and interactomics data of HEV infection obtained from available datasets, identified protease inhibitors, Retinol 38 binding agonists/receptors, insulin growth factor receptor inhibitors and PARP inhibitors.

Interaction of hepatitis B virus with innate immune system of the host cells: HBV HBx protein is known to induce apoptosis via P38MAPK and JNK pathways. Treatment of hepatoma cells with P38MAPK and JNK inhibitors i.e. SB 202190 and SP600125 respectively, rescued cells from apoptosis. This confirmed involvement of HBx protein in inducing apoptosis in both wild type and HBeAg null mutant virus infected cells. This could be possible reason for severe liver injury in individuals who are infected with HBeAg null BCP/PC mutant virus.

Role of cellular autophagy and its modulation in the replication of hepatitis E virus: Primary analysis using GFP tagged LC3 transfection in HEV infected cells showed the induction of autophagy by HEV via formation of autophagosomes and autophagolysosomes. Autophagy flux measurement clearly revealed relationship between activated autophagy and viral replication with 2-fold increase in autophagy vacuole formation. The siRNA mediated knockdown of Beclin-1 and ATG7 in HEV infected cells resulted in inhibition of HEV induced autophagy and concomitantly hampered the viral replication. With these observations it was concluded that HEV induces autophagy and utilizes it favourably during replication.

VIRAL ENCEPHALITIS

Japanese encephalitis virus molecular epidemiology and diagnostics: Epidemiological investigations suggest replacement of previously circulating GIII strains by the newly introduced GI strain.

Development of recombinant JEV GI with genetically altered flavivirus cross-reactive domain to explore in sero-diagnostic assays: As the current JE IgM ELISA makes use of antigen prepared from GIII strain, an attempt was made to generate fusion loop mutant of GI strain as antigen in IgM ELISA.

Exploring Japanese encephalitis virus GI derived virus like particles (VLP) in IgM diagnostic ELISA as an antigen: JEV GI virus like particle (VLP) was generated by transfection of recombinant mammalian expression vector (pcDNA 3.1 +)

cloned with JEV signal peptide and fragments coding C-pr-M and E protein, characterized and evaluated.The VLPs as antigen was found at par with JEV E glycoprotein in detecting IgM antibodies in samples.

Impact of climate change on JEV and West Nile mosquito abundance in coastal brackish water and wetlands: A study conducted to determine the mosquito fauna in Alappuzha district found the predominance of *Culex sitiens* (69.48%) in brackish water and *Cx. tritaeniorhynchus* (61.97%) in wet land areas.

Antiviral activity of viral RNA dependent RNA polymerase inhibitors against Chandipura virus (CHPV) infection: I*n-vitro* studies in Vero cells established Ribavirin as an antiviral drug against CHPV.

Generation of RNA vaccine candidate that protects Chandipura virus challenge in mice: A vaccine candidate based on CHPV virus G gene cloned into pGEMT-Easy vector with T7 promoter was developed and being evaluated in mice.

Trafficking of Chandipura virus in neuronal cells: Interaction of heat shock cognate 71(HSC71), and cytoplasmic actin with CHPV N protein in virus infected Neuro2a cells was confirmed.

Role of host factors in Chandipura virus infection: The protective involvement of alternative pathway of complement activation towards *in vitro* neutralization and suppression of infectivity in CHPV infection is primarily C3 and C5 mediated. Recombinant human TNF-α effectively decreased CHPV replication *in vitro* as a prophylactic and antivirus action of TNF-α is CHPV specific.

Enhanced sentinel surveillance for etiological contribution and burden of Japanese Encephalitis following vaccination in Maharashtra and Telangana: a total of 450 clinical specimens were collected from 264 hospitalized AES cases (sera=273 and CSF=177) at two sites and detected JEV, CHPV dengue and HSV-1 in 26, 11, 11 and 1 case/s respectively. Twenty three cases showed IgM positivity for both JE and dengue infections.

Development of quantitative molecular assays for diagnosis of viruses associated with acute encephalitis syndrome: Developed a multiplex qPCR assay for detection of genetic variants of JEV (genotype I and III), West Nile virus (lineage 1 and 5), CHPV and HSV 1 and 2. The newly developed assay using the target 5'UTR-nucleocapsid region is specific to JEV. QPCR assay detects HSV-1 and 2 by targeting the conserved sequence from UL 30 gene (DNA polymerase) while the assay for CHPV targets the G gene.

Public trust in JE vaccine: A qualitative study on the determinants of acceptance and hesitancy towards vaccine in various Blocks of Alappuzha District was conducted.

DENGUE & CHIKUNGUNYA

Monitoring of dengue and chikungunya serotypes, genotypes and lineages in India: 4389 samples from different Indian states in 2018 were tested in collaboration with VRDLs and NIV field units for the serotypes of dengue virus. Prevalence of different serotypes of DENV differed in different parts of India. Phylogenetic analyses of DEN 1 strains revealed circulation of Asian genotype in Kerala, Tamil Nadu, Maharashtra and Himachal Pradesh while AM/AF in other states, multiple lineages of cosmopolitan genotype of DENV-2, genotype III of DENV-3 and genotype I of DENV-4 in different regions of India.

Comparison of whole blood and plasma dengue virus RNA detection: Detection rate of DENV RNA in whole blood is higher and one step real-time RT-PCR using RNA from whole blood combined with NS1 ELISA could be the choice for diagnosis in dengue vaccine trials.

Host factors as biomarkers for chikungunya disease severity and recovery: Significant association of the cytokine gene IL-1RN 1/1 genotype with risk of developing chikungunya infection was found. An association of GG genotype of NKG2A

gene as a susceptible gene and AA genotype as a resistant gene towards chikungunya infection was indicated. Higher levels of IL-1Ra and IL-6 are suggestive of biomarkers of chronic chikungunya arthritis infection.

Lipid nanoparticles for effective delivery of siRNA in Chikungunya virus: Stearylamine based nanoparticles were found to be effective for delivery of siRNAs.

Phylogeography analysis of the Indian Ocean lineage (IOL) of chikungunya viruses: Phylogeography analysis using whole genomes of IOL strains revealed indigenous evolution in India at least at three time points, with specific mutations that conferred viral fitness in *Aedes* mosquitoes. Dispersal from India was noted to Sri Lanka, Bangladesh and China on multiple occasions.

Structure-based design and evaluation of antiviral activity of selected lead compounds against Chikungunya virus: Among different groups of compounds (xanthonoids, flavanoids and benzothioazole derivatives) investigated, Mangostein was found effective in both *in vitro* and *in vivo* studies. *In silico* studies indicated that it could interact with the envelope glycoprotein and the nsP3 macrodomain.

Repurposing of drugs towards anti-Dengue and Chikungunya viruses using the systems biology approach: Signature profiles from transcriptomic, proteomic and interactomic data of these infections from available literature and appropriate databases, identified 88 significant pathways including cyclins and cell cycle regulation, cytokinesis, FoxO signaling pathway, kinesin complex, p53 signaling pathway etc which are among the major metabolic pathways involved in DENV pathogenesis.

ArVirInd: a database of arboviral proteins from the Indian subcontinent: A database has been designed, populated and launched (http://arvirind.co.in) with information available on E-proteins and NS1 proteins of dengue, chikungunya, Japanese encephalitis, West Nile viruses including sequence, antigenic properties (B-cell epitopes), functional sites, etc.

Seroprevalence of dengue and chikungunya virus infections in Pune: A prospective population-based serosurvey using multistage cluster random sampling of 30 clusters (1654 participants) selected by probability proportional to size (PPS) sampling was undertaken in Pune city (18th March -10th April 2019). Chikungunya and Dengue IgG seroprevalence was found to be 53.2% and 87.8% respectively.

Pathophysiology of dengue virus infection using electron microscope: Differential binding affinity of DENV NS1 from different serotypes towards membrane phospholipids was reported. Molecular docking studies revealed the binding site for membrane phospholipids at the dimer interface of NS1. DENV NS1 binds and modulates the characterstics of phospholipid membranes during infection cycle.

ENTERIC VIRUSES

Hospital based surveillance of rota/non-rota enteric viruses and strains in children with acute gastroenteritis: Fecal specimens collected from 71 hospitalized children in Pune, showed presence of RV Group A in 29.5% cases. A total of 8 different G-P combinations of RVA were identified with predominance of G3P[8] (57.1%) genotype. Presence of Noro, Adeno and Astro viruses was observed in 5.6%, 12.6% and 4.2% of the cases respectively.

Assessment of diversity in group A rotaviruses in **acute gastroenteritis*:*** Full genome analysis carried out on three representative unusual rotavirus strains recovered from children having acute gastroenteritis was classified as G1-P[6]-I1-R1-C1-M1-A1-N1-T1-E1-H1, G9-P[4]-I2-R2-C2-[M1-M2_R]-[A1-A2_R]-N2-T2-E6-H2 and G9-[P4-P6_R]-I1-R1-C1-M1-A1-N1-T1-E1-H1 genomic constellations. Evidence of recombination events was found within the genes encoding VP3, VP4 and NSP1, showing combination of genetic information of genogroup 1 [M1/P[6]/A1] and genogroup 2 [M2/P[4]/A2] strains.

Identification and Molecular Characterization of Rota and Noroviruses in Neonates: Whole genome sequencing and phylogenetic analyses of

a naturally attenuated, culture adapted neonatal strain, (NIV-1740121) revealed multiple-gene reassortment events, containing ROTAVAC vaccine strain, 116E-like VP4, VP6, NSP3, NSP5 genes, VP7 gene of G12 origin and VP3 gene of porcine ancestry in a human Wa-like backbone.

Detection and characterization of Enteroviruses associated with Hand, Foot and Mouth disease (HFMD): HFMD samples (n=92) were referred from Pune and Kolhapur (n=68 cases). Seventy-five (81.52%) samples tested positive for enterovirus by RT-PCR using 5'NCR specific primers.VP1 gene sequencing of the positive strains and phylogenetic analysis revealed the presence of CVA16 [42,(59.15%)], CVA-6 [28,(39.43%)] and Echo-1 [1,(1.40%)].

Seroprevalence of Enterovirus 71 antibody among Indian children: *A study on* 500 children showed circulation of genotype D EV71 in children from 2 to 4 years.

Cytokine/ chemokine responses to EV71 in human cultured cells: Infection of human macrophages with the indigenous EV71 D genotype and the pathogenic C genotype (HFMD) could produce significantly higher IL-6 and TNF-α than C and G genotypes.

CD155/PVR Knockout Cell Strains from Human Rhabdomyosarcoma Cell Line (RD): *A* knockout RD cell line was developed (CD155/PVR) using CRISPR/Cas9 technology which rendered resistant to poliovirus infection.

Investigation of host genetic susceptibility markers to Enterovirus A71: The Single Nucleotide Polymorphism (SNP) Multiplexed assay targeting 15 genetic markers from 12 genes against EVA-71 was developed and validated.

Detection and Molecular Characterization of Potentially Zoonotic Enteric Viruses: Screening of bovine samples(n=153) collected from private cattle farms in Pune revealed presence of RVAs in 27 samples (17.64%) with a predominance of G10P[11] (51.8%), followed by unreported genomic constellations, G6P[14] (14.81%), G6P[4] (7.40%) and G10P[33] (3.70%). The G10P [33] is bovine-simian (SA11-like) reassortant strain, G6P[4] is bovine-human reassortant strain while G6P[14] strain is predominantly human.

MEASLES & RUBELLA

Genome and antigenic characterization of Indian rubella viruses: Sequence analysis of nine RuV isolates obtained from Karnataka, Kerala, Maharashtra and Odisha showed that they belonged to RuV 2B genotype. Antigenic studies showed 91.9% agreement between wild type and vaccine strains.

Measurement of virus specific IgM, IgG and neutralizing antibodies in suspected measles or rubella cases: To understand the qualitative or quantitative correlation of IgM, IgG and neutralizing antibody in the suspected measles or rubella cases, neutralization test was found more reliable and effective.

Chickenpox outbreak in a tribal population: Suspected chickenpox samples (n=36) referred from Silvassa (Dadra and Nagar Haveli), were laboratory confirmed in 33 cases as varicella zoster virus clade-1 strain.

POLIO VIRUS

National Polio Surveillance Project (NPSP), India: Screening of 8924 stool samples and 379 sewage samples from Mumbai revealed prevalence of Sabin-like poliovirus type 1 and type 3 and non-polio enteroviruses. *A*fter OPV drive, significant rise in poliovirus isolation rate was seen. Wild or circulating vaccine derived poliovirus was not identified. *A novel method for detection of polio and enteroviruses from sewage samples using polyelectrolytes has been standardized.*

In-vivo potency evaluation for the hexavalent, a combination vaccine containing Diphtheriae, Tetanus, Pertussis, Hepatitis B, Hib PRP-TT and IPV (Type 1, Type 2 & Type 3 antigens) and IPV trivalent vaccine formulation containing IPV (Type 1, Type 2 & Type 3).

Development of the Polio Essential Facility in line with the Global Action Plan III at ICMR-NIV, Pune to support work on Polio

Studies on poliovirus infections in children with immune-deficiency: Among 17 patients, (17.34%) were tested positive for enteroviruses and 5 (5.10%) tested positive for polioviruses. One SCID child was identified as a prolong excreter of P3VDPV.

BACTERIOLOGY

Seroepidemiology, maternal immune status and missed diagnosis of pertussis among young infants in India: Preliminary findings suggest low seroprevalence of pertussis antibodies in unvaccinated pregnant women.

DIAGNOSTIC SERVICES & DIAGNOSTIC REAGENT FACILITY

ICMR-NIV, continued to provid diagnostic support to the country and tested more than 60,000 samples. Inactivated viruses as positive control including Zika, KFD, Yellow Fever (17D) and CCHF has been supplied to various VRDLs across India and SEARO countries through WHO.

A total of 12823 JEV/DENV/ CHIKV MAC ELISA kits were supplied under the National program.

NIV, Bangalore unit tested ~10,000 samples for viruses including polio, measles/ rubella, congenital rubella, severe acute respiratory syndrome, Zika virus, KFD virus, Scrub Typus for AES and fever rash syndrome (FRS, Leptospirosis etc. The VRDL initiated project of 'Establishment of network of laboratories for managing epidemics and natural calamities' at ICMR-NIV Kerala Unit received 12,952 samples from 10,452 patients during the year and tested 18,952 samples. The total number of samples tested by the Mumbai unit was around 13,000.

Fig. 32: COVID-19 team of ICMR-NIV, Pune.

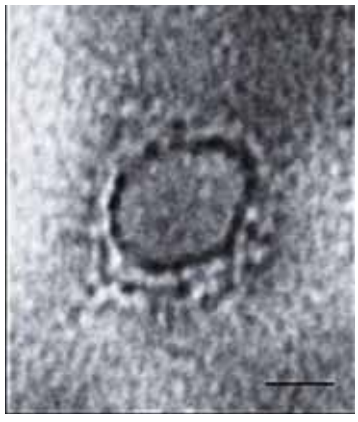


Fig. 33: First Transmission electron microscopy imaging of SARS-CoV-2.

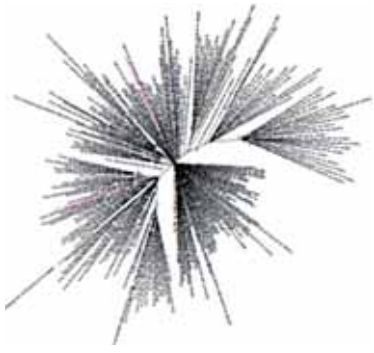


Fig. 34: Full genome sequences of the first two SARS-CoV-2 from India.

Fig. 35: Shipment of diagnostic reagents for SARS-CoV-2 to other centres;

Fig. 36: Iran Mission (March 1 – 18, 2020).

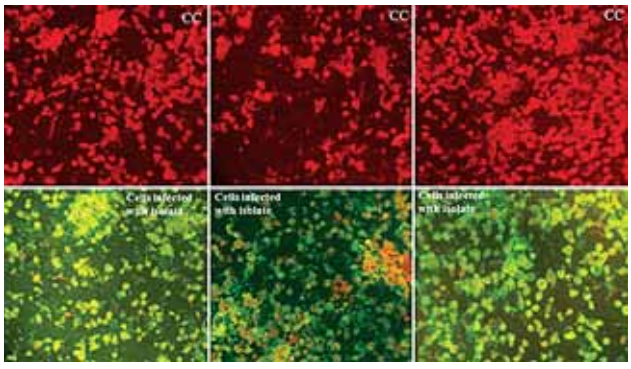


Fig. 37: First isolation of SARS-CoV-2 from clinical samples in India.

Fig. 38: Training & capacity building program 'Biological Emergency for First Responders for SARS-CoV-2' (February 25, 2020)

Fig. 39: Establishment of Nipah diagnosis set-up at GMC Ernakulam- June 2019.

ICMR – RAJENDRA MEMORIAL RESEARCH INSTITUTE OF MEDICAL SCIENCES, PATNA (ICMR-RMRIMS)

COMMUNITY BASED STUDIES

Evaluation of diagnostic facilities available for PKDL at grass root level in highly endemic districts of Bihar

A cross-sectional study was conducted in 31 PHCs of 2 highly endemic districts of Bihar using WHO's Service Availability and Readiness Assessment (SARA) tool. It was found that most of the PKDL cases are diagnosed clinically supported by rk39 test. Only 10% of Govt. health facilities have slit-skin examination facility and that too at district hospital level. Treatment facility is not consistently available at the periphery level.

Embedding diagnostic and surveillance of VL into the primary health care system

This study aimed to assess various diagnostic tests for VL to establish the best diagnostic algorithm in secondary health care setting. Patients with acute febrile illness, captured from both hospital and field, were subjected to various diagnostic tools. The result revealed that qPCR had higher positivity followed by rK39 ELISA and rK39 strip test. Urine ELISA had the lowest positivity. Based on the follow-up data, it was inferred that combination of qPCR and rk-39 ELISA may be a good option for better diagnostic approach for VL.

Evaluation of Health systems for VL under Post-elimination phase

Interim analysis revealed that health system needs to be strengthened in terms of trained human resources, logistic management, early diagnosis, diagnostic facility specially for PKDL/ relapse/ co-infected cases, post-treatment follow-up, etc.

CLINICAL STUDIES

Safety and efficacy assessment of AmBisome in treatment of PKDL as compared to Miltefosine

Safety and efficacy of AmBisome (5 mg/kg b.w. twice a week for 6 infusions) in indoor setting (n=50) was compared with 12-weeks treatment with miltefosine (n=50), the standard treatment for PKDL implemented in kala-azar elimination programme. It was observed that miltefosine had higher cure rate (86.9%) with lesser adverse events than AmBisome (cure rate 78.7%).

Randomized trial of AmBisome® monotherapy and combination of AmBisome® and miltefosine for treatment of VL in HIV positive patients.

In HIV-VL co-infected cases, combination of AmBisome® (30 mg) plus miltefosine (2.5 mg/kg b.w.) for 14 days showed better cure rate and

lesser side effect than AmBisome® alone (40 mg) for treatment of VL.

BASIC & APPLIED RESEARCH

Cytopathological and Immune cells involvement in leucocytes trafficking in PKDL

Inflammatory response with infiltration of mononuclear cells consisting of mostly histiocytes and lymphocytes was observed very high in papulo-nodular lesions as compared to macular lesions. Up-regulated CD62L and down-regulated CD11b were observed in macular cases. CXCL-10 plays a role in migration of innate cells to the inflammatory sites. Cytokine level of IL-2 was observed to be high in macular lesions. Possible defect in certain chemokine (CXCL-10) and cytokine (IFN-γ & TNF-α) co-ordination importing leucocytes to inflammatory dermal tissue in macular cases was observed.

Enoyl-acyl carrier protein-reductase in type II fatty acid synthesis pathway as a promising drug target in *Leishmania donovani*

The sequence analysis of *L. donovani* Enoyl-acyl carrier protein-reductase (LdENR) showed 99% similarity with the available putative sequence. Molecular docking and dynamics of Triclosan (TCL) done with modelled structure of LdENR was found satisfactory. Expression of LdENR gene had no significant variation amongst Amphotericin B sensitive and resistance strains of *L. donovani*. Wet lab studies showed efficacy of TCL against *L. donovani* with MIC_{50}= 30 µM (Fig. 40).

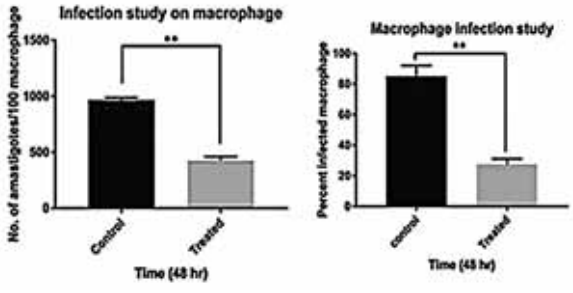


Fig. 40: Anti-leishmanial effect of TCL: (a) number of infected macrophages per 100 macrophages in absence and presence of LKZ. (b) number of amastigotes per 100 infected macrophages.

Evaluation of Luliconazole to restore Amphotericin B susceptibility in *Leishmania donovani* infected murine model

In silico docking analysis revealed that the ligand Luliconazole (LKZ) had good interaction with Lanosterol C14α demethylase having G score -6.185 and the ligand efficacy 0-634 (Fig. 41.). *In vitro* wet lab analysis as anti *L. donovani* promastigotes and intracellular amastigotes revealed $IC5_{50}$: 30µM and CC_{50}: 270µM.

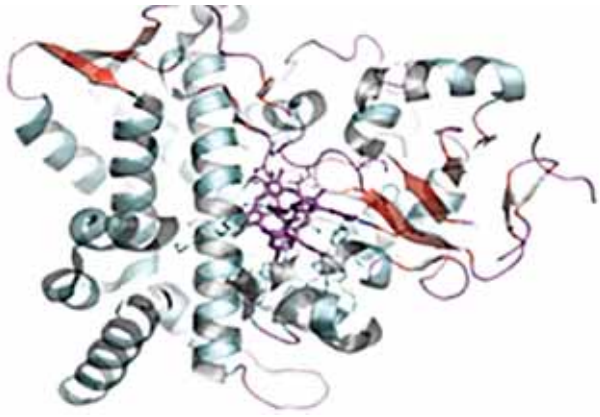


Fig. 41: Docking of LKZ with Lanosterol C14α demethylase.

Assessment of Vitamin D concentration and parameters linked to Kala-azar disease progression

The study suggests that Vitamin D concentration is much lower in asymptomatic cases than VL cases and may contribute in development of full blown disease as well as severity of disease. Study on correlation of Vit.D with clinical-pathological scores and other immunological profile is underway.

Analysis of Vitamin D receptor gene polymorphism in VL and PKDL

In the present study, PKDL (n=76), VL (n=60) patients and healthy subjects (n=28) were included to assess the probable involvement of four single-nucleotide polymorphisms of the *VDR* gene (rs731236, rs7975232, rs1544410 and rs2228570) in susceptibility/ resistance to VL and PKDL. Frequency of Fok1 C allele was observed significantly higher (p = 0.149) in both VL and PKDL as compared to healthy controls. However, no significant difference (p>0.05) was observed

in allelic and genotype distributions of Bsm1, Apa1, Taq1, Fok1 polymorphisms between VL and PKDL.

Impact of ultraviolet rays penetration on increasing incidence of PKDL

The effect of solar Ultra-violet radiations on PKDL patients (n=242) have been assessed and compared with healthy controls (n=30). Most of the PKDL patients had complaints related to intense sun light such as skin irritation, skin reddening or both. Labourers and farm workers were found more affected with PKDL than other categories of occupations having less sun light exposure. Further, alteration in expression of Toll like Receptors and other key cytokines were observed during PKDL progression.

Role of ornithine decarboxylase of *L. donovani* in immunopathogenesis and to evaluate its vaccine potential against VL

Gene from Ornithine decarboxylase (ODC) of *L.donovani* was experimented as a potential DNA vaccine. Immunization with Ld-ODC-encoding DNA (Ld-ODC construct) induced specific protective cellular immune response against VL in experimental animal model.

Role of Protein disulphide isomerase (PDI) primed dendritic cells with host protective CD4+T cells in protection against VL

The recombinant protein disulphide isomerase (rPDI), when used as an immunogen with murine DCs, showed inhibited leishmanial parasite load in immunized BALB/c mice. Splenic macrophages produced more IL-12, GM-CSF and reduced IL10 with this immunogenic material. Thus, DCs primed with rPDI might have a role in protection against leishmania infection.

Role of Mevalonate Kinase of *L. donovani* in host invasion

It was observed that both the intracellular and secreted LdMVK, an unique protein of *L. donovani* – Mevanolate Kinase, is essential in the survival of the *L donovani* within the host. MVK expression was found upregulated during oxidative stress and parasite viability was reduced in presence of MVK inhibitor. In the amastigote form, the protein was found localized in the membrane and flagellar pocket along with the glycosomes (Fig. 42). The secreted MVK was found to immunomodulate the host, thus facilitating parasite entry. The study suggests involvement of LdMVK in VL pathogenesis.

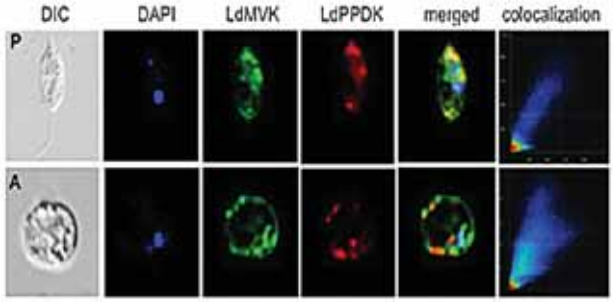


Fig. 42: Immunofluorescence images acquired with confocal microscope showing localization of LdMVK in glycosomes of *L. donovani* promastigotes and glycosomes, membrane and nucleus of *L. donovani* amastigotes. Differential interference contrast (DIC); DAPI (blue); rabbit anti-LdMVK (green); rabbit anti-LmPPDK (red); merged image (merged).

Evaluation of derivative (SP15 family protein) of *P. argentipes* saliva protein towards restriction of experimental *Leishmania* infection

The 13.6 kDa (Pag SP02) DNA construct of *P. argentipes* was used to induce delayed type hypersensitivity (DTH) response in mouse model. About 10-15 fold reduction in *Leishmania* parasite burden was observed in experimental mice immunized with sandfly salivary gland Homogenate (SGH) and Pag SP02 plasmid of SP15 Saliva protein of Sandfly as compared to different control group of mice. This clearly suggests that Pag SP02 plasmid of SP15 sandfly saliva protein may further be explored as vector based vaccine candidate for leishmaniasis.

BIOINFORMTICS

INTD-DB: A comprehensive knowledgebase of inhibitors and small-molecule compounds against Neglected Tropical Diseases

TrypInDB - a user-friendly, freely accessible, online database of inhibitors and small-molecules of leishmaniasis, trypanosomiasis, etc. (http://trypindb.biomedinformri.com) includes more than 22,000 experimentally (in-vitro or in-vivo) verified small molecules or inhibitors against >100 different enzymes. This database has also been integrated in earlier developed LeishInDB (http://leishindb.biomedinformri.com).

TUBERCULOSIS

Systematic pulmonary TB case finding among severely malnourished children admitted to nutritional rehabilitation centres (NRCs)

Out of 203 severe acute malnourished children examined at NRCs of Bihar, gastric aspirations were done in 197 cases, of which 3 samples were found positive for PTB infection (1 by CBNAAT and 2 by TRUNAAT). Evaluations of all SAM children for PTB were completed before discharge from NRC.

VIRUS RESEACH AND DIAGNOSTIC LABORATORY (VRDL)

Apart from facilitating routine diagnosis of 22 viruses, including JE, Dengue, Chikungunya, Zika, Enterovirus, Swine flu, Influenza, HSV 1 & II, HAV, HBV, HCV, HEV, etc., the VRDL provided investigational support to the State Govt. of Bihar during various viral outbreaks during the period.

Scrub Typhus and Leptospira have been detected first time in Bihar as causative agent of acute encephalitis syndrome (AES). Genome wide T and B cell epitope mapping of chikungunya virus by molecular docking revealed three epitopes ALFAKTHNL, ATVPFLLSL, and TLYPERSTL having higher antigenicity based on higher binding energy than the reference epitopes.

Since the beginning of COVID-19 pandemic in Bihar, VRDL of this Institute came forward to support state Govt. in COVID-19 testing. After feasibility assessment and quality assessment by ICMR-NIV, Pune, this centre was approved as the first ever centre in Bihar for RT-PCR of COVID-19.

EXTRAMURAL RESEARCH

TRIBAL HEALTH

Environmental Reservoirs of Cholorae Sero Groups in the Tribal Areas of Odisha

The main objective of the project was to find out the reservoirs of V. cholerae serogroups in the flowing water bodies by direct culture method and using molecular tools. During the field study, efforts were done to isolate different serogroups of V. cholerae from water bodies like river, nala, chua from the study blocks. The V. cholerae O139 strains from river water and reports were submitted to the concerned health authorities. People were made aware not to use the river water for cooking and washing utensils. As a result of which, a possible cholera outbreak was averted. 18 V. cholerae O1 strains were detected from the planktons and stool samples which showed close similarity among themselves through multiplex PCR assays. The major reservoirs of V. cholerae in the flowing water bodies like river, stream was detected in the partial stagnant condition of water and also in the water bodies which is a major breakthrough of this study. V. cholerae O1 strain was isolated from the stream water collected in the chua which was contaminated and caused a cholera outbreak during a marriage ceremony, celebrated in April, 2019.

Health Assessment of Villagers of Tamner Block, District Raigarh, Chhattisgarh

The study was carried out to find out the morbidity, mortality and nutritional status of the population residing in Tamnar Block of Raigarh district. A total of 5233 individuals from 33 villages were screened. The majority of the population (61.2% were using community piped water supply for drinking purposes. About 11.2% of the households had tubewell as a source of drinking water, while 22.9% were using open well for drinking. The proportion of pre-school children with underweight

was about 42.7%. Among the adult population, about 8.8% of males and 6.6% of the females had grade III chronic energy deficiency. The prevalence of hypertension was followed by anemia and fungal infection among the adult population. A majority of the currently pregnant women had received some kind of antenatal care. Among under-five years of children, BCG vaccination was 96.1% followed by DPT.

TRIBAL HEALTH RESEARCH UNIT AT NIE, CHENNAI

The study results on health needs assessment of selected hill tribes (Palliyar and muthuvan) in Western Ghats of Tamil Nadu revealed diverse socio, economic and cultural practices on various aspects of their health and reproductive health. Their main sources of their income are by foraging the forests, or working as farm hands, or plantation workers. Majority of them are illiterate and do not seek care from the state health system for their health problems and prefer domicililary delivery with the help of TBAs for varied reasons. They are unable to avail any of the government maternity benefits because of the home deliveries and n-possession of Aadhar card, and Bank account. Fear of loss of wages by the parents is one of the main reasons for not taking their child to the vaccination site. Prevalence of hypertension is seen due to excess use of salt to preserve the cooked food for long time. Water scarcity and lack of sanitation is a common sight in tribal villages. The numbers of childless couples are increasing and infertility is common.

Assessment of Nutritional Status and Health Seeking Behavior Among Siddi Tribe in Karnataka

Malnourishment and nutritional deficiency are reported to be the major health issues among Siddi tribe in Karnataka. The current study intended to assess the attitude toward nutritional and health aspects among Siddis to observe indigenous ritual, behavior, belief and practice for general illness, maternal and new born care, reproductive and sexual health issues, role of traditional medicine among tribal population and integrating the usage of other systems. Hemoglobin estimations among the children of all the age groups indicated that they were moderate to mild anemic with lower haemoglobin contents. Health seeking behaviour indicated that 90% of the ill individuals consulted doctors, while of the remaining a majority resorted to self medication and use home remedies, while few did not take any treatment. The study documented 27 species of plants for 15 ailments from Siddi tribe. More than 50 representatives of the Siddi tribe have been trained through field level workshops.

TRIBAL HEALTH RESEARCH UNIT AT RMRC, BELGAUM, (PHASE II)

The Kathodi-Katakari Tribe do not have any major specific health issues, concerning to declining of their population. Low Hemoglobin level in all the age groups is issue of concern, which is mainly associated to Microcytic hypochromic anemia with Eosinophilia. The nutrients deficiency, especially Vitamin-A, is also a factor of concern. The level of personal and community hygiene is very low and has to be improved to reduce the chances of preventable and infectious diseases. Looking in to the nomadic pattern of their lifestyle and migratory patterns, the reduction in their number in Karnataka may be related to their migration to the neighboring states. Tribal communities are weaned away and forgetting their own heritage of age old traditional health practices. They are willing to learn and use the local herbal resources, but they are in need of persuasion and proper guidance to practice the traditional therapies/home remedies for their primary healthcare needs.

TRIBAL HEALTH RESEARCH UNIT AT RMRIMS, PATNA , (PHASE II)

Out of 38929 (52.8% male and 47.2% female) population surveyed, 24524 (tribal: 10581 and non-tribal: 13943) individuals aged ≥15 years were clinically examined as per the study protocol and of them 713 (Tribal: 462, non-tribal: 251) were found symptomatic for pulmonary TB (PTB). The AFB

positivity through culture was found higher than microscopy in both tribal and non-tribal population. Considering positivity by culture, prevalence of PTB (0.448%) in tribal population was higher than non-tribal population (0.11%).

Drug-susceptibility testing (DST) were done for anti-tuberculosis drug-resistance surveillance for the culture positive samples. Out of 62 culture positive samples we observed 13 samples resistant for Rifampicin and Isoniazid and 49 were drug sensitive. Out of 13 resistant cases 9 from tribals and 4 from non-tribal group. Out of which 47 (10.17%) tribals and 15 (6%) non-tribals were found positive for pulmonary tuberculosis.

Tribal Health Research Unit at VCRC, Pondicherry (Phase II)

From both the qualitative and quantitative tests, it is revealed that the G6PD deficiency cases are prevalent in all the 6 tribes surveyed in Koraput and Malkangiri districts with varying degree. In total, 4.7% (71/1519) G6PD deficient cases were found among the tribal population of Koraput and Malkangiri districts. Overall, the G6PD deficiency was predominant in Gadaba tribe (8.6%) followed by Koya (6.7%), Paraja (3.9%), Bonda (3.7%), Bhumia (2.8%) and Kandha (2.3%). Since, the study area is endemic for malaria, G6PD deficiency can cause problems in the individuals mainly when it is complicated by the association of vivax malaria because of 14 days treatment of primaquine. Therefore, it is recommended to do G6PD deficiency testing before the treatment with primaquine for each confirmed P. vivax and P. falciparum with gametocyte cases. Since, all the surveyed CHCs showed the prevalence of G6PD deficiency, the study should be continued to other tribal communities present in the region.

TRIBAL HEALTH RESEARCH UNIT AT DMRC, JODHPUR

Of the total 7100 tribal students screened for sickle cell anemia 17.52% reported positive for sickle cell anemia. A total of 629 household investigated. Amongst them 17 were reportedly suffering from TB & out of these 17 cases 13 opted for treatment. Only 28% people were aware of TB. Among the 395 women, 351 (89%) were anemic and out of 195 adoloscent girls, 165 were anemic.

Estimate the Burden of TB among the Tribal Population and Develop an Innovative Health System Model to Strengthen TB Control in the Tribal Areas - Multicentric Study, Phase II

This study aimed at generating community-based primary data on the prevalence of pulmonary tuberculosis, the challenges in accessing the health care services and the factors that influence health care seeking behaviour. The estimated prevalence of sputum positive tuberculosis in the study sample was 394/100,000 population. The estimated prevalence at car Nicobar Island per 100,000 population was found to be 735.3 in 2001-02 and then showed a decline to 241.6 in 2013-14 and to 242 in 2015-17. The estimated prevalence of sputum positive pulmonary tuberculosis was one third of that estimated in 2001-02. Even though there was a decline in prevalence of TB, the emergence of MDR-TB is a challenge. TB, along with hypertension and fever are perceived to be the most important health problems faced by the community. Although traditional medical practices are prevalent in a section of the community, majority of the population utilize modern medical facilities. They all knew that TB was curable and the facilities where the treatment was available. They have good idea about the importance of diet, isolation of patients, clean environment and avoiding alcoholism and smoking in preventing the spread of TB.

NORTH EAST REGION

Novel Malaris Surveillance System Along International Borders of North East Region, India

The study utilizes MoSQUIT, an Android based mobile software developed by C-DAC, Pune in collaboration with RMRC Dibrugarh. Malaria

endemic areas along the international borders of Tripura and Assam are hilly and remote without proper road network. The project has been implemented in Tripura along the Bangladesh Border and Assam along the Indo-Bhutan border. So far, 1494 case records have been obtained from Tripura (233 malaria positive). In Assam, 800 malaria cases have been recorded out of 1769 fever cases. MoSQuIT is expected to help in the continuous monitoring of malaria in the community, plan for control measures and detect both spatial and temporal changes in malaria epidemiology.

Morbidity, Mortality, Nutritional Status and Adherece to Art Among HIV Infected Children: a Cohort Study

Children of both sexes were infected with HIV more or less equally. Majority of the infected children were above 4 years. Only 2 children of enrolled 256 children expired due to HIV-TB co-infection and pneumonia during the short follow up. Contact with healthcare providers and NGO's were important predictors for initiating ART. Round 16% did not adhere to ART. Adherence to ART was mostly affected by side effects of the drugs developed after initiating ART, thereby indicating proper counseling while starting and following up this population. Forgetfulness and distance to ART center were other important factors for adherence. Changes in nutritional status of the children could not be elicited adequately because of short follow up.

Integrated Brief Intervention for Alcohol Abuse to Improve Anti-Tubucular Treatment Outcome: Controlled, Randomized Clinical Trial

The problem of alcoholism is prevalent in the Sikkimese society here, so also tuberculosis is also frequent especially among the poorer socio economic strata of society. Amongst TB patients, the problem of alcohol intake is there but, it is more likely that alcohol intake along with poor nutrition and other risk factors lead to the occurrence of TB and its late detection at times, due to negligence on the part of the patient. During the course of the study, it has been observed that in most of the patients once the diagnosis of tuberculosis is made,they stop taking alcohol till the time their treatment is going on, and may revert back to alcohol once their treatment course is over or they are feeling better. It is also observed that the problem of alcoholism occurs more with patients suffering from tuberculosis who are defaulters, relapse after treatment etc.

Genotypic Characterization of Circulating Rota Viral Stains Among Children with Acute Diarrheal Disease in a Tertiary Care Setup of Tripura

The study aimed to determine the proportion of viral diarrhea and circulating Rota virus strains contributing to Acute Gastroenteritis among children below 5 years of age group enrolled in tertiary care hospital in Tripura. Stool samples collected from children ≤ 5 years between the periods of August, 2016 to March, 2019 were subjected to preliminary antigen detection of Rotavirus by ELISA followed by molecular analysis by Semi-nested PCR. The results showed 252 (39%) of the total samples to be positive for Rotavirus, the common genotypes identified were G3P [8] 75% followed by G1P [8] 16% along with some other combinations such as G2P [4], G3G12P [8], G1P [4]. The disease was predominant among male than female within the age group of 0-1 year. Although the infection was encountered throughout the year, there was an elevation in the diarrheal cases in the months of December to February. Among the rotavirus negative samples Adenovirus contributed 12% of the diarrheal cases followed by Norovirus that attribute 10%.

Comparative Study of Red Cell Antigen Profile Among Malaria Infeted Atients and Normal Population form Assam and Mumbai

In this study, the prevalence of P. falciparum cases (68.61%) was found to be high, followed by P. vivax (28.68%) and P. falciparum and P. vivax mixed cases (2.71%) in the population of Assam. Frequency of A group was significantly lower in

Malaria cases (27.06%) than healthy individuals (35.41%) suggesting a protective role of A blood group while the AB group showed increased risk towards malaria. A total of 11 different Rh phenotypes were identified in this population, where around 74% of individuals were homozygous for D antigen while RhD negative individuals were very rare in this region. Duffy Fy (a+b-) phenotype was the most common followed by Fy (a+b+) and Fy (a-b+) while Fy (a-b-) was absent in this region. No significant difference was observed in the frequencies of Rh and Duffy phenotypes among malaria cases and healthy individuals.

o Only Kna, McCa and Sl1 in Knops blood group system and Ge (+/+) in Gerbich were identified in all the cases and healthy individuals screened. In CR1, a significant association was observed with rs2274567 SNP in Exon 22 where the frequency of A/G genotype was lower in Malaria cases (35.27%) as compared to healthy individuals (45%). In Intron 27 HindIII polymorphism also, a significant association was observed where the frequency of the LL genotype was lower in cases (18.61%) than the controls (26.92%) while the frequency of HL genotype was higher in cases (54.6%) than controls (44.6%).

ANTI MICROBIAL RESISTANCE

Initiating Antimicrobial Stewardship Activities in Hospitals in India

All these projects were funded to establish the structure and process of antimicrobial stewardship in their hospitals. The hospitals during this period created antibiograms, created hospital specific treatment guidelines and implemented formulary restrictions for higher generation antimicrobials.

VIROLOGY

Elucidation of The Role of Endothelial Cell Signaling Pathways in Vascular Permeability Modulation in Dengue Virus Infection

The present project focused on elucidation of the endothelial cell signaling pathways involved in vascular permeability modulation in Dengue. Two major endothelial cell pathways, Angiopoeitin signaling pathway and Spliingosine signaling pathway, were focused in the study. We found that both these pathways play role in the DENV-induced trans-endothelial cell permeability. Blocking key targets in these pathways using specific inhibitors including Angiopoeitin -1 and Sphingosine - I - phospahte (S-1-P) were found to alleviate the increase in permeability. Our study further reinforced the role of VE-cadherin internalization that result in the destabilization of the adherens junction (AJ), in the permeability changes using a direct virus infection model. In the study, we cloned coding regions of DENV proteins and suitable expression vectors were generated for studies to understand the specific role of each of these proteins in vascular leakage. A lentivirus-based transduction system was established to generate HMEC cells that stably express the DENV viral proteins; and can be used for permeability studies. In animal models, when we gave a single dose of S- I -P or its analogue and FDA-approved molecule, FTY720, there was significant reduction of symptoms. However, this dosing could not prevent mortality. So, there is a need for optimizing the dose and timing of injection. Our study reveals possible newer approaches in managing the vascular permeability increase in dengue virus infection.

Effect of Sex Steroid Hormones on Replication of Hepatitis E Virus

This study was designed to know the effect of pregnancy related hormones on HEV replication in-vitro. We could recruit 66 pregnant women with viral hepatitis (HEV IgM positive) in this study out of which only 14 were FHF and collected ten fecal samples after consent from HEV pregnant patient. A quantitative amount of HEV virion was present in only 20 patients' serum and 2 fecal samples. The pregnancy hormone (Estrogen, progesterone and beta human chorionic gonadotropin) levels from all the patients and healthy pregnant subjects were to determined. Huh7 Cell was tested for the toxicity of pregnancy hormone and found that

higher concentrations increase cytotoxicity in case of progesterone and hCH whereas the estrogen has no effect throughout the all concentrations. HEV virus from Faeces of the pregnant women with viral hepatitis was isolated using ultra-centrifugation. Since we could not propagate HEV obtained from serum/fecal sample of pregnant women we used an alternate method to culture the HEV-1 clone obtained from Dr. Emerson (HEV R-luc) as it is an infectious clone of HEV-1 and has very high efficiency to infect hepatic cell lines S10-3. We successfully infect S10-3 cell lines with the HEV R-luc RNA and study the effect of progesterone and human chorionic gonadotropin hormone on replication of HEV on hepatic cell lines. Significant difference on replication efficiency of HEV clone even at lower dose of hCG i.e. 5 miu/ml and 25 miu/ml (p=0.02 and 0.009). However as the concentration of hCG increases from 25 miu/ml to 50 miu/ml it showed lower expression of HEV RNA then it has at 25 miu. Progesterone at lower dose has no significant impact on replication of HEV (5 ng/ml to 40 ng/ml) as measured by RLU unit. However as the concentration increases form 40 ng/ml to 60 ng/ml significant high expression of HEV RNA (p=0.0313) was observed as measured in RLU unit.

Establishment of a Novel Electronic Surveillance System for Dengue in Pune: an Initiative for Smart Cities Mission

This well-planned pilot study in a Pune ward generated data on dengue disease and Virus surveillance for 3 consecutive years.

An electronic system was developed for dengue surveillance in one ward that can be adapted to the whole city and for other infections.

Age-stratified sero survey for DENV confirmed hyperendemicity and estimated new" infections per year.

VECTOR BORNE DISEASES

Monitoring of Insecticide Resitance in Malaria Vectors in Jharkhand State

The above study was undertaken in 12 districts (suggested by NVBDCP) of Jharkhand state. The state is highly endemic for malaria contributing 7% of the total malaria cases of India. An. fluviatilis was confirmed resistance to DDT (4%) in 8 districts studied while susceptible to deltamethrin(0.05%) andpermethrin(0.75%). An. culicifacies was confirmed resistant to DDT (4%) in all the 12 districts, confirmed resistance to malathion in one district, susceptible in 4 districts whereas it was found possible resistance in 7 districts. Against deltamethrin An. culicifacies was resistance in 3 districts, susceptible in 2 districts, whereas possible resistance in 7 districts. Permethrin was resistant in 5 districts while in the other 7 districts its response was under possible resistance category. Other pyrethroids, cyfluthrin and lambda cyhalothrin was confirmed resistance in two districts while it comes under possible resistance category in 4 districts. *An. annularis* was confirmed resistant to DDT (4%) in 6 districts, possible resistance in 2 districts to malathion (5%) and susceptible in other 4 districts. The resistance in vectors (especially *An. culicifacies*) to almost all the classes of insecticides particularly synthetic pyrethroids, is posing a challenge to the recent trend of declining malaria.

An. minimus showed possible resistance to DDT (4%) in Noamundi PHC (West Singhbhum district) and susceptible to all other insecticide used.

Spatial & Temporal Variations of Potential Malaria Vector(S) And Associated Species of Anopheles in the Islands of Nicobar District

A total of 27 villages in three districts of Andaman & Nicobar archipelago were covered longitudinally for various entomological parameters, focusing on anophelines. The per dip density in Nicobar district recorded the highest, both for culicines and anophelines. Tehsil wise dip per density of anophelines ranged from 0.05 to 3.1. Anopheline immatures were recorded from 23 different habitats. Six habitats were common for anophelines in the three districts. A total of twelve anopheline species were identified from different water habitats.

Anopheles sundaicus was collected from 13 of the 18 different habitats, showing its diverse habitat distribution. This was followed by An. barbirostris and An. kochi, which was collected from 12 habitats. While, An. tessellatus was collected from two habitats, viz, rain water pool and mud pool. The habitat, viz, pond, was observed with the maximum number of anopheline species (n=8). In adult resting collection, the per man hour (PMH) density of anopheline mosquitoes ranged from 0.01 to 0.19 in the three districts. Six anophelines species were recorded in resting collection, and *An. sundaicus* was the dominant species. South Andaman recorded the highest man landing rate, while N & M Andaman the lowest. In the landing collection in Nicobar District, An. sundaicus alone was collected, while Andaman districts recorded seven species. The peak biting time for this species was 21-22 hours. Altogether, 430 full fed anophelines were tested for their blood meal source, of which 128 (25.4%) were *An. sundaicus*. High proportion of An. sundaicus has fed on cow (42.52%) and goat (61.4%). Almost 1.4% of anophelines had fed on three hosts. Human blood index (HBI) was highest for *An. sundaicus* (0.28), and was found to be significantly different from An. kochi and An. aconitus. A new molecular form of *An. barbirostris* was identified from Andaman and Nicobar Islands, which was closely related to An. barbirostris form A (A3). The An. dirus collected was found to be An. baimaii by molecular assay. All the specimens collected from the three districts of Andaman and Nicobar Islands revealed the presence of one molecular form, based on the sequences of mitochondrial COI and nuclear ribosomal region ITS2. GPS coordinates of the potential breeding habitats of anophelines were recorded and maps were constructed using ArcGIS ver.10 software.

Distribution of Single Nucleotide Gene Variantions in the Leptin Receptor and its Significance as a Susceptibility Biomarker for Visceral Leishmaniasis in North Indian Population of Bihar

Leptin receptor polymorphism is associated with VL or leptin has a role in modulation of immune response in VL. In this study five common polymorphism in the Ob-R gene, namely K109R, Q223R, S343S, K656N and P1019P polymorphisms, in VL patients were investigated. All five polymorphisms were associated with amino acid substitutions in the Ob-R. Receptor activation requires initial binding of leptin to a composite binding site formed by the Ob-R dimer or oligomer. The results of the present association study provided evidence for the relationship between Q223R variant and Visceral Leishmaniasis at least in endemic area of Bihar. Taken together, these findings indicate that mutation in Ob-R can be a cause of Visceral Leishmaniasis, at least in the endemic areas of Bihar. This link between genotype and VL suggests new approaches for prevention or treatment of VL. The study depicted that the polymorphism in Leptin receptor (Ob-R) is associated with increased susceptibility to visceral leishmaniasis. The Q223R and K109R polymorphism is remarkable examples of a common genetic polymorphism having a major effect on disease susceptibility in VL.

Identification of Clinico- Immunological Determinants For Macular Vs. Polymorphic Post Kala-Azar Dermal Leishmaniasis (Pkdl)

The above study showed the ratio of polymorphic: macular PKDL is now almost equal to 1:1, as opposed to previous reports of an overwhelming presence of almost 90% polymorphic cases in the PKDL population. The parasite load, at disease presentation was also significantly higher in the polymorphic variant compared to the macular type. There was a difference in response to anti-leishmanial therapy between the two variants also, with the parasite load decreasing significantly in the polymorphic cases after completion of treatment with LAmB. But in macular PKDL, it decreased by only 42% as opposed to 86% in polymorphic cases. Histopathological analysis also shows that there are differences in the overall immunopathology between the two clinical variants with varying type and intensity of the dermal infiltrate, thus suggesting that differences may also exist in the status of different immune markers. This, in turn, may lead to a different impact on the disease

pathogeneisis in macular PKDL and its response towards anti-leishmanial therapy, thus requiring patient stratification to ensure appropriate treatment regimen, based on the lesional type.

Genetic Characterization of Darc Gene and DBP and Estimating the Baseline Antibody Response Against Parasitic Duffy Binding Protein In *P. Vivax* Infected Patients

The above study depicted that for DBP Gene: Out of 43 samples, 10 samples were microscopically positive but negative for diagnostic PCR. Out of the remaining 33 samples, 1 was excluded due to poor sequencing. Alignment with the 33 samples of Plasmodium vivax DBP gene did not show any single nucleotide polymorphisms (SNP). However, a much more intensive study with remaining sample size might help in providing a better insight. However, amino acid changes were reported for DBP gene when compared with Sal I reference strain. Among 32 patient samples (isolates), one was ignored because of poor sequencing. All polymorphic sites showed the monomorphic mutation (changed into one amino acid-type). DARC and Duffy Binding Protein are two important components required in the pathogenesis of Plasmodium vivax associated malaria. The DARC gene plays an important role in acquiring malaria due to *P. vivax* and *P. vivax* is dependent on binding of the Duffy Binding Protein (DBP) to the Duffy Antigen Receptor for Chemokines (DARC) on erythrocyte. Further the polymorphism in these might reflect the severity of the disease. Genomic sequencing of DARC gene and PvDBP gene will help in establishing the link between acquiring complicated vivax malaria cases and altered genetic sequence of DARC and PvDBP.

Monitoring of Insecticide Resistance in Malaria Vectors in Endemic Districts of Uttar Pradesh, India

An. culicifacies which is the principle malaria vector in Uttar Pradesh was found resistant to DDT 4% in all the 10 districts and against malathion possible resistance was observed in 8 out of 10 districts. In Badaun district malathion was found susceptible and in Gautam Budh Nagar it was resistant. Deltamethrin showed possible resistance in 9 out of 10 districts and in Banda district resistance was observed. The species was found susceptible to cyfluthrin in 5 districts, while in remaining 5 districts possible resistance was found. Thus, results indicate that An. culicifaciesis reported resistant in all the 10 districts to DDT and possible resistance to malathion in 8 of 10 districts, while to pyrethroids, deltamethrin and cyfluthrin the species is reported mostly possible resistance. The terrain-wise data revealed almost no variations in susceptibility.

Bionomics of Malaria Vector(S) Sibling Species Composition and to Establish Their Role in Malaria Transmission in North East Region of India

To improve the existing malaria control strategies, a comprehensive study was undertaken to identify the species and distribution of sibling species complexes of the vectors and biological variations of vector species that are prevalent in different areas of NE India. Entomological study conducted during the study period reveled that density of the primary vectors i.e., *An. minimus* and *An. baimaii* was low. Although the density of Anopheles sp. viz., *An. vagus*, *An hyrcanus* and *An. annularis* were comparatively higher. Use of insecticide impregnated bed nets and insecticide residual spray (IRS) acted as a factor in decreasing the vector population. Insecticide susceptibility assays also shows that the vector species are still susceptible to DDT 4% and Malathion 5%. Insecticide bioassays could not be performed on *An. philippinensis*/ *An. nivipes* as its density was very low during the study period. Sibling species analysis based on the ITS2 gene reveals the presence *An. minimus*, *An. varuna* and *An. jeyporiensis* of *An. minimus* complex in both the states. Moreover, PCR analysis based on the D2 region genes showed that An. baimaii type of An. dirus complex was present in the study areas.Entomological study conducted during the study period reveled that density of the primary

vectors i.e., *An. minimus* and *An. baimaii* was low. However, density of Anopheles sp. viz., *An. vagus*, *An. hyrcanus* and *An. annularis* were comparatively higher. Use of insecticide impregnated bed nets and insecticide residual spray (IRS) acted as a factor in decreasing the vector population. Insecticide susceptibility assays also shows that the vector species are still susceptible to DDT4% and Malathion 5%.

A Pilot Scale Bio-Ecological Studies on *Ae. aegypti* Population In Delhi Towards Developing an Alternate Dengue/Chikungunya Control Strategy

Bio-ecological studies on *Ae. aegypti* population was carried out in Barela and Shahpura blocks of Jabalpur district Madhya Pradesh where dengue outbreak occurred in the year2008 and sporadic cases of dengue occurred every year. The present study provided substantial information about Aedes breeding habitats, relative proportion, spatial and temporal distribution and dengue infection rates in the natural population. Out of 39111 and 32360 containers in 5158 and 5230 households of both the blocks. A total of 753 Aedes mosquitoes (79 *Ae. aegypti*, 641 *Ae. albopictus* and 43*Ae. vittatus*) collected from barela and 607 Aedes (66 *Ae. aegypti*, 528 *Ae. albopictus* and 26 *Ae. vittatus*) collected from shahpura were tested of which none were found positive. Since there are no pools found positive; therefore, the minimum infection rate (mir) is zero. During adult mosquito collection, very few numbers of *Ae. aegypti* (10.6%) and *Ae. vittatus* (3.6%) were caught however, Ae. albopictus (86%) was found in very high numbers specially in August and September months. In BG sentinel traps, no mosquito was trapped except only two Ae. agypti from Barela and one *Ae. albopictus* from Shahpura which were trapped in the months of September and November only. The present study gathered very good information on vector population, distribution and breeding preferences which can be useful supplement for management strategies against the dengue vectors.

A Pilot Scale Bio-Ecological Studies on *Ae. aegypti* Population In Delhi Towards Developing an Alternate Dengue/Chikungunya Control Strategy

The study concluded that a total of 2443 *Ae. aegypti* in 455 pools were tested for presence of DENV. Through Rt-PCR only two pools were found positive in Dwarka which was reared from larva collected park in Dwarka (1 pool during March and 1 during October). The presence of virus in F1 mosquitoes signifies Transovarial Transmission in Aedes. Alternate peaks of dengue cases are observed in the case reporting. Dengue data collected from MCD showed that there is alternate increase in cases in both localities of study area. Aedes population of both the areas were found susceptible for synthetic pyrethroids and were resistant to DDT. The Immature form was found to susceptible for temephos for both study sites. Additionally the intervention was conducted by the field teams like source reduction and application of temephos wherever, it was needed they have provided IEC material to both the inhabitants study sites which were provided by MCD. A total of 3445 houses in Rohini (Population 16488) and 3925 houses in Dwarka (Population 16816) were surveyed. In both localities, breeding was observed in coolers, flowerpots, Overhead Tanks OHTs), plastic drums, cement tanks, tyres, iron tanks, bird pots, mud pots, and solid waste. In Rohini, a total of 12413 containers were checked out of which 206 found positive whereas in Dwarka, a total of 14333 containers were checked out of which 375 found positive. Plastic drums and OHTs were identified as key containers in both Rohini and Dwarka respectively. Larval productivity was found high during September and reduces there in March again one short peak appears during March and April. There is sudden decrease after May due to high temperature. Month-wise comparison of Container Index (CI), Breteau Index (BI) and Pupal Index (PI). Till duration, peaks of CI, BI is observed in the month of March whereas PI is maximum in the month of April in Rohini. In Dwarka CI is

highest in the month of May, BI in February and PI in March. Adult collection from the houses using aspirator from Rohini and Dwarka

A Pilot Scale Bio-Ecological Studies on *Aedes aegypti* Population For Developing Alternate Dengue Control Strategy

The above study was conducted in two clusters in urban, and two clusters in peri-urban areas under Port Blair and Ferrargunj Tehsils respectively .For enumeration, door to door survey was carried out to estimate the number of family members in each household. The demographic details in each village was recorded, including the goe co-ordinates. In mosquito immature survey, a total of 1055 households were inspected for Aedes breeding, of which 3870 water holding containers were examined. Of these, 516 water holding containers (13%) were found to support Aedes larvae. A total of 3232 pupae were collected. The Stegomyia indices with respect to houses and containers were highest in Garacharma (HI=60.0) and Chouldari (CI= 24.47). The Breteau index value was highest in Chouldari (BI= 88.66) and lowest in Dollygunj (BI= 15.86). The pupal index (PI) estimated per household was highest in Chouldari (PI= 602.38). Five types of water holding containers were consistently observed to contain Aedes spp. in all the four village clusters. In most of the potential habitats, the container index was highest recorded from Garacharma village. A total of 1210 Aedes species were identified, of which, 943 (77.9%) were Ae. aegypti and 267 were Ae. albopictus. By prokopack aspirator, 104 households were examined, spending 17.5 hours, and a total of 94 *Ae. aegypti*, and 149 *Ae. albopictus* were collected. In BG Sentinel trap collection a total of 28 traps were installed in different houses and 124 adult mosquitoes were trapped, and Ae. aegypti formed 10% of the collection. For Dengue and Chikungunya virus infection, 61 Aedes mosquito pools (15 *Ae. aegypti* and 46 *Ae. albopictus*) were tested, and all were found negative for the two viruses. Information generated in the project will facilitate in identifying potential breeding habitat of Aedes mosquitoes and thus help in the development of alternate dengue control strategy, in order to interrupt the transmission of dengue/chikungumya/ zika viruses.

A Pilot Scale Bio-Ecological Studies on *Aedes aegypti* Population in Delhi Towards Developing an Alternate Dengue/Chikungunya Control Strategy

The study was conducted in two study sites Todiyarpet and Adyar in Chennai, Aedes aegypti breeding was observed to be high during November/December which corresponds to the monsoon (Northeast) season with diverse breeding habitats such as natural, water storage containers and discarded container habitats. The density of *Ae. albopictus* was found to be more in Adyar (Zone XIII) although *Ae. aegypti* breeding was high in Tondiarpet (Zone IV). This may be due to the presence of large vegetation coverage in Adyar (Zone XIII) which also favours sylvatic breeding of other Aedine mosquitoes and Zone IV with an erratic water supply and hence more storage practice. In general, *Ae. aegypti*, *Ae. albopictus* and *Ae. vittatus* could be collected in Adyar (Zone XIII), probably due to the geo-ecological area with large vegetation coverage. Moreover, *Ae. aegypti* was the predominant vector species in both the study sites except for the monsoon period, where Ae. albopictus also contributed to the breeding in the area. *Ae. aegypti* could be collected throughout the reporting period in both zones. BG-Sentinel traps collections revealed the presence of more Aedes aegypti in outdoor traps. The susceptibility of immature *Ae. aegypti* to WHO diagnostic dose of Temephos (0.02 ppm) observed 100% mortality after 24 hours indicating its susceptibility.

Monitoring of Insecticide Resistance in Malaria Vectors in Madhya Pradesh State

Bio-ecological studies on Aedes aegypti population was carried out in Barela and Shahpura blocks of Jabalpur district Madhya Pradesh where dengue outbreak occurred in the year2008 and sporadic cases of dengue occurred every year. The present

study provided substantial information about Aedes breeding habitats, relative proportion, spatial and temporal distribution and dengue infection rates in the natural population. Out of 39111 and 32360 containers in 5158 and 5320 households of both the blocks, a total of 417 and 595 containers in 301 and 435 households of these blocks respectively were found positive for Aedes larvae with 5.8, 1.06, 8.08 and 26.6 HI, CI, BI and PI in Barela and 8.3, 1.8,11.3 and 21.3 in Shahpura. Disused containers are the most preferable breeding habitats at both the sites. The other key containers are the mud pot disused and overhead tank cement. The peak prevalence of Aedes emergence was found mainly in August and September in both the areas. The pupae per person were very low in both the areas. During adult mosquito collection, very few numbers of *Ae. aegypti* (10.6%) and *Ae. vittatus* (3.6%) were caught however, *Ae. albopictus* (86%) was found in very high numbers specially in August and September months. In BG sentinel traps, no mosquito was trapped except only two Ae agypti from Barela and one *Ae. albopictus* from Shahpura which were trapped in the months of September and November only. The other mosquitoes trapped were Armigeres, Culex and Anopheles. All the three Aedes mosquitoes i.e., aegypti, albopictus and vittatus were tested for detecting DENV/ CHIKV using RT-PCR of CprM gene of DENV and Envelope gene of CHIKV, but none was found positive showing Minimum infection rate (MIR) zero.The present study gathered very good information on vector population, distribution and breeding preferences which can be useful supplement for management strategies against the dengue vectors.

A Pilot Scale Bio-Ecological Studies On Aedes Aegypti Population for Developing Alternate Dengue Control Strategy

The study was conducted in four clusters *viz*. Ashok Nagar, Kurunji Nagar, Lawspet and Rajaji Nagar. Insecticide susceptibility and infection rate were depicted through this study. Adult susceptibility to the insecticides, DDT, Malathion and Deltamethrin (for the monsoon, Oct-Dec and cold season, Jan-March) was determined using WHO susceptibility test kit. The results showed that *Ae. aegypti* was completely resistant to malathion (0.8%) and DDT (4%) and for deltamethrin 0.05% it was under 'Possible resistance' category.A total of 616 pools of *Ae. aegypti* mosquitoes (143 pools from Ashok Nagar, 151 from Lawspet, 223 from Kurinji Nagar and 99 from Rajaji Nagar) obtained from day time indoor resting collections using Prokopack aspirator were screened by PCR for the presence of dengue and chikungunya virus. Of these, 42 pools were positive for chikungunya (Ashok Nagar-7, Kurinji Nagar 15, Lawspet 7, Rajaji Nagar 13) with a minimum infection rate (MIR) of 19.5 (LCL 14.65 - UCL 25.48) and 3 for dengue (Kurinji Nagar 1, Lawspet 2) with a MIR of 1.39 (LCL 0.37 - UCL 3.73). One pool from Lawspet cluster showed positive for both dengue and chikungunya virus infections.

ZOONOSIS

Molecular Epidemiology of Trichinellosis And Toxoplasmosis In India: Addressing Neglected Zoonotic Diseases in a One Health Context

The study aimed to determine the prevalence of Trichinella and Toxoplasma infections in pigs and seroprevalence of human trichinellosis and toxoplasmosis in selected populations of two states of North India *viz*. Punjab and Uttaranchal. In this project, a total of 1194 (for Trichinellosis) and 1296 (for Toxoplasmosis) pig tongue tissue samples were collected, out of which, 362 samples were tested for the presence of Trichinella and 405 samples were tested for Toxoplasma. The samples were collected from different slaughterhouses/ shops in Ludhiana, Patiala, Bathinda districts of Punjab and from Tehri Garhwal, Pauri Garhwal and Haridwar district(s) in Uttaranchal. The study result confirms the existence *Trichinella spp*. and *Toxoplasma gondii* in slaughter pigs in North India. For the first time, zoonotic nematode larvae of Trichinella species have been isolated and

later confirmed molecularly by PCR and sequencing. High molecular prevalence of protozoan parasite Toxoplasma gondii has also been recorded in the slaughter pigs. The detection of antibodies against Trichinella and Toxoplama among human risk groups also confirmed the exposure of human population to these zoonotic parasites. Since, pigs are the most important animal species as a meat source and for food security in India, existence of these zoonotic parasites in pig production are an important food safety concern in North India.

LEPTOSPIROSIS

Development of Recombinant Antigen Based Diagnostics for Bovine and Human Leptospirosis

The study aimed to clone and express the recombinant protein(s) coding gene (Lsa 27/ Ompl37/LigB) of pathogenic Leptospira in *E.coli* system and to evaluate the recombinant protein as a diagnostic antigen in immunoassay and development of recombinant protein-based diagnostics (LAT/ ELISA) for serodiagnosis of leptospirosis. In this project the samples were collected from cattle associated with abortion and reproductive disorders as well as serum samples from human associated with pyrexia. The diagnostic sensitivity and specificity of LAT was assessed in comparison with Microscopic Agglutination Test (MAT). The study concludes that recombinant mixed antigens/protein based LAT has been technologically advanced in the form of Kit (Bovine LeptoLAT) and can be applied as initial screening test for detection of antibodies against Leptospira for diagnosis of leptospirosis in bovine/human and is an alternative to MAT as it is specific, sensitive , low cost and a simple test format.

Development of Diagnostic Method Based on Loop-Mediated Isothermal Amplification (Lamp) for Rapid and Early Detection of Leptospirosis

The study relies on using molecular markers for detection of Leptospirosis. The marker gene LipL32 is unique to pathogenic Leptospira while LipL21 is found in non pathogenic strains. The study uses the principle of loop-based isothermal amplification for rapid detection of pathogenic Leptospira. The assay was validated using clinical samples and was compared with MAT which is the standard diagnostic test for Leptospirosis. The study results confirm that LAMP shows higher sensitivity (92.45%), specificity (82.08%) positive predictive value (67.12%) and negative predictive value (96.49%) in comparison to MAT. The developed assay is rapid, easy to perform and does not depend on sophisticated equipment as well as it can be used in resource-poor settings too (on field). The findings also suggest that a LAMP based diagnostic kit would allow clinicians to correctly diagnose leptospirosis cases against other febrile diseases with similar symptoms.

Kap Studies on Risk Factors of Ocular Leptospirosis in South India and Using KAP as a Parameter of Impact Evaluation Of The Disease

The study aims on two objectives. The first one is to quantitatively analyze the Knowledge, Attitude and Practice (KAP) towards Leptospirosis among rural and urban population and the second was to analyze the same among undergraduates and post graduate medical students of a South India. The areas of study were selected on the basis of addresses of leptospirosis patients who attended the hospital during and after epidemic outbreak. The survey was done in Madurai district which included 902 participants from rural and 1074 participants from urban. And the second included 778 undergraduate students from six medical colleges of Tamil Nadu and 446 postgraduate students from two postgraduate institutions. The study result confirms that vulnerable and rural populations were found to be less knowledgeable on risk factors and they had poor practice patterns. Education had significant impact on knowledge and attitude of urban population, however their practice did not improve with education. Hence it concludes that frequent and systemic public education on causes

and risk factors of Leptospirosis is mandatory. The next survey of 1024 medical students reveals that the post graduate medical curriculum significantly improves student's knowledge on leptospirosis. The study also shows urban student awareness is better than rural students.

Perseverance of Macrophage Migration Inhibitory Factor (Mif) in Pulmonary Leptospirosis

The study aimed on profiling of MIF in serum of patients with leptospirosis with different clinical manifestations, role of MIF in the pathogenesis of leptospirosis by in vivo using knockout mice and screening for MIF small molecule inhibitors and MIF antagonists for treatment of pulmonary hemorrhages by *in vivo*. *In vitro* MIF knockdown model was prepared to analyze the underlying mechanism of MIF regulated leptospiral pathogenesis. A total of 19 pyran compound and 7 pyrano derivatives were screened for anti-MIF activity. The study result confirms that higher expression level of circulating MIF was observed in laboratory confirmed leptospirosis cases than other febrile cases and healthy control.This indicated that the level of serum MIF to use as marker for monitoring. The findings also suggests that leptospiral LPS triggers the upregulation of MIF m-RNA and protein expression in surrogate model in a time dependent manner. The data from luciferase assay indicated that CREB are positive regulator of expression of the MIF gene. As well significant anti-MIF activity was noticed in serum of pyran compound administered mice. The selected pyran compound is non-toxic to cells and having non-hemolytic activity even in higher concentration, thus revealing their biocompatibility and suitability for biomedical applications.

TUBERCULOSIS

Evaluation of Liver Specific Micro RNAS (Mir 122 Mir 192) as Prognostic Markers of Anti-Tubercular Drug Induced Liver Injury

This study has been designed for the early detection of ATT drug's induced liver injury, where liver specific microRNAs are being evaluated for their potential as a pre diagnostic biomarker for DILI.

Species Indentification and Response to Appropriate Treatment F Sympotomatic Pulmonary Non Tuberculous Mycobacterial Disease Amount Patients Treated For Tuberculosis In Tamilnadu

Diagnosis of NTM lung lisease was done by a combination of clinical, radiographic and bacteriological criteria. 135 patients was refered to as a presumptive case of pulmonary NTM from RBTCP centers, of whom only 110 patients registered for further testing. Out of 110, 48 patients was started on appropriate treatment after the identification of the mycobacterial species. A total of 10 species of NTM were identified in the study and out of them the three most frequently isolated pulmonary NTM are *M. kansasii* (50%), *M. intacellulare* (31.35%) and *M. abscessus* (8.3 %).

Repurposing Econazole and Adding to the Shorter Who Regimen for Mdr Tuberculosis (Reswmen) Study

Phase one of the study with 24 subjects have been completed and report submitted. Experts approved the Phase 2 of the study to assess the safety, efficacy, pharmacokinetics of Econazole in patients with MDR-TB. Phase 2 of this study was just initiated. The study will help in reducing the duration treatment to 3 – 4 months in place of the current recommendation of 4 – 6 months.

Validation of Indigenously Developed Technolgies for the Diagnosis of Extra Pulmonary Tuberculosis Multicentric Validation

The study demonstrated good yield of the indigenous nucleic acid amplification test (NAAT) based technology, TruNat. The assay is rapid, affordable, offers high-sensitivity when tested in a blinded, multi-centric validation protocol, the assay was successfully validated for test accuracy and feasibility at all the three sites, using the laboratory reference standards and the WHO

validated technology Xpert MTB/Rif. Salient findings being:

- TruNat gave a higher yield in detection of TB in fluids and pus samples, yield at par with GeneXpert in biopsy samples and inferior to GeneXpert in Lymph node and CSF samples.
- Sensitivity of detection by TrueNat in comparison to MGIT culture was 62% while Specificity was 85%.
- Sensitivity of detection by TrueNat in comparison to GeneXpert was 74% while Specificity was 90%.
- Sensitivity of detection by TrueNat in comparison to MGIT culture and GeneXpert taken together was 80.6% while Specificity was 90.9%.
- Sensitivity of RIF resistance detection by TrueNat MTB/RIF in comparison to MGIT culture DST was 95% while Sensitivity of RIF resistance detection by Xpert MTB RIF in comparison to MGIT culture DST was 94.4%.

Multicentric Validation of TB-Detect and TB-Concentration and Transport Kit and Tb DNA Extraction Kit for the Diagnosis of TB and Drug Resistant TB

TB Detect' kit was found to be better in comparision to centrifugation by filteration during sputum sample processing. It has shown an increment over direct smear microscopy and can be used in resource limited laboratories. TB Concentration and Transport and TB DNA extraction bio safe kits and can provide a readymade solution for concentrating sputum on device at a microscopic center and can be utilised in safe transportation of sputum at ambient temperature.

Prospective Multicentre Study to Assess the Diagnostic Accuray of the Truenat Mtb And Rif Assays in Intended Settings of Use-Pahse-II

WHO has endorsed the Truenat MTB, MTB Plus and RIF-Dx assays and released recommendations in their guidelines. The WHO in its report already endorsed the Truenat based on the intrim result of the study. Indigeneous diagnostic technologies for diagnosis of TB and MDR/XDR-TB developed by Indian scientist and endorsement of the TrueNat by WHO will enable other low and middle income countries to procure TrueNat for diagnosis of TB and Rifampicin resistance, thus supporting TB elimination in developing countries.

Tuberculosis among Homeless Persons Chennai City

The low rate of active TB in shelter homeless group one smear positive in 1076 persons, compared with other group (two smear positive in 318 pavement dwellers).

DIARRHOEAL DISEASES

An Approach to Identify the Environmental Drivers Modulating Rotavirus Seasonally

Rotaviruses identified as the predominant cause of infection, followed by Adenovirus (6%), Astrovirus (3%) and Norovirus (3%). Co-infections persisted at a rate of ~10% in the population. Astroviruses were often found to infect concurrently with rotaviruses and were identified in 42% of total co-infection cases. Noroviruses of GII genotype was found in 86% of the patients with norovirus infections. A key finding of this study was that the propensity of rotavirus infections was independent on *E. coli* phylotypes housing the host gut as diverse phylogroup types of *E. coli* were found associated with rotavirus positive stool samples.

LEPROSY

Programmatic Implementation and Comparision of MIP Vaccine Immunoprophylaxis and Fifampicin Chemoprophylaxis Under the National Leprosy Eradication Programme (NLEP) in High Endemic Setting

A total of 1126 leprosy contacts were vaccinated. The report suggest that the attack rate in leprosy after MIP implementation is 2.51 per 1000 per

year. However, the data provided is only for 1 year follow up which is insufficient time for a disease like Leprosy since it has a long transmission period. The main barriers identified were continued migration, distance to vaccination centers ie PHC of the respective village due to which few patients could not be vaccinated

Multicentric Trial to Study the Effect of Early Active Mobilization as Compared to Three Weeks Immobilization Following Tendon Transfer Procedures for Claw Hand

A total of 112 patient recruited in intervention arm and 110 patients recruited in control arm at the end of 4years from all five centres. The outcome of the study showed better degrees of deficit correction for delayed arm compared to control arm, however, due to inadequate sample size, it could not conclusively prove. The non-inferiority of the Early mobilization could not be established

OTHER MICROBIAL INFECTIONS

Cytotoxin Associated Gene L Polymorphisms in *Helicobacter Pylori* and Response to Gastric Integrin & Disintegrin Metalloproteases

H. pylori strains having polymorphism of cagL at D58 and K59 shows positive association with Gastric cancer.

Understanding the Role of Quorum Sensing and Other Mechanisms Regulating Persister Cell Formation Against Antibiotics in A Baumannii

Combination treatment with tobramycin and colistin inhibits persister cell formation in *A. baumannii*

Early Detection of Haemophilus Ducreyitreponema Pallidum, Herpes Simplex Virus Type 1 And 2 From Patients with Genital Ulcer Disease by Multiplex Pcr in a Tertiary Care Hospital

The use of Multiplex PCR significantly improves diagnosis of Genital ulcer disease

REPRODUCTIVE & CHILD HEALTH

ICMR is undertaking research in the field of reproductive health through its research institution National Institute of Research in Reproductive Health, Mumbai as well as extramural research projects. These studies are aimed to protect and enhance the reproductive health of people through research and development of technologies and programmes for field applications which can be incorporated into National Programmes.

INTRAMURAL RESEARCH

ICMR - NATIONAL INSTITUTE FOR RESEARCH IN REPRODUCTIVE HEALTH, MUMBAI (ICMR-NIRRH)

FEMALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Deciphering the Putative Epigenetic Mechanisms Pertaining to Polycystic Ovary Syndrome (PCOS)

Environmental milieu has a substantial impact on PCOS development and it exerts its effect through epigenetic modifications. We are interested in tissue-specific epigenetic alterations in PCOS development. Previously, we reported >3000 differentially methylated genes in ovarian granulosa cells (GCs) of PCOS women compared to controls. Few differentially methylated genes such as *AKR1C3, CASR, RETN, MAMLD1,* and *TNF*, which predominantly contribute to hyperandrogenism, premature luteolysis, and oocyte development defects, were explored as novel epigenetic candidates in mediating ovarian dysfunction. Methylation status of these genes matched with our NGS data, and their transcript expression patterns correlated with their hypo- or hypermethylation status. We plan to study global 5-hydroxymethylation (5hmC) levels and 5hmC profiling in PCOS women.

PON1 Expression, Activity and its Relationship with Oocyte and Embryo Quality in Women with PCOS undergoing Assisted Reproductive Technique

Intracellular oxidative stress in granulosa GCs was higher in women with PCOS than in controls. Expression of crucial antioxidant enzymes namely; glutathione peroxidase, glutathione reductase and superoxide dismutase was significantly lower in GCs of PCOS women. Also, these trends matched with respective enzyme activities in follicular fluid which indicates the significant contribution from GCs in maintaining redox homeostasis in follicular environment. Further, the transcript levels of the rate limiting enzyme for synthesis of reduced glutathione i.e., glutamate cysteine ligase was significantly lower in GCs from women with PCOS compared to controls. These observations indicate compromised redox homeostasis in oocyte microenvironment of PCOS.

Understanding Follicular Angiogenesis in Women with PCOS

Follicular growth arrest in women with PCOS may be due to alterations in angiogenesis. Earlier we reported altered expression of proangiogenic genes in GCs of PCOS women. We found similar expression of VEGFA and lower expression of bFGF in follicular fluid of PCOS women. The angiogenic potential of follicular fluid investigated by tube formation and scratch assay using HUVECs showed significantly lower angiogenic capacity in PCOS women. Lower expression of angiogenic factors in GCs and compromised follicular fluid angiogenic capacity may lead to defects in follicle vasculature formation and thus may contribute to follicular defect in ovary of PCOS women.

Unraveling Pathogenetic Mechanisms of PCOS by Whole Exome Sequencing

As phenotypic, ethnic and geographic variations contribute to differences in genetic susceptibility, it is important to examine the associations of these variants in Indian population. We continued genotyping intronic variants in LHCGR, THADA and DENND1A and investigated their associations with PCOS susceptibility. Additionally, we have initiated genotyping of two polymorphisms of c9orf3 gene, found in both Caucasian and Chinese GWASs and are considered to be evolutionarily conserved markers. We found rs2479106 polymorphism of DENND1A was significantly associated with increased risk of PCOS development, while rs13429438 of THADA and rs13405728 of LHCGR showed no association. Furthermore, preliminary findings show that the genotype frequency distribution of rs4385527 but not the rs3802457 polymorphism of c9orf3 is significantly different between PCOS and controls. Our study therefore indicates that genetic predisposition for PCOS may be population specific and thus genetic profiles need to be determined in the Indian context.

Analysis of Mitochondrial DNA Sequence Variants in Polycystic Ovarian Syndrome in Women with Insulin Resistance

Mitochondrial DNA (mtDNA) copy number was found to be reduced in PCOS women, compared to control women suggesting mitochondrial dysfunction may contribute to pathogenic mechanisms in PCOS. Numerous common to rare variants, including some novel variants were identified in mtDNA Displacement loop in PCOS women which might have led to mitochondrial dysfunction and consequently low mtDNA copy number.

Effect of Yoga on Physical and Emotional Health of Infertile Women with Polycystic Ovarian Syndrome (PCOS)

This is a joint collaboration between ICMR-NIRRH and Kaivalya Dham Institute of Yoga. Women with PCOS experience emotional effects like depression/anxiety and infertility further adds to this stress. This project was formulated to study the effect of guided Yoga intervention on physical and emotional wellbeing of infertile women with PCOS and to understand the acceptability, barriers and facilitating factors for introducing Yoga intervention in this group. A training module focussed on Yoga and PCOS was prepared in consultation with Kaivalya Dham Institute and distributed to all the study participants. Pre and post intervention improvement in emotional wellbeing, physical, endocrine, biochemical parameters, ovulation, conception at end of 12 weeks were assessed. Preliminary findings suggest that Yoga intervention has beneficial effect in improving the HDL profile, anxiety and cortisol levels.

Identification of Novel Genes and Pathways for Lean and Obese PCOS

A systematic and comparative study on lean and obese PCOS with respect to gene, pathway and comorbidity analysis has been done using in silico methods. Analysis of differentially expressed genes across tissue types for lean and obese PCOS revealed that majority of them were downregulated for both lean and obese PCOS. Ovarian and endometrial tissues shared several commonly dysregulated genes, suggesting an important role of this cross-talk in PCOS pathophysiology. Several fundamental pathways for cellular homeostasis were affected in lean and obese PCOS. The gene-disease network is

denser for obese PCOS with a higher comorbidity score as compared to lean PCOS.

Updation of an Online Database for PCOS

The PCOSKB database developed in 2015 was updated and now holds information on 533 genes, 145 SNPs, 29 miRNAs, 1150 pathways and 1237 diseases associated with PCOS. This data were retrieved based on evidence gleaned by critically reviewing literature and related records available for PCOS in databases such as PubMed, KEGG, DisGeNET, OMIM, GEO, GO, Reactome, STRING, NCBI Gene, UNIPROT and dbSNP. Since PCOS is linked with several comorbidities, a variety of data mining algorithms for comorbidity and network analysis are integrated in PCOSKBR2. It is freely accessible at http://pcoskb.bicnirrh.res.in/.

Building and Analyzing Gene Network for Polycystic Ovary Syndrome (PCOS)

Polycystic ovary syndrome (PCOS) is one of the leading causes of female subfertility. A number of genes have been reported in literature to be associated with PCOS. However, the genetic etiology is still unclear. This study is aimed at using a global approach to gain useful insights about the pathophysiology of PCOS. The gene disease network for PCOS was generated using genes identified from literature and gene expression data from GEO database. 100 novel candidate genes with high probability to be associated in PCOS pathology were identified.

Clinical Phenotypes and Genetic Regulation of Endometriosis in Indian Women

MOUs were signed with The University of Queensland, Australia as well as with twelve Collaborating Centers all over India. Three-day intense training was provided to research staff working at collaborating institutions from December 12-14, 2019 at ICMR-NIRRH, Mumbai. An electronic database for collecting national data on endometriosis was developed. As a part of the celebration of endometriosis awareness month, an educational brochure on endometriosis was developed. National Clinical and Genomic database of endometriosis will be developed with a plan to establish National Bio-repository of serum, plasma, DNA of women with endometriosis.

Studies to Evaluate the Effect of Metformin on Endometrial Functions

This study was undertaken to evaluate direct effects of metformin on endometrium. In vitro proliferation and upregulation of receptivity markers in Ishikawa and HEC-1A endometrial cells at low concentrations of metformin was previously reported. A microarray approach was employed to understand differential gene expression at high and low concentrations of metformin in HEC-1A endometrial cells. The data show 481 and 71 differential genes at 10 mM and 50 µM respectively, compared to control ($p<0.05$). Mitochondrial protein synthesis was one of the biological processes upregulated at low concentration of metformin and cell division, cell cycle and mitosis were among the down-regulated biological processes at high metformin concentration. In-vitro data showed activation of pmTOR at low concentration of metformin and downregulation at high concentration of metformin. Data so far conclude that low dose of metformin activates mTOR without activation of AMPK; however, at high concentration inhibition of AMPK is dependent on mTOR. Activation of mTOR at low concentration may involve endometrial cell proliferation and further studies are in progress to understand mechanisms of activation of mTOR in endometrial cells in response to metformin.

Pathways to Oncogenesis in the Pathophysiology of Endometriosis

Somatic mutations and common Loss of heterozygosity events in oncogenesis-associated genes have been documented in endometriotic lesions. There also exist data to suggest dysregulated DNA Damage Response (DDR) in endometriotic lesions. However, it remains to be unequivocally established whether eutopic

endometrium from women with endometriosis also displays dysregulated DDR. Endometrial expression of 84 DDR genes in women with and without endometriosis was assessed. Out of these, 12 genes were upregulated by at least 1.5 fold in the mid-proliferative phase eutopic endometrium from women with endometriosis, compared to those without the disease. In the mid-secretory phase eutopic endometrial samples, 14 DDR genes displayed differential expression, of which 13 were upregulated and one gene was downregulated in women with endometriosis, compared to those without the disease. The array data were validated at protein level for GADD proteins. Further, higher number of γ-H2AFX (an indicator of DNA damage) foci was observed in the mid-proliferative as well as mid-secretory phase eutopic endometrial samples from women with endometriosis, compared to women without endometriosis. Data so far are indicative of higher DNA damage and elevated DDR in eutopic endometrial samples from women with endometriosis, compared to women without endometriosis.

Pregnancy Outcomes in Indian Women with Endometriosis and Biomarker Correlation: A Cohort Study

Seventy-three women with endometriosis were recruited during reporting year and so far, a total of 234 women with endometriosis have been recruited from 6 study sites in all over India. The most common subtype reported was ovarian endometrioma (OMA) [39.1%], followed by deep infiltrating endometriosis (DIE) (31.2%) and superficial peritoneal endometriosis (29.7%). There was left laterality for endometriotic lesions in Indian woman with OMA and DIE. Vascular and red endometriotic lesions were most common endometriotic lesions. Further analysis is ongoing to study pregnancy outcomes in women with endometriosis.

Role of Homeobox Gene HOXA10 in Pathogenesis of Endometriosis

The aim of this study is to understand the roles of HOXA10 gene in the pathogenesis of endometriosis. Mice transgenic for HOXA10 shRNA have been developed which have lower than normal levels of HOXA10. Endometriosis was induced in these animals by surgery. The results revealed that in the transgenic mice the lesions were fibrotic and underwent epithelial to mesenchymal transition (EMT). It was proposed that loss of HOXA10 may lead to EMT which is responsible for fibrotic stroma observed in ectopic endometrium of women with endometriosis.

Understanding the Molecular Basis of Embryo Implantation

Implantation of the embryo is a rate-limiting step of successful pregnancy and any defects in the process can lead to infertility. Failure of embryos to implant is a major cause of poor success rates of assisted reproduction. The aim of this project was to investigate the fundamental mechanisms by which embryo breech the endometrial epithelium and lead to decidualization of stromal cells. Using mice as study model it was demonstrated that at the site of implantation, there is flattening of luminal epithelial cells and there is switch in expression of markers associated with epithelial to mesenchymal transition (EMT). Altered expression of transcription factors like HOXA10 and TWIST2, which are associated with EMT, was also observed.

Understanding the Molecular Mechanisms of Gonadal Development in the Mouse

Failure of gonad development leads to disorders of sex development and infertility in many individuals. However, the cause of failure of gonad development in many cases is unknown. The present study aims to understand the changes in genetic programs that occur in the XX and XY gonads and determine how these programs are governed by the Lim homeobox gene Lhx2. Using RNAseq of XX and XY gonads, a number of sex-biased genes were identified whose expression is altered during the course of sex determination. These genes belong to diverse pathways and have sex-specific biological functions. Genes involved in meiotic program were altered in Lhx2 knockout XX embryos while the Lhx2 knockout XY embryos showed altered

expression of genes associated with cell migration. Together these results imply the sex specific roles of Lhx2 in gonad development.

MALE INFERTILITY AND ASSOCIATED REPRODUCTIVE DISORDERS

Development and Validation of a PCR based Technology for Detection of Yq Microdeletions in Diagnosis of Male Infertility

In this translational research project, it was proposed to develop an assay for detection of Yq microdeletions, a major genetic cause of male infertility. Using previous datasets a multiplex PCR was developed using 16 STS markers that can detect Yq microdeletions. The reproducibility, sensitivity and specificity were tested. The related documents have been submitted to ICMR for technology transfer. A commercial partner has been identified for technology transfer.

Development of a Microfluidic Device for Good Quality Sperm Selection for Assisted Reproductive Technologies

Sperm motility is one of the major factors of male infertility. It is perceived from several studies that chemotaxis orients the movement of sperm towards the egg, increase the velocity of the sperm and thereby its ability to fertilize the egg. Failure in bringing the sperm in close proximity to the egg either due to certain chemotactic factors missing in the follicular fluid or due to lack of response to these factors on the part of sperm may be one of the causes manifesting as female infertility, male infertility or both. A microfluidic device has been developed which allows studying sperm chemotaxis in vitro. Using this device, differences in sperm motility response to ovulatory- and preovulatory oviductal fluid in rats was demonstrated. Further, a few chemo-attractants have been identified from ovulatory oviductal fluid which are presently being validated. This study will be extended to investigate presence of these chemo-attractants in follicular fluid of infertile women and study response of sperm from infertile men to these chemo-attractants.

Microtubule (MT) Dynamics and Sperm Function: Involvement of Tubulin Acetylation/ Deacetylation

Sperm microtubule (MT) dynamics is being investigated and so far, data from asthenozoosperm suggests that the threshold levels of sperm MT acetylation/deacetylation along with microtubule-associated proteins (MAPs) are important for MT dynamicity and may play a crucial role in regulating sperm motility. Characterization of MAPs in sperm would be undertaken.

Genetic and Epigenetic Changes in Imprinted Genes in Male Partners of Women Experiencing Recurrent Spontaneous Abortions

Recurrent Pregnancy Loss (RPL), defined as the loss of two or more pregnancy affects 1-2% of couples in the reproductive age. Although several maternal and paternal etiological factors are known to contribute to RPL, nearly 50% of the cases remain idiopathic. Studies are going on to understand the involvement of sperm epigenetic factors in RPL. DNA methylation levels of selected imprinted genes implicated in embryo development were evaluated in the spermatozoa of men whose partners are experiencing RPL. A significant decrease in the global 5mC levels and aberrant methylation of imprinted genes in the sperm in the RPL group was observed suggesting that these could contribute to the etiology of RPL. Further, receiver operating characteristic (ROC) analysis to determine whether the differences in methylation levels of imprinted genes observed in RPL group could be used as diagnostic markers to detect the "epigenetically abnormal" spermatozoa revealed that global 5mC level is the best candidate with highest diagnostic efficiency and can be a good diagnostic candidate to be explored at the clinical level. Among the imprinted genes studied, the IGF2-H19 DMR and ZAC were the best candidate genes. The feasibility and diagnostic potential of these markers need to be further investigated in a clinical setting.

Idiopathic Recurrent Pregnancy Loss: Possible association with Paternal Exposure to Endocrine Disruptors and Epigenetic Modifications in Sperm

Studies have been undertaken to investigate genomewide DNA methylation changes, histone retention and histone modification as well as methylation of imprinted miRNA cluster on chromosome 14 and 19 in spermatozoa of male partners of RPL cases. Histone H3 lysine 4 trimethylations (H3K4me3), a key histone modification involved in transcriptional activation of gene expression was studied using flow cytometry. A significant higher level of H3K4me3 modification was observed in the RPL group spermatozoa in comparison with fertile controls. In addition, since endocrine disruptors affect sperm epigenome, efforts are being made to explore the possible association of paternal exposure to endocrine disruptors (Bisphenol A and phthalates) and sperm epigenetic modifications in male partners of RPL couples.

Investigations on Obesity Induced Epigenetic Changes in Germ Line of Adult Male Rats

Studies on paternal obesity induced changes in the sperm methylome using two rodent models, one genetically-inherited and another high fat diet-induced demonstrated genes involved in developmental pathways namely Wnt, Hedgehog, Notch and TGFbeta signaling pathways to be differentially methylated. The methylation changes correlated with the expression of some of these genes in the resorbed embryos sired by the diet-induced obese males suggesting paternal diet-induced obesity could partially transmit the defective epigenetic signatures of developmental importance via sperm leading to embryo loss.

2.7 Developing a Gene Based Database on Male Infertility

A gene-based database is being developed which holds information on genes, their associated diseases, gene ontology, pathways and references for their role in male infertility. The database currently holds information on approximately 1500 genes, which are functionally validated to be associated with male infertility. This resource would prove useful to researchers interested in understanding the genetic basis of male infertility.

Identification and Characterization of Sertoli and Leydig Cell Homing Peptides

In the present study, attempts were made to identify the Sertoli and Leydig cell ligands using phage display approach. Sertoli cell homing peptides were identified using in-vitro (TM4) followed by in-vivo (mouse model) bio-panning approach. Out of total 148 peptides, SCHP1 and SCHP2 were selected and further validated for their specificity and homing abilities to Sertoli cells. SCHP1 and SCHP2 peptides were found to have significantly higher homing ability to Sertoli cells compared with the scrambled SCHP1 and SCHP2. In future experiments these peptides will be tested for their ability to home Sertoli cells in an in-vivo system and targets of the peptides will be identified. Sertoli cell homing peptides can be used as ligand for targeted drug delivery to testis.

RTI/ STIS/HIV/ MICROBICIDES

Development of a Multistrain Probiotic *Lactobacillus* Formulation effective against Reproductive Tract Infections

Vaginal microbiota of healthy women and women with bacterial vaginosis (BV) were characterized using 16s rRNA V3-V4 region sequencing (HiSeq Illumina). Alpha-diversity analysis showed significant differences in microbial diversity between the groups. Abundance of *Lactobacillus* was significantly low in BV samples. Principal coordinates analysis showed a distinct clustering of samples from the two groups. Species-level analysis revealed that the vaginal microbiota of healthy women was dominated by *L. crispatus*; whereas *L. iners* was detected with 80% and 100% prevalence in normal and BV flora respectively.

Significant difference in microbial diversity and species richness was observed in women with BV and normal microbiota during their luteal phase. The study provides insights into the vaginal microbiome of Indian women. This will enable us to unravel the microbial biomarkers and explore the prospective candidate probiotics for restoring the vaginal microbiota.

Investigation of Integrin α4β7 Expressing Immune Cells in Sexually Transmitted Infections / Reproductive Tract Infections (STIs/RTIs) and HIV

During the reporting period, potential factors involved in altering the frequency of integrin α4β7 expressing T cells during HIV infection were examined. MAdCAM-1, the natural ligand for integrin α4β7 is known to co-stimulate T cell proliferation and its levels were found associated with higher frequency of integrin β7 expressing effector memory T cells in healthy controls. However, despite higher levels of MAdCAM-1 in HIV infected individuals, the frequency of integrin β7 expressing effector memory T cells was not found to be higher than those in healthy controls. Transforming growth factor-β1 (TGF-β1), a multipotent cytokine reported to promote HIV latency, was also found to be elevated in infected individuals. This in turn may influence the frequency of integrin β7 expressing effector memory T cells by modulating their responsiveness to MAdCAM-1 mediated proliferation. Further studies are needed to evaluate the effect of these events on HIV pathogenesis.

Variants of Human Leukocyte Antigen and their Possible Association with HIV Transmission

Human leukocyte antigen (HLA) molecules have been consistently associated with HIV transmission. Our studies suggest that HIV infection may cause an increase in HLA-C expression. This is in contrast to the existing reports indicating that HIV downregulates HLA-A and HLA-B at the cell surface and leaves HLA-C unaffected. HLA-C cell surface expression in treatment naïve HIV-1 infected cases was significantly high than those on treatment. This was also evident in the viral load paired HLA-C expression analysis in those 9 cases that showed a highly significant reduction in the viral load 1 month after treatment. This suggests that HLA-C expression decreases due to lowering of viral load. Further, HLA-C expression in HIV infected treated individuals was found to be significantly lower than the expression seen in the HIV-1 naïve individuals. However, the expression in HIV infected treated individuals was significantly higher compared to their exposed uninfected spouses. There are no reports stating that ART has any direct effect on HLA expression. Thus, it is unclear how this reduction in HLA-C takes place. It is plausible that HLA-C expression increases in response to HIV infection, and is reduced due to reduction in HIV viral load after initiation of ART.

MENOPAUSE AND OSTEOPOROSIS

Bone Exercise for Life: An Intervention Model on Bone Health and Quality of Life among Menopausal Women

Data from 440 peri/menopausal low-income women regarding awareness of osteoporosis revealed that women were not aware of risk factors like bone loss soon after menopause, premature menopause, hyperthyroidism, misri use, thin built, etc. Though women were aware about prevention of falls, importance of exercise/yoga and calcium rich diet for improving bone health, they were not practicing it as a part of their day-to-day lifestyle. Some barriers spelt by them were lack of family support/ time, no facilities for exercise or yoga, financial reasons etc. Data of 6 FGDs indicated that participants unanimously agreed that women have general need to take care of their bone health via adhering to modalities: 30 minutes' walk without overstraining body, exercise, yoga, diet, avoiding stress and no tension. Sarcopenia assessment was not evident among these women and they were trained to walk with estimation of the flat foot and

guidance on how to walk daily. Pictorial booklets on yoga protocol were published in English and Marathi, along with detailed document in English. Community awareness generated by this study may inculcate community acceptance of preventive and therapeutic measures for osteoporosis, thus eventually helping them to improve their quality of life.

Osteoporosis Screening and Intervention Programme Using AYUSH Approach: A Community based Programme in Maharashtra State

Public health program was undertaken to sensitize general community, health-care professionals, policy makers and public on menopausal osteoporosis and the burden of this disease was assessed using a camp approach. Twenty-two screening and treatment camps for osteoporosis were conducted. A total of 2250 post-menopausal women were screened for osteoporosis out of which 857 osteoporotic women were recruited and administered Ayurvedic treatment (Tab Ghanavati /laksha Guggul) for a period of 3 months. Atraumatic fractures, thin built, menopause and tobacco or misri use were significantly associated with osteoporosis while sedentary lifestyle and family history of hip fracture did not relate. Leg cramps were significantly associated with osteoporosis. Trend for osteoporosis was seen among menopausal women and significantly associated with years since menopause. *Vata*, *Pitta*, *Vata Pradhan* or *Pitta Pradhan Prakruti* had strong association with osteoporosis. Till date, 607 patients have been followed up. The camp approach has helped generate awareness regarding i) osteoporosis as a silent disorder and bone health; ii) prevention of fractures; iii) importance of walking and exercise in optimizing musculo-skeletal health and iv) importance of diet for wellness. The camps have also succeeded in sensitizing women about non-communicable diseases like hypertension, diabetes and anaemia.

MATERNAL AND CHILD HEALTH

Evaluation of Factors affecting Innate Immunity in Women with Pre-Eclampsia

Serum levels of SP-A, SP-D and MBL and P4/E2 ratio are consistently maintained during pregnancy. Collectins, Surfactant protein A (SP-A), Surfactant protein D (SP-D) and mannose binding lectin (MBL) are a group of innate immune molecules regulated by steroid hormones. Reduced levels of SP-A and SP-D during early gestation exhibited significant association with severe early onset preeclampsia (EOPE). About 15% of pregnant women undergo a missed abortion (MA), wherein they do not experience cramping and vaginal bleeding. Dysregulation of immune molecules and steroid hormones contribute to early pregnancy loss. In order to determine serum profile of collectins throughout normal pregnancy and to explore their predictive potential during 8-12 weeks of gestation for MA, prospective cohort of pregnant women was examined at DY Patil Hospital, Navi Mumbai and Nowrosjee Wadia Maternity Hospital, Mumbai. The serum levels of SP-A and SP-D were significantly downregulated in normal pregnant women in all three trimesters compared to non-pregnant women and were not significantly different across the three trimesters. Although progesterone (P4) and estrogen (E2) levels increased progressively during the pregnancy, the P4/E2 ratio remained constant in all three trimesters with no significant change among the trimesters similar to serum collectin levels. Fourteen women from the cohort underwent MA during the 14-20 weeks of gestation and exhibited a significant downregulation in the serum levels of SP-D during 8-12 weeks of gestation. At the best cut-off level of SP-D (725.5 pg/ml), the serum SP-D levels could predict impending MA with a sensitivity of 57.14 % and specificity of 93.3%. The P4/E2 ratio showed significant decline at 8-12 weeks in MA women compared to the normal-pregnant women and a significant positive correlation with SP-D. Dysregulated serum levels of SP-D and P4/E2 ratio during the early first trimester may predict occurrence of MA. A significant inhibition of the HTR8/SVneo cell proliferation and migration in the presence of a recombinant fragment of human SP-D suggested the relevance of SP-D in placental development.

Developing an Immunochromatography Based Strip Test for Analyzing PlGF Concentration

for Prediction of Risk for Developing Preeclampsia

Analysis of urine samples from pregnant women by an in-house ELISA and commercial ELISA demonstrated a correlation of PlGF levels with neonatal birth weight. In samples from healthy women (taken in the third trimester), it was observed that when PlGF levels were lower than 80 pg/ml, birth weight of the baby was lower than 2.5 Kg. This indicated that apart from being a marker for pre-eclampsia, PlGF might serve as a marker for IUGR in non-pre-eclamptic women.

Maternal Near Miss (MNM) Review and Corrective Measures at Selected Tertiary Hospitals in Maharashtra

The main objective of this study is to identify the challenges in the process of implementation of the MNM guidelines and provide feedback to Government of Maharashtra. The study duration is of two years (2018-2020). Data collection phase was from February 2019 - January 2020, in which MNM events were reviewed and interviews of survivors of near misses were conducted. MNM review committee meetings were conducted every month in two tertiary care hospitals. During these meetings, recommendations were given to address the gaps identified based on the three delay model. The total number of MNM identified in one year were 228. Corrective measures based on recommendations given by the MNM committee were taken at both the hospitals. Data cleaning and analysis will be completed in July 2020.

Maternal Near Miss Review and Corrective Measures at District and Women's Hospitals in Maharashtra - Funded through PIP of Government of Maharashtra

NIRRH is providing technical and monitoring support to Government of Maharashtra in operationalizing the MNM guidelines at five district/women's hospitals in Maharashtra i.e. Nasik, Parbhani, Ratnagiri, Akola and Nanded. The overall objective is to implement the MNM-R Guidelines developed by Government of India and take corrective measures at the selected hospitals. The total number of MNM cases identified and forms filled in software at the selected hospitals (April 2019 - March 2020) was 75. Out of these, the major adverse events were Hemorrhage-47 and Hypertension-21. MNM-R meetings were conducted at all the selected hospitals. During these meetings, recommendations were given to address the gaps identified based on the three delay model.

Detection of Infections Associated with Preterm Births

Bacterial infection is a common cause of preterm births and vaginal colonization of certain bacteria predisposes the mother to deliver preterm. Eight bacteria were shortlisted which are commonly found in vagina of women with preterm delivery. A PCR assay was optimized using DNA from standard strains. A multiplex format has been devised and the assay is being tested for sensitivity and specificity.

Improving Reproductive Health Seeking Behavior and Service Utilization by Tribal Women through Involvement of Self Help Group (SHG) Women in Maharashtra

An experimental study was conducted in two tribal blocks of Nasik district (Kalvan and Surgana) in Maharashtra, from May 2018 - November 2019. In the study block (Kalvan), the trained SHG women in selected villages conducted education sessions on reproductive morbidities for other women in the community. No interventions were provided through the SHG women in the control block (Surgana). Out of the 505 women with reproductive morbidities referred by the SHG women, 328 (65%) percent availed services at the health facilities. The study demonstrated feasibility and acceptability of utilizing the potential of SHG women for improving reproductive health seeking behaviour and service utilization by tribal women. This model could be scaled up in other areas of Maharashtra and India to address neglected reproductive health needs of women with the existing human resources.

Enhancing Male Participation in Interventions to Prevent Unintended Pregnancy

The objectives of the study are to i) develop and implement intervention [Counselling Husbands and Wives to Achieve Reproductive Health and Marital Equity (CHARM2)]; ii) evaluate the impact of CHARM2 on spacing contraceptive use and iii) assess the quality, scalability, replicability and sustainability of CHARM2. A total of 20 subcenters were randomly allocated to intervention and control groups of Junnar taluka, Pune district. A total of 1200 women aged 18-29 and their husbands; not using permanent contraceptive methods and not willing to have child in the next one year were randomly selected from villages under subcenters after obtaining informed consent. Preliminary analyses showed that majority of women have attended school and have at least one child. It was found that women experiencing physical violence were significantly less likely to use condoms than women not experiencing violence.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and the Effect of Early Intervention in Management of the Disease in Tribal Populations: Research cum Intervention Study

Sickle cell disease (SCD) is an important public health problem in India with highest prevalence in tribal areas with increased risk for severe morbidity. Presently there is no national neonatal screening programme in India. The current study is undertaken to establish a newborn screening program for SCD, to understand the magnitude of SCD, barriers in implementing the programme and to measure the benefit of early comprehensive care of affected babies. It also aims to evaluate a genotype-phenotype correlation to understand the role of genetic modifiers in the disease severity. The study was initiated in Dec 2019. Initially, meetings with the District Health Officials and community awareness activities were conducted. A CME was organized on SCD for Medical Officers. Total 549 new-borns were screened for SCD. Initial 345 samples were tested by point of care test-Haemotype SC followed by HPLC. So far, two babies were sickle cell homozygous and 38 were sickle cell heterozygous. The babies with SCD are being followed up for the trait at 6 weeks for confirmation of diagnosis and screening of family members followed by genetic counselling.

Development of a Non-Invasive Evaluation Protocol for Detection of Congenital Cytomegalovirus Infection in Newborns

Congenital cytomegalovirus (CMV) infection is a leading cause of birth defects as well as childhood mortality and morbidity. Newborn screening is important for early detection of infection and clinical management. A total of 391 neonates in a tertiary care hospital were screened by the CMV PCR assay. Out of these, 7 were found to be infected based on presence of CMV DNA in saliva samples while 43 were found to be exposed to the virus based on presence of CMV DNA only in their stool samples. Follow up of some of these 43 cases revealed presence of CMV in saliva samples. These results suggest that presence of CMV DNA in stool samples may be a good indicator of underlying infection. However, the potential utility of screening of stool samples for early detection of CMV infection in neonates needs to be further explored.

Community Based Screening and Management of Latent TB among under-Five Children from Urban Slums in Mumbai

Childhood tuberculosis (TB) accounts for approximately 27% of the global burden of TB and contributes 8–20% of TB-related deaths in India. The diagnosis and treatment of Latent TB infection (LTBI) forms an integral component of WHO's End TB Strategy. The present study is a community based study in urban slums in collaboration with Tertiary Hospital and Health post (MCGM), aiming to screen under-five children at risk for LTBI as per WHO guidelines with estimation of Interferon Gamma Release Assay (IGRA-Quantifern Gold Plus). The study also aims to assess adherence to treatment and progression of disease during follow up among diagnosed patients and assess acceptability of

testing and treatment of LTBI among parents. The study was initiated in September 2019. Apparently, healthy children in 6 months to 5 years age group who were underweight as per WHO criteria and children having household contacts with TB were included in the study. Total 216 children have been recruited so far. It was observed that IGRA was positive among 6% children of which 5.1% children were positive on basis of both TST (≥ 10 mm) and IGRA. Children suspected for LTBI were evaluated at BJ Wadia Hospital - TB Clinic and were screened for active TB by work up X-ray Chest and Gene Xpert. None of the children so far had active TB infection. Children diagnosed of having LTBI have been started on INH prophylaxis as per the guidelines and are being followed up.

GENETIC RESEARCH CENTER

Functional Study of Voltage-Gated Calcium Channel Gene Mutations in Schizophrenia Using Induced Pluripotent Stem Cells (iPSCs): A New Approach for Developing a Cellular Model

In this study, 5 families were analysed; 3 having history of multigenerational positive history of schizophrenia including affected first-degree relatives. Whole exome sequencing trio samples of all the affected members have been carried out. Next Generation sequencing analysis revealed almost 25129 variants after annotation. Upon prioritization, 21 variants are found to be statistically significant. Pathway analysis was carried out using all prioritized variant; however, no common pathway was identified. Further analysis revealed a common pathway (i.e. glycosaminoglycan pathway) in all 5 families. Thus, an altered glycosaminoglycan pathway may have a causative relationship with schizophrenia in this cohort. Microarray analysis identified presence of copy number loss in 7q35-q36.1 region, encompassing the CNTNAP2 gene. Interestingly, hemizygous loss of entire gene has also been detected in an affected sister of family 4. The CNTNAP2 gene is known to be associated with autism spectrum disorder and schizophrenia. Therefore, a hemizygous loss of CNTNAP2 may be a causative factor for schizophrenia in the family 4.

Identifying Cytogenetic Abnormalities in Cases of Disorders of Sex Development

The objective of this study was to screen the patients of Disorders of Sex Development (DSD) for SRD5A2 mutations and determine the pathogenicity of mutations in causation of DSDs. A cohort of 50 paediatric and adolescent patients with 46 XY DSD with ambiguous genitalia was studied. All the patients had no Mullerian structures and no adrenal involvement. All other syndromic conditions like congenital adrenal hyperplasia, ovo-testicular DSD, gonadal dysgenesis, persistent mullerian duct syndrome, syndromic DSD were also not observed. The entire exons and exon-intron boundaries of SRD5A2 gene were amplified. Direct sequencing of SRD5A2 gene revealed the presence of 3 different mutations (p.L89V, p.R246Q and p.E57X) and 2 intronic polymorphisms (rs522638 and rs632148) in 29 children (58%) (along with 4 children having parental consanguinity). Out of the 3 mutations, the p.L89V in exon 1 was the recurrent commonest variant present followed by p.R246Q present in exon 5 of SRD5A2 gene. A nonsense mutation p.E57X was found to be present in only one patient. Mutations p.L89V and pR246Q have been reported widely in various ethnic groups; however, mutation p.E57X was reported only in Indian patients. Overall, the study presents a spectrum of mutations present in SRD5A2 gene and the clinically variability among mutation positive patients.

STEM CELL BIOLOGY

Regenerating Diabetic Mouse Pancreas by Manipulating Endogenous Stem Cells

An innovative protocol was developed to enrich pluripotent very small embryonic-like stem cells (VSELs) from adult mouse pancreas and pancreatic islets. This simple and robust protocol can enrich VSELs from any solid organ. VSELs

were enumerated by flow cytometry as 2-6 µm, viable cells with a surface phenotype of *Lin⁻CD45⁻ Sca-1⁺* and a 10-fold enrichment. VSELs increased in numbers (from 0.725% to 1.142%) in diabetic mouse pancreas in an attempt to restore homeostasis but were unable to as their niche is possibly affected by streptozotocin treatment. Transplanting mesenchymal cells as 'paracrine providers' from bone marrow into the diabetic pancreas and treating with a nano-formulation of resveratrol- XAR-reversed diabetic symptoms and results are ready for translation.

Investigating the Effects of Neonatal Exposure to Estrogen and DES on Mouse Testicular Stem Cells

Endocrine disruption during neonatal life with estradiol and DES was found to directly affect the testicular stem cells (VSELs and SSCs) that express ERα and ERβ. VSELs increased in numbers after endocrine disruption; however, their differentiation into c-Kit positive germ cells was markedly affected along with disruption of p53 and NP95 expression. Excessive self-renewal of VSELs and reduced p53 levels after DES treatment led to initiation of testicular cancer in 9 out of 10 mice. NP95 is an epigenetic regulator crucial for transitioning pluripotent stem cells into committed progenitors. NP95 disruption resulted in global hypomethylation and blocked differentiation of VSELs into cKit positive germ cells and suppressed meiosis thus explaining reduced sperm count and sub-fertility. Thus, data were generated suggesting altered stem cells biology as the underlying mechanism to explain reduced sperm count, infertility and testicular cancers due to endocrine disruption.

Studies on Stem Cells and Niche Interaction in Mice and Sheep Ovary

Surface epithelial cells and stem cells (VSELs and OSCs) were gently collected after enzymatic digestion from adult mouse ovaries during different stages of the estrus cycle. Maximal numbers of VSELs/OSCs were found during estrus and metestrus phase of estrus cycle whereas the germ cell nests were mostly observed during metestrus along with expression of pre-meiotic germ cell marker Stra-8. Results supported the presence of stem cells in the adult ovary that are modulated by the circulatory hormones to undergo neo-oogenesis and primordial follicle assembly. This was in contrast to existing paradigm that a female has a fixed ovarian reserve by birth. This newly emerging insight will provide novel strategies to tackle POI, POF, PCOS and ovarian cancers in future.

Investigating the Effects of Follicle Stimulating and Steroid Hormones on Uterine Stem Cells

Stem cells (VSELs and EnSCs) were studied in adult mouse uterus during different stages of estrus cycle. VSELs were maximal during estrus and metestrus phases of estrus cycle and VSELs/EnSCs expressed receptors for pituitary and steroid hormones [FSHR, ERα, ERβ, PR]. Data were also generated to show that intrinsic changes in the uterine stem cells by endocrine disruption result in a non-receptive endometrium in adult life rather than altered levels of ovarian hormones. Expression of FSHR on uterine stem cells explains extragonadal action of FSH on the uterus. Expression of ERα and ERβ make the uterine stem cells vulnerable to endocrine disruption and provide a stem cell basis for various pathologies like non-receptive uterus, endometriosis, fibroids and endometrial cancers.

NATIONAL CENTER FOR PRECLINICAL REPRODUCTIVE AND GENETIC TOXICOLOGY

8.1 MicroRNA Regulation in Prostate and Ovary upon Exposure to Endocrine Disruptors

Endocrine disruptors like Bisphenol-A (BPA) mimic endocrine hormones and cause various developmental and reproductive disorders in animals and humans. Differentially regulated expression of miRNA Let7 family and their target genes HMGA1, HMGB1 and AR were analysed.

HMGA1 and HMGB1 are high mobility group proteins classified on the basis of functional DNA-binding motifs. A significant decrease in the expression of HMGA1 was observed in the prostate tissue of perinatally BPA exposed F1 rats. Androgen Receptor (AR) and HMGB1 expressions in the prostate tissue of perinatally BPA exposed F1 rats were found to be significantly upregulated. This overexpression of AR is responsible for the promotion of metastasis induced by EMT in the prostate tissue. Findings suggested that BPA can induce cancer in the prostate tissue of perinatally exposed F1 generation male rats.

Deciphering the Molecular Mechanism of Triclosan on Hypothalamus Pituitary Gonadal Axis

The present study was undertaken to decipher the effect of Triclosan (TCS) on hypothalamus-pituitary-gonadal axis and to investigate whether TCS exposure affects male reproductive system through an epigenetic mechanism. Pregnant dams (F0) were administered with different doses of TCS (0.1, 4, 40 and 150 mg/kg b. wt. /day) by subcutaneous injection during gestational and lactational periods. Expressions of steroid hormone receptors and two enzymes (StAR and aromatase) involved in the regulation of steroidogenic pathway were checked. Perinatal exposure to TCS altered the mRNA levels of steroid hormone receptors (AR, ERα and ERβ), StAR and aromatase in the testis of F1 male rats at postnatal day 75. Altered expression of steroid hormone receptors and steroidogenic enzymes may affect the process of spermatogenesis and steroidogenesis respectively leading to subfertility in F1 male rats.

Deciphering the Effects and Mechanism of Action of Butyl Paraben on Fertility

The present study was undertaken to decipher the effects of gestational and lactational exposure to n-butyl paraben on sexual maturation and fertility of F1 generation male and female rats and understand the mechanism of action of n-butylparaben. F0 dams were injected subcutaneously with different doses of n-butylparaben during the gestational and lactational periods. Daily Sperm Production (DSP), sperm transit time and quantitative effect on seminiferous tubules were studied on adult F1 male rats at post-natal day (PND) 75. Results demonstrated that exposure to n-butylparaben accelerates sperm transit time, thus resulting in reduced fertility in F1 male rats. The exposure during critical period of development to butylparaben results in perturbed HPG axis of F1 male rats through estrogenic/anti-androgenic action.

An Endocrine Disrupter- Atrazine induced Epigenetic Regulations in the Male Germ Line Following Perinatal Exposure

Atrazine ATR (2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine), is a widely used pre- emergence herbicide. The present study was undertaken wherein F0 dams were treated with various doses of ATR subcutaneously from gestational and lactational periods. ATR (high dose) treated males showed significantly altered serum testosterone and estradiol levels at PND75. Significant reduction in sperm count and motility was noted in all ATR treated groups. ATR exposure changed testicular expression of steroid nuclear receptors (AR, ER-α/β) at mRNA level in F1 males with significant upregulation of ERα at all doses at PND75. Fertility assessment of ATR exposed males paired with naïve female showed increased pre-implantation losses and decreased litter sizes as compared to control. Adverse developmental effects on F2 foetuses were also noted. Altered expression of steroid hormone receptors might affect the process of spermatogenesis and steroidogenesis leading to subfertility in F1 male rats exposed perinatally to ATR.

Cellular and Molecular Effects of Cypermethrin on Reproductive Functions of Male and Female Rats

Cypermethrin (CYP) is a potent endocrine disruptor having estrogenic and anti-androgenic effects. CYP

exposure significantly affected the reproductive organ development and functions at all doses in rats. Disrupted estrous cyclicity, histological changes in ovary and uterus, presence of multi-oocyte follicles, altered circulatory steroid hormone levels and their respective receptors were observed. The expression profiles of oogenesis markers (mitotic and meiotic) of granulosa cells and oocyte such as *Amh*, *Gdf9*, *Ccnb1* and *Pcna* were also altered in all CYP exposed groups. Further, the expression of HOXA10 and α-SMA, which are important for uterine integrity and function, were found to be altered. These observations highlighted the detrimental effects of CYP exposure during the sensitive window of development, which can manifest into reproductive dysfunctions at adulthood.

REPRODUCTIVE CANCERS

Improving Access for Screening of Common Cancers and Non-Communicable Diseases among Women in Tribal Block of Maharashtra: Challenges in Implementation

This project was developed in joint collaboration with state health system and Model Rural Health Research Unit (MRHRU), Dahanu with the objective of implementing screening of common cancers and Non-Communicable Diseases (NCDs) among women in tribal block of Maharashtra involving the state health system and community and identifying facilitating factors, barriers for implementation at program and community level. In-depth interview with health care providers (Medical officers, ASHAs and ANMs in Ashagad PHC) and sub centres was completed. In addition, FGDs with eligible women and facility survey have been completed. Findings of FGDs revealed that ASHAs play a key role in providing comprehensive and culturally appropriate care to communities; however, they were overburdened and needed support from the health system. Findings of FGDs of eligible women suggested that distinct differences existed among the tribal people concerning their knowledge on health, awareness and treatment-seeking behaviour. Interventions could change tribal cultural beliefs and increase knowledge also to improve the quality of health care in tribal areas.

Deciphering the Role of PSP94 and CRISP3 in Ion-Channel Modulation

Expression of two ion channels that are thought to be affected by CRISP and/or PSP94 proteins was evaluated in various prostate cancer cell lines. P2X5 channel, a purinergic receptor activated by ATP, was found to be expressed by prostate cancer cells. Preliminary experiments showed that in the presence of PSP94, PC3 cells showed decreased Ca influx when stimulated with ATP.

PSP94 as an Adjunct Marker for Serum PSA for differentiating between Benign Prostatic Hyperplasia (BPH) and Prostate Cancer (PCa)

A study in patients with serum PSA values between 4-20 ng/ml was undertaken to ascertain whether PSP94/PSA marker could aid in reducing the number of biopsies in patients having lower urinary tract symptoms and prostate diseases. Interim data analysis for correlation of serum PSP94/PSA marker in eighty prostate biopsy samples indicated that PSP94 along with PSA is a better indicator to differentiate between BPH and PCa cases. Estimation of PSP94/PSA ratio may obviate the need to take repeated biopsies from patients with prostate pathophysiology. Validation of PSP94/PSA ratio in larger sample size is in progress.

In-Vitro and In-Vivo Functions of Cell Surface Estrogen Receptors in the Context of Prostate Cancer

Estrogens have emerged as potent agents contributing to the pathogenesis of cancers of various solid tissues and prostate cancer is no exception. Robust experimental evidence implicating estrogens in the initiation and progression of prostate cancers are available. Existing data also suggest modulation in the expression of nuclear estrogen receptors with prostate cancer progression. Our interest has been to complement this knowledge by unraveling the significance of extranuclear estrogen receptors in the pathophysiology of prostate cancer using in-vitro and in-vivo approaches. Our previous

in-vitro studies demonstrated the presence and functional significance of estrogen binding proteins on the cell surface (csERs) of non-tumorigenic and tumorigenic prostate cancer cell lines. It was observed that the estradiol binding to csERs leads to activation of specific kinases, phosphorylation of cytoskeletal proteins, and consequently, epithelial-mesenchymal-transition in tumorigenic cells. Further csERs were detected in the prostate of a mouse model of prostate cancer -Transgenic Adenocarcinoma of Mouse Prostate (TRAMP). Genotyped animals were grouped according to the histopathological stage of prostate tumors and assessed for the presence of csERs in prostate tumors. Studies revealed that the percentage of cells that bear csERs are higher in prostate tumors, as compared to normal prostates. Further, the proportion of cells bearing csERs was found to increase with the progression of prostate cancer in TRAMP. This indicates a key role of csERs in prostate cancer pathogenesis.

Intervention to Increase Breast Cancer Awareness and Breast Self-Examination among Women in the Community- A Multiple Approach

The aim of the study was to increase the awareness about breast cancer and breast self-examination. A community level survey was conducted among 480 women of age 18 to 55 years from low socio-economic strata. The awareness about breast cancer, signs and symptoms, risk factors, breast self-examination and clinical breast examination was provided by experts. Significant increase in awareness risk, signs and symptoms of breast cancer was observed following the intervention.

In-vitro Evaluation of Vaginal Lactobacilli Isolated from Indian Women for Potential anti Cervical Cancer Activity and Elucidating its Possible Mechanism of Action

Selected Lactobacilli was investigated for elucidating the mechanism underlying their anti-cancer effects on different cervical cancer cell lines. Levels of E-cadherin, MMP9 and hCG were detected, post treatment with lactobacilli culture supernatants. Treatment with M92B, M118, and M129, notably upregulated E-cadherin levels in HeLa, SiHa and CaSki. Additionally, downregulation of MMP9 and hCG was observed in HeLa, SiHa and C33A cell lines treated with M129 and M269A. Lactobacilli metabolites induced elevated levels of anti-inflammatory IL-10 cytokine in HeLa, SiHa and CaSki cells. All the isolates reduced secretion of pro-inflammatory cytokines IL-1β, IL-6, IL-8 and TNFα in C33A and CaSki cells; whereas only M118 and M269A isolates could induce this effect in SiHa cells. However, treatment with culture supernatants of pathogens (*G.vaginalis, E.coli, S.aureus*) induced inflammatory cytokine production. Furthermore, certain lactobacilli treatments significantly downregulated the expression of apoptotic genes (caspase 8 and 9) in all four cervical cancer cell lines. Also, M269A induced transcriptional downregulation of autophagy related genes ATG14, BECN1, PRKAA2 in HeLa cells. Further research is ongoing to investigate the expression of E6 and E7 oncoproteins of HPV genes in cervical cancer cell lines treated with *Lactobacillus* metabolites.

Immune Response Genes: Variants and its Association with Cervical Cancer

To understand the association of host immune response gene variants with HPV infection and further complications, 223 cervical cancer cases; 176 HPV infected women with healthy cervix and 100 women with healthy cervix and without any infection were screened. The results highlighted a polymorphism in exon 5 of CD86 gene, which forms the extra cytoplasmic domain region along with the highly conserved exon 4. However, another polymorphism in CD86 gene at +2379G/C position in 3'UTR region affected binding ability of miRNA there by affecting CD86 expression and T cell activation. Twenty two SNPs in cytokine genes were studied in this population. Their allelic and genotypic frequencies were compared with other populations. Genotypic frequencies in all populations were significantly different from Indian population. Polymorphisms in IL-6 gene -174G/C

and TGFβ G/C codon 25 were significantly associated with cervical cancer. GG genotype was significantly higher in both genes in cervical cancer and HPV positive group as compared to controls. Cytokine levels for IL-6, IFNγ and IL-12 were significantly elevated in cervical cancer cases as compared to controls. IL-12 and IFNγ were similar in both treated and untreated cervical cancer cases, but IL-6 levels were significantly higher in untreated cases as compared to treated cervical cancer cases. IL-6 levels in treated cervical cancer cases were similar to that of control group. So, IL-6 can be used as a prognostic marker.

Primary Screening of High Risk HPV DNA by a Low Cost Molecular HPV Test for Early Detection of Cervical Precancers and Cancers among Women in Urban and Rural Community of Maharashtra

The study aims at identifiying various high risk HPV genotypes in the selected urban and rural community and comparing the results of genotyping, VIA and cytology with careHPV positive and hybrid capture II. The community sensitization and awareness activities have been initiated and conducted at Anganwadi Jijamata Nagar and ICMR family welfare clinics. A KAP survey has been initiated among the women attending clinics before enrolment to assess their knowledge on cervical cancer. Till date 130 women have been enrolled in the study. Samples for hybrid capture 2 and pap smear have been collected. Data are being analysed.

Evaluating the Potential of Trop2 as Immunotherapeutic Target for Ovarian Cancer

The N-terminal proteolytic cleavage of Trop2 was shown to occur by a transmembrane serine protease, matriptase. Alanine substitution mutants showed a novel way of regulation of cleavage of Trop2 dimers by matriptase. Trop2 was also shown to be liberated by cancer cells via exosomes. Anti-Trop2 antibodies inhibited invasive ability of Trop2 expressing cancer cells.

Assessing Trop2 Expression and its Correlation with anti-Trop2 Immune Status in Ovarian Cancer Patients

Ascetic fluids from 35 ovarian cancer patients have been collected so far. Trop2 expression at RNA and protein level was tested in the cells separated from the ascetic fluid of 21 patients. Varying levels of Trop2 expression was seen in different patients. 8 out of 21 patients showed high levels of Trop2 transcript whereas 10 patients showed high Trop2 at protein level. The cell free ascetic fluid was also tested for liberated or cleaved Trop2 fragments and only 6 out of 10 patients with high Trop2 showed the presence of Trop2 in the ascetic fluid.

Exploring the Therapeutic Potential of Peptides Targeting Lysophosphatidic Acid Receptors in Ovarian Cancer

Lysophosphatidic acid (LPA) is one of the key molecules involved in ovarian cancer metastasis. LPAR2 and LPAR3 are overexpressed in ovarian cancer. LPA-LPAR interaction activates signalling pathways leading to cell proliferation, cytoskeletal changes, angiogenesis, cell adhesion, and invasion leading to cancer metastasis. Peptide molecules have shown promise for cancer treatment. Targeting LPAR with LPAR binding peptide may disturb LPA-LPAR interaction and might delay ovarian cancer metastasis. The present study aims to identify the peptides targeting LPAR using phage display peptide library approach. Expression of LPARs at mRNA level in normal mice organs and cancer cell lines was assessed. Ovary expressed all 5 LPARs at significant level, followed by uterus compared to other organs. Similarly, the expression of LPAR (1-6) at protein level in the cell lines as well as other mouse organs will be checked. LPAR3 has been selected for identification of the LPAR binding peptide by phage display biopanning approach.

HEALTH TECHNOLOGY ASSESSMENT

HTA on Long Acting Reversible Contraceptive Methods in India

Several input parameters were derived from literature review, primary costing study and analysing secondary data and used in the decision analytical models. The results suggested that Implanon NXT is a safe and cost-effective contraceptive that could be considered for program introduction after conducting a feasibility and acceptability study, creating awareness, phased top-down approach for introduction into program. Pre-insertion counselling, preparedness for management of side-effects, efficient follow-up and tracking mechanism for users are other pre-requisites.

HTA of Uterine Balloon Tamponade for Management of Postpartum Haemorrhage

Among three uterine balloon tamponades, condom and ESM UBT were found to be cost-effective. However, available evidence on clinical effectiveness of ESM UBT was not very robust. It was recommended that a well-designed random controlled trials needs to be conducted to assess the clinical effectiveness of these methods including the health care provider's perspectives on use of these methods.

Public Health Importance

- The following policy briefs were prepared:
  a. Expanding Informed Contraceptive Choice for Indian Women: Will Nexplanon Matter
  b. Enhancing Utilization of Adolescent Health Services
  c. Involvement of Self Help Group (SHG) Women to improve health seeking behavior of tribal women
  d. Genetic testing (CFTR-mutations) in Indian men with congenital bilateral absence of vas deferens (CBAVD) before undergoing Intracytoplasmic Sperm Injection (ICSI)
  e. Genetic testing for non-obstructive azoospermia and oligozoospermia
  f. A Model for Addressing Burden of Snakebites in Rural India through Health System Capacity Building
  g. Reducing TB burden. Screening Aspergillosis in ATT non-responders.
- MRHRU Dahanu has been recognized as the 38th Sentinel surveillance hospital for diagnosis of Dengue and Chikungunya since October 2017.
- Newborn screening project through MRHRU has helped in identifying newborns with sickle cell trait or disease. This will help in better management of children born with this disease. Family members of these children are screened for this genetic disorder and offered genetic counselling.
- Low PlGF levels in the urine in third trimester of pregnancy were found to be associated with the low birth weight of the baby.
- Receiving Operating Characteristic analysis of DNA methylation of global and imprinted genes demonstrated Global 5mC level in spermatozoa to be a good candidate with highest diagnostic efficiency for paternal epigenetic factors in recurrent pregnancy loss.
- Paternal obesity affects sperm methylome of genes involved in developmental pathway and the methylation status correlated with the expression of some of these in the resorbed embryos sired by the obese male rats suggesting transmission of aberrant epigenetic signature of the spermatozoa to embryo leading to embryo loss.
- Cypermethrin, an endocrine disruptor, affects expression of genes involved in steroidogenesis and gametogenesis thereby affecting male and female fertility.
- Newborn screening for CMV infection is important for timely intervention and clinical management.
- Development and characterization of a mouse model for endometriosis to show how the steroid hormone receptors in the ectopic endometrium are altered providing an explanation for steroid resistance.
- Commercialization of the assay for Y chromosome microdeletion is under process

ICMR-NATIONAL ANIMAL RESOURCE FACILITY FOR BIOMEDICAL RESEARCH, HYDERABAD (ICMR-NARFBR)

Animal experimentation in Bio-medical research continue to remain crucial to find out better ways to understand, prevent, treat and cure diseases as currently there are no existing alternatives to substitute the biological systems. World over, new drug research as well as tests meant for assuring the quality, safety and efficacy of pharmaceutical products /vaccines/ recombinant products are based on experiments involving animals. The use of animals for research is essential for the development of new and more effective methods for diagnosis and treatment of diseases that affect both humans and animals. Virtually every breakthrough in new drug/vaccine development has been the direct result of research in animals.

Major research areas

Use of innovative methods for testing of drugs, vaccines, recombinant products, herbal medicines, genetically modified and other new molecular entities and modern medical devices. It also has research and development schemes for developing alternatives and validated testing approaches for treatment of human and animal diseases.

Evaluation of therapeutic efficacy and understanding the mode of action of a polyherbal formulation on streptozotocin - nicotinamide induced diabetic cardiomyopathy: In vitro and In vivo studies

Diabetic cardiomyopathy (DCM) is multifactorial. In the current study, centre made an attempt to prepare poly herbal formulations (PHF) with different medicinal plant extracts and to evaluate its beneficial effects in the protection of DCM. Team evaluated the effects of PHF on experimentally induced DCM in mice and H9C2 cell lines.

From this study, so far centre has observed fruitful beneficial effect against diabetes and its associated DCM. From the TOBEC and DXA studies, it was found that PHF shown significant effect on regulation of physiological parameters. From the biochemical analysis, it was revealed that PHF demonstrated significant protection against inflammation, oxidative stress, and cardiac fibrosis and also prevented the pathological alterations in tissue level which were confirmed with histo pathological analysis (TEM).

Centre also observed that PHF exhibited noteworthy effect against DCM via activation of Nrf2 pathway in PHF treated cell lines and experimental animals as well.

Fig.1: The 15th PEC meeting was held on 22nd June 2019, the committee reviewed the progress of works of construction in the institute and made suitable recommendations.

Fig. 2: The institute has organised ICMR-NARF Haritha Haram program on 9th August 2019. The District Collector and Magistrate Medchal - Malkajgiri, Dr M.V.Reddy, I.A.S was invited as the Chief Guest along with other local leaders who participated in the program. Staff has planted more than 1000 saplings on this occasion.

Fig. 3: The 16th PEC meeting of the NARF Institute has been held on 1st November 2019. The Committee reviewed the progress of works of the construction in institute and made suitable recommendations.

EXTRAMURAL RESEARCH

BASIC REPRODUCTIVE BIOLOGY AND FERTILITY REGULATION

Phase-III Clinical Trial with an Intravasal Injectable Male Contraceptive – RISUG®

As per the recommendation of Drugs Controller General of India (DCGI), under this task force study, the following activities are going on currently:

- After the approval of experts and after pilot testing the questionnaire to obtain data on the psycho-social and behavioural aspects and sexual activity of the RISUG® injected couple has been sent to all the participating centre with a request to collect the data urgently.
- The data is being collected.
- The clinical reversibility protocol has been prepared for undertaking the study.
- The testicular biopsy / FNAC study was carried out at the centres to know the exact status of spermatogenesis in the testes. Normal spermatogenesis is seen in both the testes and it is concluded that normal spermatogenesis remains ongoing in the testes of subjects after 3 to 5 years of RISUG® injection.
- Follow up of the RISUG® injected subjects is going on for assessing the safety and efficacy of the drug.

Phase I-II Clinical Trial on Safety, Immunogenicity and Probing Efficacy of the Revived Recombinant Vaccine against human Chorionic Gonadotropin (hCG)

To determine the safety and immunogenicity of hCGβ-LTB vaccine in sexually active women and its ability to prevent pregnancy without impairment of ovulation and derangement of menstrual regularity and bleeding profiles the clinical trial is going on at AIIMS, New Delhi and Sir Ganga Ram Hospital, New Delhi.

For immunogenicity and safety, total 50 sexually active healthy women are to be enrolled at two centres (25 subjects at each centre) and Total 05 subjects in each dose group (i.e. five doses of 100, 200, 300, 400 & 500 µg of protein vaccine) will be enrolled

The enrollment details of the subjects in both the centres is given below:

Table 1: The enrollment details of the subjects in both the centres.

Centres	Screened	Pre-immunization investigations done	Primary vaccination completed	Enrolled in Study	Being followed up	Excluded and Reason/s of exclusion form study
AIIMS	11	11	7	7	7	4 (1 low progesterone, 1 out of station, 1 discontinued, 1 Refused since husband not willing)
SGRH	10	4	4	4	3	6 (1 hypothyroid, 1 refused IUCD, 1 skin allergy, 1 ANA+, 2 Low progesterone) 1 (Refused after enrollment)
Total	**21**	**15**	**11**	**11**	**10**	**11**

In AIIMS, New Delhi, all the 5 subjects of first dose 100 µg and 2 subjects of second dose 200 µg has been enrolled while in SGRH only 3 subjects of first dose 100 µg has been enrolled and followed up is going on.

National Registry of ART Clinics and Banks in India

National Registry of ART Clinics and Banks in India is under the process of establishment, as per the provisions of ART (Regulation) Bill. Under National Registry, around 1866 ART Clinics and Banks have been identified. Out of 528 approved ART clinics, only 09 clinics are IUI clinics and out of 544 under process ART clinics, 33 are IUI clinics. The status of these ART Clinics and Banks are given below as Table No. 2.

Table 2: The status ART Clinics and Banks.

S. No.		ART Clinics	ART Banks	Total
1	Total no. identified	1652	214	1866*
2	Total no. enrolled	528	-	528
3	Total no. of confirmed Clinics and Banks under process	761	214	975
4	Total no. of Clinics and Banks yet to respond	361		361

*** Two ART clinic enrollment cancelled**

Zone-wise distribution of ART Clinics and Banks in India are given below as Fig. No. 4 & 5.

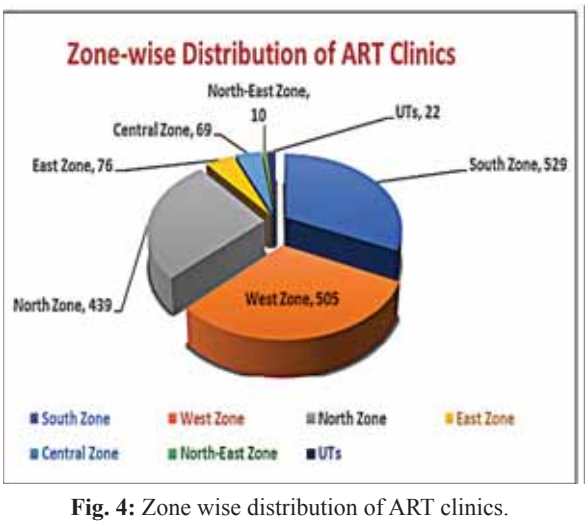


Fig. 4: Zone wise distribution of ART clinics.

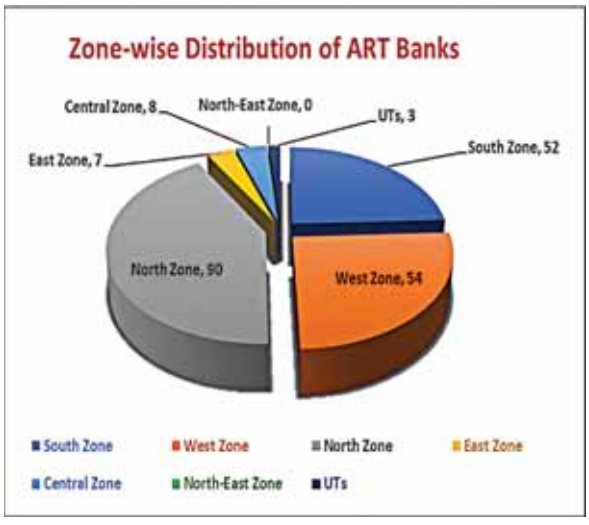


Fig. 5: Zone wise distribution of ART Banks.

Other activities of the ICMR National Registry are given below:

- In view of the ongoing COVID-19 pandemic, ICMR is currently formulating guidelines for resumption of ART Clinic services on a National level to avoid any sort of disparity between protocols to be followed by ART Clinics all over India. These guidelines are aimed at minimising the chances of spread of COVID-19 infection to patients and ART clinic staff and are under the process of finalization.
- To obtain online monthly data from all the enrolled ART clinics regarding all their activities related with treatment and management of infertility, their outcome and side effects if any, a detailed Online performa has been designed which is under process of finalization.
- Based on the guidelines developed by ICMR National Registry and approved by DGFT, the ICMR National Registry has issued 13 NOC's for export of human embryos / gametes for the treatment of infertile couple themselves.
- The guidelines developed by the ICMR National Registry on import of frozen human embryos and/ or gametes are being debated with DGFT and currently, the DGFT is considering the provision of importing frozen human embryos and/ or gametes.
- The National Guidelines for Accreditation, Supervision and Regulation of ART Clinics in

India were developed by ICMR in 2004 which were approved by Govt. of India in 2005. Since, ART is very dynamic science and so many new technologies are being developed since 2005. Therefore, the ICMR National Registry is in process of revising the above-mentioned National Guidelines in the light of current ART technologies being developed and practised around the world.

Evaluation of a Progesterone Vaginal Ring as a New Contraceptive Option in India - An Indo-US collaborative study under CRHR of DBT

The results of this study show that the PVR is non-inferior to the IUD in its efficacy to prevent pregnancy. Both methods were highly effective in preventing pregnancy. The probability of subjects becoming pregnant was slightly higher in the PVR group (0.7%) compared to the IUD group (0.4%). The difference in the pearl index of the PVR and IUD groups with the upper limit of 95% CI was 0.37, which was well within the specified limit of 2.5% non-inferiority margin.

Pregnancy - Pearl Index after Use of Product (Efficacy Population)

Table: 3: Pregnancy - Pearl Index after Use of Product (Efficacy Population).

	PVR	IUD
Number of woman -years (per 100 users)	323.1	286.8
Number of Pregnancies	2	1
Pearl Index (95% CI)	0.62 (0.55, 0.69)	0.35 (0.29, 0.41)
Difference between the pearl indices (95% CI)	0.27 (0.17, 0.37)	

Abbreviations: CI = confidence interval; IUD = Intrauterine Device; PVR = Progesterone Vaginal Ring

The continuation rates of subjects in PVR group when compared to the IUD group was similar at one month and gradually reduced as the study progressed. One reason driving the higher discontinuation rate in the PVR group was ring expulsion. According to the study protocol, if a subject lost her ring during the study or if the ring could not be retrieved then she was discontinued from the study. At all-time points, the majority of PVR subjects experienced prolonged amenorrhea compared to IUD subjects (median days: 405 days vs 120 days).

Kaplan-Meir plot of lactational amenorrhea

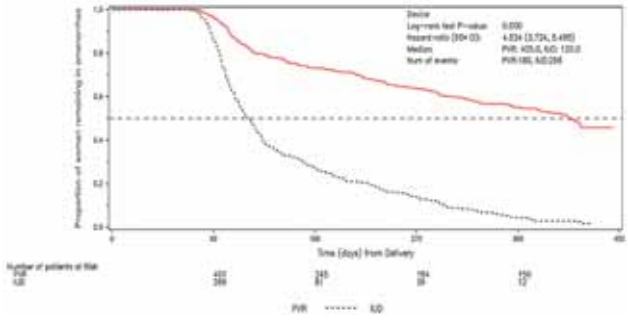


Fig. 6: IUD=intra-uterine device, VR=progesterone vaginal ring.

The use of PVR or IUD did not have any notable effect on breast feeding and supplemental feeding episodes among the infants. Infants from both groups did well in terms of growth (height and weight). The use of PVR and IUD in subjects with child bearing potential over the 12-month period was safe and did not result in treatment-related SAEs or maternal deaths. The PVR device was well accepted among subjects opting for this device. The treatment emergent adverse event (TEAEs) occurring in subjects were similar between the PVR group (24.2%) and the IUD group (23.0%) and were usually mild or moderate in severity. Two SAEs (seizure and excessive bleeding) were reported in IUD group of which one (excessive bleeding) was considered to be probably related to the study drug. The most frequently reported AEs in the PVR group compared to IUD group were vaginal discharge (PVR: 5.2%, IUD: 3.3%), metrorrhagia (PVR: 3.7%, IUD: 2.1%), vaginal infection (PVR: 2.2%, IUD: 1.5%), medical device discomfort (PVR: 2.0%, IUD: 0%), and amenorrhea (PVR: 2.0%, IUD: 1.2%). The most frequently reported AEs in the IUD group compared to PVR group were menorrhagia (IUD: 9.4%, PVR: 4.6%) and back pain (IUD: 2.7%, PVR: 1.3%). The most common AEs leading to discontinuation were menorrhagia (PVR: 8 [1.7%], IUD: 17 [5.2%]), vaginal discharge (PVR: 4 [0.9%], IUD: 0), vaginal ulceration (PVR: 4 [0.9%], IUD: 0).

A similar proportion of infants in PVR group (28.3%) and IUD group (30.9%) experienced AEs/morbidities; however, none of these AEs/ morbidities were considered related to the study drug. A total of 7 infants, 4 (0.9%) in the PVR group and 3 (0.9%) in the IUD group experienced SAEs, two of which resulted in death. None of the infant SAEs were considered related to the study drug. The infant growth in the PVR and IUD group were similar as assessed by the WHO MGRS standards and confirmed that neither PVR nor IUD affected infant growth. Among PVR users, the majority of subjects felt it was easy or very easy to put the ring in the vagina at all acceptability assessment time points (3 months [87.4%], 12 months [93.9%] and at early termination [78.6%]). A small proportion felt it was difficult to put the ring in the vagina (3 months [7.6%], 12 months [3.8%] and at early termination [9.8%]). Among IUD users, comparatively fewer subjects felt that the procedure for inserting the IUD went very easily or easily (3 months [74.3%], 12 months [74.9%] and at early termination [65.4%]). The rest of the subjects felt the procedure for inserting the IUD was neither easy nor difficult (3 months [16.6%], 12 months [17.0%]; early termination [12.7%]). Some subjects found insertion of the IUD difficult and very difficult (3 months [9.1%], 12 months [8.1%] and at early termination [21.8%]). The majority of subjects in the PVR and IUD groups were satisfied with the use of their contraception method and a high proportion of subjects were either very satisfied or satisfied with the PVR and IUD (3 months: 90.6%, 12 months: 98.0%) and IUD (3 months: 92.2%, 12 months: 93.4%) method. A higher percentage of subjects who discontinued early from the IUD group were dissatisfied (41.8%) compared to subjects who were dissatisfied and discontinued early in the PVR group (25.4%).

The clinical study reported has been formulated and approved by the DSMB and the Project Advisory and Review Committee for submission to the drug regulators DCGI for consideration of PVR as an additional user-controlled contraceptive option for lactating women for extended post-partum until one year and more. The study partner from HLL Lifecare responsible for transfer of technology of PVR will initially import the device and evaluate the demand for the method outside clinical trial settings so that acceptability could be evaluated and demand for the method could be evaluated in existing programme settings.

Regulate the reproductive health issues of human from Jammu and Kashmir region

To explore the knowledge about various health issues in both males and females to analyse the mechanism of development and progression of reproductive cancer, urological and gynaecological disorders which in long term may help in making personalized medicine. Total 544 blood samples collected where 239 were primary infertile and 64 were secondary infertile couples. Age was found higher in males for both primary and secondary infertile couples with statistically significant ($p<0.05$) while BMI was higher in males and females for primary and secondary infertile couples respectively. Semen analysis has been done on minimum of 200 sperm samples for morphological abnormalities of head midpiece and tail. Parameters, Large head, small head, round head, Amorphous head, Double head, Abnormal head morphology, bent neck, Thick midpiece, Cytoplasmic droplet, Short tail, Multiple tails, Abnormal midpiece morphology, Abnormal tail morphology and Motility grade A were found statistically significant ($p<0.05$) comparted with control group. The study will try to fill the gap in literature from Jammu and Kashmir State and the data can also help state Govt. to frame policies reading the same.

Feasibility of multigene panel for diagnosis and management of Autism Spectrum Disorder in early neonatal period(<7days)

This study will evaluate the validity and feasibility genetic testing as a screening test for prediction of future of ASD by identifying the specific genetic changes which may be etiologically responsible for causing ASD in the Indian population. Understanding the biologic factors that contribute

to condition can lead to individual treatment and understanding of genetic variations can then lead to understanding of future treatment. The study will add to the global pool of knowledge related of the genes involved in the causation of ASD and its associated syndromes. Total of 25 Autism affected subjects from Indian state Uttar Pradesh and Kerala were enrolled in the study. A detailed phenotypic characterization was performed in all the patients. Additional 15 samples were in transit from KIMS Trivandrum making the number of samples to 40. Mood disorder, Intellectual disability, Speech disorder were found in all the subjects while no subjects has been found with Self-injury and Deafness. Only 4 with Motor coordination problems, 3 with Epilepsy, 5 with Sleep disorder has found and only 2 were not affected with ADHD. Chromosomal microarray (CMA) analysis was completed in 10 subjects as the first line of screening method. CMA analysis identified copy number variation in the complete genome and also has the ability to genotype 200,000 SNPs presents throughout the genome. Extensive searches and analysis of microarray data has been done to identify previously reported and novel pathogenic variation associated with subjects. This study has potential to compliment the RBSK program proposes to use the existing framework and budgetary provisions for the benefit of the population. Early detection and early therapy will lead to better outcomes and improve community trust and participation and effective healthcare delivery.

National Centre for Technology in Family Welfare (NCTFW)

National Centre for Technology in Family Welfare (NCTFW) was established as a continuing program with expertise and specialties to expeditiously respond to technological problems which are in the National Family Welfare program. The long-term continuous monitoring of physiological parameters may aid in development a data mining algorithm-based model to predict preterm birth. 70 units of RISUG prefilled syringe and specification and testing methods was submitted to IPC Ghaziabad. Visit to Sonipat IITD was made from IIT Delhi Hauz Khas for laboratory planning and design, site assessment, laboratory design assessment, GMP facility required for drug and device development and testing etc. Visit was carried out to supply Standard Maleic Anhydride sample to IPC Ghaziabad, for clarification of endotoxin testing method and for RISUG syringe handling method sterility testing protocol. GMP laboratory design and planning for scientific experiment at IITD Sonipat. GMP manufacturing and marketing certification for male injectable contraceptive (RISUG). Simultaneously standardizing gamma irradiation-based biopolymer development, scale up manufacturing, standard development, standard testing procedure for drugs and medical devices, and interaction with several governmental bodies. Male injectable contraceptive (RISUG) manufacturing for mass usage and its advance version for prostate cancer prevention. The NCTFW is a technological program addressing technological issues of the ongoing National Family Welfare Programme of the Ministry of Health and Family Welfare, Govt. of India.

Development of dendritic cell vaccine for the treatment of recurrent/metastatic reproductive cancers

The study intends to use the entire repertoire of tumor antigens for priming DC that were generated in-vitro with patient tumour cells. SPAG9 has been found to be expressed in various cancers like ovarian, breast, cervical cancer. The use of primed DC with SPAG9 protein as vaccines may help on generation of cytotoxic T lymphocyte response in addition to any pre-existing humoral response. Such stimulus may help in eliminating residual tumour cell much more effectively. The study ensures early diagnosis in cost effective manner and also better blood-based biomarkers for follow up after therapy will ensure identifying much before clinical relapse and instituting effective therapies before frank relapse. So far 39 samples were collected from epithelial ovarian cancer patients at the time of surgery (before or after neoadjuvant chemotherapy). The percentage of tumour was determined by a trained cytologist.

Cells were frozen with 10% DSMO containing freezing mixture and stored in liquid Nitrogen. A comprehensive analysis and evaluation of various combinations of selected antigen antibody system will be used for development for autoantibody profile involving different panels or array of TAA in the research initiative will be useful for diagnosis of different types of cancer.

MATERNAL HEALTH

Women's Reproductive Health

ICMR Polycystic ovary syndrome study (PCOS): A Multicenter study across India

To generate nation-wide data on prevalence of PCOS, its comorbidities and any variations in Phenotypes or treatment responses among Indian women, this study is being undertaken at 10 sites representing various geographical regions of India. The objectives of this study are to estimate the prevalence of PCOS including in urban and rural population in India including burden of metabolic and other comorbidities among Indian women. The study also assesses efficacy of treatment of oral contraceptive pills vis-à-vis metformin on PCOS at two centres.

The study is in an advanced stage and has completed about 70% of all enrolments, while the investigations to confirm diagnosis and assess comorbidities are ongoing in enrolled women. The table below shows the overall progress of the study.

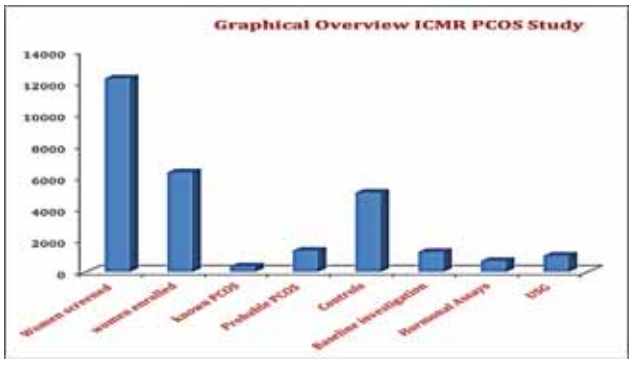


Fig. 7: ICMR PCOS Study.

Capacity building through HRRCs for screening of common cancers (oral, breast and cervical)

This study is being undertaken at 4 ICMR HRRC centers to create awareness regarding oral, breast and cervical cancer among women attending out-patient and in-patient services in tertiary care hospital and to provide facility for opportunistic screening of oral, breast and cervical cancer to women attending out-patient services in the department of Obstetrics & Gynecology. The study also aims to provide pre-service and in-service training to doctors and nurses for screening of oral, breast and cervical cancer in tertiary care hospitals. The study operationalizes the Government of India guidelines for screening and management of common cancers. The study has completed one year and screened around 900 women.

Smokeless Tobacco and Reproductive Health

Assessment of harmful effects from smokeless tobacco (SLT) and areca nut use remains to be neglected among females, especially pregnant women. Hence, a study aiming to understand SLT and areca nut use and consequence in women of reproductive age as a means to develop training and behaviour change intervention models for cessation is ongoing. The study is examining the association between socioeconomic factors of SLT use among women of reproductive age and adverse pregnancy outcomes using Demographic and Health Surveys in selected south Asian countries (Afghanistan, India, Nepal, Maldives and Pakistan).

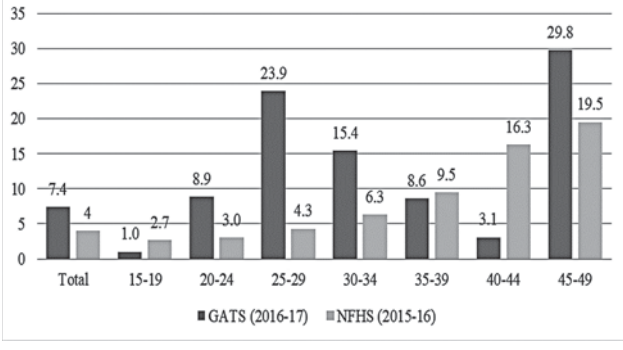


Fig. 8: Percentage of Pregnant Women, reporting any kind of SLT use in India.

ICMR Registry of PPIUCD and Centchroman Contraceptive Users

The Government of India has introduced some new contraceptive methods in its programme including (Post partum IUCD) PPIUCD and Centchroman. This ongoing study at 6 sites is planned to understand the satisfaction and continuation rates among women using Centchroman and postpartum IUCD and to document the side effects/adverse effects of Centchroman and PPIUCD. Findings at one year are tabulated.

Table: 4: Infertility and Pregnancy loss: Assessment and Interventions

Total women counselled		16903	
Total women Recruited		3457	
		PPIUCD	Centchroman
Numbers in each group		3032	401
PPIUCD Expulsion		162	
PPIUCD Removal		165	
Centchroman Stopped			58
Centchroman not taken			37
Total follow up	6 weeks	1349	202
	3 months	814	171
	6 months	439	25
	12 months	0	0
Lost to Follow up		26	9

Immuno-modulatory effect of Intralipid in women with recurrent implantation failure with elevated uterine Natural Killer cells (RCT)

Objectives of this study are to evaluate the role of NK cells in implantation failure and to study the immunomodulatory effect of intralipids in women with elevated NK cells undergoing fresh IVF/ICSI on implantation rate and clinical pregnancy rate. The observation of increased Natural killer cells (NK cells) in the endometrium of women with reproductive failure has suggested they may play a role in this pathogenesis.

Molecular Analysis of promising immune-regulatory pathway involved in Recurrent Pregnancy Loss (RPL)

This study aims to investigate the role of HLA-G and FOXP3 polymorphisms in the regulatory sequences (3'UTR and promoter) in women with recurrent pregnancy loss in comparison with parous women and estimates the circulating sHLA-G and FOXP3 levels among RPL and parous women and anti- (IL-4, TGF-β) inflammatory cytokines among RPL and parous women. Reduced levels of HLA-G and FOXP3, a master regulatory transcription factor of Treg cells may impact the anti-inflammatory milieu during pregnancy. The genetic alteration in these genes may disturb the pregnancy outcome. The ongoing study will assess any relation of the pathway with RPL.

Psychosocial Dynamics of Pregnancy Loss: Development of a Multidimensional Scale & Development and Efficacy (a Randomized Control Trial) of a Group Psychological Intervention Module

Pregnancy loss is a painful and traumatic event that can occur at any time during the pregnancy. The ongoing study aims to provide efficacious psychological treatments for females who have experienced pregnancy loss. These treatments will be in the form of manual or e-modules formats which are presently non-existent in India. Once it is done through present RCT study, these females either at the hospital or at their home can use both manual and e-modules.

MATERNAL HEALTH

ICMR Centre for Advanced Research in Mechanisms leading to Preeclampsia

The Centre is undertaking studies to examine the possible factors involved in the pathology of preeclampsia at early and later stages of gestation and establish the role of long chain polyunsaturated fatty acids (LCPUFA) and micronutrients in mechanisms associated with preeclampsia. A total of 1076 pregnant women have been recruited early in pregnancy and followed at 4 time points until delivery. Information on subject's clinical history, medication, SLI, physical activity, 24-hour dietary recall, food frequency questionnaire, ultrasonography and color Doppler measures were recorded at each time point. Biochemical analysis of various parameters is ongoing. Children are

being followed up for anthropometry at various time points and developmental assessment at 2 years of age. Preliminary analysis suggests that

- Women who develop PE have a higher age, BMI and blood pressure right from early pregnancy until delivery as compared to non-PE women
- Percent women in the PE group conceiving through IVF and IUI was higher as compared to the non-PE group and delivered by caesarean section
- Majority of the women in the PE group were nulliparous. TSH levels were observed to be higher in women with PE in early pregnancy
- Fetal measurements by USG such as BPD, HC, AC and fetal weight at 32-35 weeks were lower in women with PE as compared to non-PE group
- Doppler measure such as mean uterine artery PI was higher in PE as compared to non-PE group
- Women with PE had placentae with lower thickness and had a higher percent of bilobed and irregular shaped placentae
- Babies born to mothers with PE had a lower birth weight, length and head circumference. The percent of SGA babies was higher in the PE group as compared to non-PE group.

Gene specific methylation analysis of selected candidate genes *PlGF, FLT-1, HIF1A, HIF3A* and *PEMT* shows significantly disturbed methylayion patterns. This disturbed methylation patterns of genes may influence the process of placental angiogenesis in women with preeclampsia.

To study feasibility of Oral TDF-containing PrEP, administered, once daily orally to men having sex with men (MSM) and transgender women (TGW) in India.

This prospective two-site cohort demonstration project using observational study design would assess retention, acceptability, adherence, potential unintended consequences, such as changes in use of condoms, risk perception and behavior and other HIV preventive interventions with oral PrEP given through community settings and at clinical facilities and MSM and TGWs. During the reporting period, study preparatory activities were completed. Community sensitization and mobilization was initiated following protocol training. The number of community sensitization and mobilization activities conducted in reporting period are given in the figure below.

Fig. 9: Several preparatory activities.

Fig. 10: Community Engagements meetings.

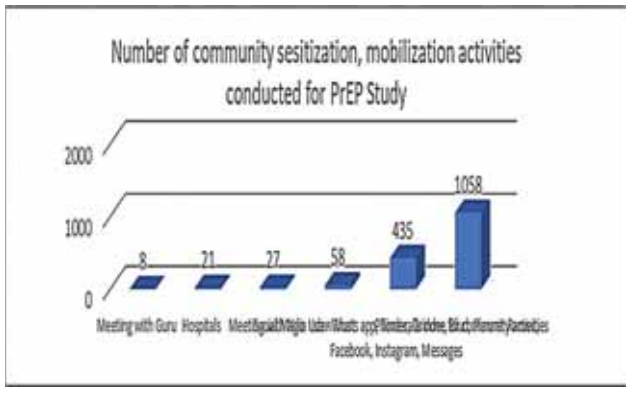


Fig. 11: Number of community sensitization & mobilization activities.

Study enrolment was initiated in January 2020 and a total of 350 individuals have been contacted/pre-screened, 114 have undergone screening and 60 subjects enrolled.

Development of Fetal Growth Nomograms Standards Specific to the Indian Antenatal Population

Assessment of the fetal growth is an essential part of prenatal care; the aim being to detect suboptimal growth as restriction of the fetal growth has immense implications for the neonatal wellbeing. This study aims to establish a reference for fetal growth pattern in our population based on serial ultrasound scans right from early pregnancy so as to provide an effective reference tool to be uniformly applied in our health systems and ultrasound software to detect suboptimal fetal growth. The study has completed one year.

The effectiveness of Peanut Ball device during labor on maternal & neonatal outcomes and stress level in low-risk primigravid women - A Randomized controlled trial

The objectives of this study are to determine the effectiveness of the use of a peanut ball device during labor in terms of maternal outcomes such as the pattern of uterine contractions, duration of active stage of labor, duration of the 2nd stage of labor, nature of delivery, need for pain medications, perception of pain and occurrence of Post-Partum Haemorrhage and neonatal outcomes. The study is about to complete one year.

Prevalence, Procreation, Persecution and Prevention regarding Caesarean-Section Deliveries/Births: A Systematic Review and Meta-Analysis

This study is being carried out with an objective to assess the prevalence of CS deliveries across different regions of the world, stratified by type of health facility, rural-urban settings, age groups, socioeconomic status and education level of the delivering women, major indications, risks associated with unnecessary CS and prevention thereof. The study has begun in January 2020.

Quality of intra-partum and immediate post-partum care of mothers and newborns: An implementation research to improve performance of LaQshya program

LaQshya initiative has been launched to fast track quality of care, with a 360-degree approach towards (a) structural and (b) process improvement around labor room and maternity OT in Government facilities. In this proposed study, district health system shall entirely lead and implement the LaQshya interventions as desired under the program guideline; the research team shall closely observe, document bottlenecks, and co-create strategies to overcome these in partnership with health system and primary implementers. The overall implementation strategy will be to catalyze the working of the health system leveraging currently available human as well other resources and accelerate the process of improvement.

ICMR research initiative on Gestational Diabetes Mellitus (GDM)

A prospective multi-centre observational cohort study would be shortly initiated to evaluate maternal and fetal outcomes in women diagnosed with GDM or normoglycaemia using IADPSG criteria, among women diagnosed with normoglycaemia by DIPSI criteria. The study findings may enable government and concerned authorities to revise policies for GDM diagnosis in health programs. To assess the implementation of the GOI guidelines for the diagnosis and management of GDM at different levels of health care delivery at both rural and urban settings across India and determine the challenges, a multisite mixed method prospective cross- sectional study in collaboration with the state and district health system would be carried out across six regions of the country. Based on the results of this situational analysis, a multipronged intervention package model for implementation at district level would be developed.

CHILD HEALTH

Comparative effectiveness of two mobile-based strategies on adherence to IMNCI guidelines for managing children suffering from pneumonia: a cluster randomized control trial.

The study aimed at developing two mobile based strategies and comparing their effectiveness in adherence to the guidelines – one by providing a job aid to health workers and other by knowledge enhancement of caregivers**.** e-IMNCI app was found useful as a job aid, which was apparent from the marked difference between assessment, classification, referral and treatment of the sick children using IMNCI guidelines. It proved to be a better strategy over the SMS based mobile strategy for adherence to IMNCI guidelines, through rigorous qualitative data analysis, as mothers didn't have cell phones and mostly messages were sent to the cell phones of their husband or in-laws.

Indian adaptation and validation of the adapted ASQ-3 (ages and stages questionnaire). scale for Indian infants) in Indian children 2 to 24 months of age: A multicentric study.

This project evaluated sensitivity, specificity, positive and negative predictive values of Indian adaptation of ASQ-3 (Ages and Stages Questionnaire) as a developmental screening tool as compared to reference standardized tool (DASII- Developmental Assessment Scale for Indian Infants) in at risk Indian children 2 to 24 months of age (for each individual age group). The overall sensitivity of Indian adaptation ASQ in detecting developmental delay was 94% and specificity was 83% with a negative predictive value of 82.3%. Sensitivity of Motor domains (gross motor, fine motor) of Indian adaptation of ASQ-3 was 98.1% and specificity was 85.4% with a negative predictive value of 93.6%. The tool can be used for Neurodevelopment screening across India in peripheral health center.

A pilot study to determine causes of deaths in under five children in tertiary hospital setting using minimally invasive tissue sampling technique (MITS)

To assess feasibility and acceptability of minimally invasive tissue sampling (MITS) a pilot project is ongoing at Safdarjung Hospital New Delhi, ICMR National Institute of Pathology, New Delhi with funding support from Bill and Melinda gates Foundation to build capacity for performing MITS in a tertiary hospital setting and to standarise the methodology including grief counselling. Formative research identified the facilitators, barriers and potential opportunities related to MITS. Finding suggest that MITS is likely to have higher acceptability for deaths in children and stillbirths, where post mortem procedure was hitherto believed to be unfeasible. Paediatrician, obstetrician and gynaecologist and pathologist were trained on MITS at Maputo children Hospital in Mozambique. Till date 154 out of 200 proposed MITS (150 in under five children and 50 still birth) has been performed. Overall acceptance for MITS is around 50%. Tissue and non-tissue (blood, CSF, urine, nasopharyngeal and rectal swabs) samples collected are being processed for determining causes of deaths.

Establishment of Health and Demographic Surveillance System in Dibrugarh district, Assam (Dibrugarh –HDSS)

This is first HDSS under ICMR (Dibrugarh-HDSS) started in the year 2019 covered a total population of 1, 06,769 from 60 villages and 20 tea gardens predominantly representing tea garden community. Census of 60 villages and 20 tea gardens have been completed. Demographic and health data have been collected at individual level has been collected. Proportion of male population is 49.6% percent and female 50.4% percent, majority of the population is in the age group of 20-29 years. All these data were entered using unique mobile application software developed for this purpose.

Fig. 12: Study areas (villages).

Fig. 13: Study areas (tea gardens).

National Registry for Rare and other inherited disorders

The registry has been initiated at 20 sites for 6 major disease conditions (Storage disorders (LSDs & GSDs), Small Molecule IEMs, Hematological Disorders, Skeletal dysplasias, Primary Immune deficiencies, Neuromuscular Disorders) for which treatment is available. It is a hospital based registry that aims to to generate hospital based prevalence data on rare diseases and collect epidemiological and phenotypic data of affected patients. Data will be entered on online ICMR portal. Preparatory activities are ongoing, data collection and entry will follow soon.

To study the bacterial aetiology, antimicrobial sensitivity pattern resistance determinants and associated risk factors of neonatal sepsis in 4 different districts of Assam has been initiated

Study is ongoing since 2019 July. Culture positivity rate was found to be 54.5%, 34.1% and 23.3% from Tinsukia civil hospital (n=22), Silchar Medical College (n=102) and Barpeta Medical College(FAAMC)(n=202) respectively. The most common bacteria isolated from LGB, Tinsukia was CoNS (18.2%) followed by *Staphylococcus aureus* (9.1%) and *Klebsiella* (9.1%). *Klebsiella* pneumoniae (17.1%) was the common bacteria isolated from neonatal sepsis cases from SMCH, Silchar (17.1%) and FAAMC, Barpeta (48%). The gram-negative bacterial isolates from all the three sites showed resistance to the βlactam antibiotics. Amplification of the genes for carbapenem and cephalosporin resistance were carried out with multiplex primers. MLST for the isolates (*E. Coli*, *K. pneumonia* and Acinetobacter species of 7 pairs of housekeeping were amplified.

Formative Research To Ascertain Feasibility, Acceptability, Barriers And Enablers To Develop An Effective Delivery Model For Improving Adoption And Coverage Of Eight Contact Antenatal Care In Primary Health Care System Of India: An implementation research

New guidelines of WHO for positive pregnancy experience recommends eight antenatal contacts. There are challenges in implementing the 8 contacts particularly in resources (capacity of health personnel including supply chain management) countries to deliver the new ANC Model. In order to develop context specific model formative research project to ascertain feasibility, acceptability, barriers and enablers to develop an effective delivery model for improving adoption and coverage of eight contact Antenatal care in Primary Health Care System of India has been planned at five states- Maharashtra, Odisha, Gujarat, Karnataka and Uttarakhand. Project has been technically approved.

Research Capacity Building project for north east region

In order to build capacity among faculties of medical colleges, universities and research institutes for carrying out research in health and biomedical sciences to address local health issues in the North East states, Seed Grant scheme was initiated in 2011. During this year 196 concept proposals were received in different disciplines of biomedical and

health sciences. Of the 46 concepts approved, 34 full proposals were submitted for further evaluation. Total 12 new projects were approved for funding, and twenty projects are ongoing in various areas of health sciences. Seven were completed and 14 papers have been published.

Centre for Advanced Research in Childhood Respiratory Diseases

This CAR was established at AIIMS in 2019 to develop India specific diagnostic protocols, treatment algorithms and preventive measures for paediatric respiratory diseases in children. Major projects in interstitial lung disease in children, point of care testing for Primary Ciliary Dyskinesia in Children, respiratory complications of Primary and Acquired Immunodeficiency Disorders in Children are being undertaken including capacity building of medical college hospitals across India for management of chronic respiratory disorders in children, improve diagnosis.

Centres for Advanced Research on paediatric kidney disease at AIIMS

Major projects ongoing under the center are for management of nephritic syndrome- RCT comparing the efficacy of therapy with low dose daily prednisolone versus long term alternate day prednisolone, efficacy of prednisolone on alternate days converted to daily therapy during infections, *vs.* levamisole in frequently relapsing nephrotic syndrome. Registry and biorepository has been set up for hemolytic uremic syndrome, specimens are being stored; whole exome sequencing for atypical hemolytic uremic syndrome and genetic variations in primary vesicoureteral reflux is being studied. Guidelines on management of HUS and parent education material on nephrotic syndrome (Hindi, English) and hemolytic uremic syndrome have been published.

ICMR Advance Centre for Evidence Based Child Health Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh

The PGIMER, under the aegis of ICMR has established Advanced Centre for Evidence Based Child Health in Advanced Pediatric Centre (APC), PGIMER, Chandigarh in November 2020. During the 7 months of tenure (Nov 2019-August 2020), the centre has conducted 2 short courses/ workshops. In these workshops, 198 participants were trained in critical appraisal of different areas such as randomized controlled trials, observational studies and Systematic reviews. Teaching methods for Evidence Based Child Health/ Clinical Practice were also introduced. Different sessions for intervention, diagnostic, systematic review studies and literature search were taken by the expert faculty members (plenary and group sessions). Candidates who attended these short courses were clinicians, faculty members, Ph.D students, technical staff, nurses and other paramedics. The center has produced 1 Meta analysis entitled "Efficacy and Safety of Anti-malarial Drugs (Chloroquine and Hydroxy-Chloroquine) in Treatment of COVID-19 Infection: A Systematic Review and Meta-Analysis", 1 update on systematic review entitled "Palliative drug treatments for breathlessness in cystic fibrosis", 1 editorial entitled "Use of Face Masks in COVID-19". The center also successfully registered 2 protocols in Prospero for systematic review for upcoming year. Our 5 articles including letter to the editors are under review. During the COVID-19 pandemic followed by lockdown many activities of the centre were conducted on online platforms such as zoom and google meet.

Capacity Building for North East Region in Evidence Based Medicine

Background: An online mentoring approach in combination with the onsite mentoring would be effective in using the resources to the fullest. The ECHO (Extension for Community Healthcare Outcomes) model could be adopted for the online approach, as it would be easy for the healthcare workers to attend the sessions and interact without being compelled to travel. **Method :** The online sessions on evidence-based medicine has been conducted for healthcare professionals (pediatricians and research scientists) in the

northeastern region of the India. These sessions were conducted by collaborating with ECHO (Extension for Community Healthcare Outcomes) to connect with a number of medical colleges, Health facilities and ICMR MRHUs in the Northeastern region of the country. Practice-based learning modules and didactic presentations were conducted in this mentoring process. Sessions on evidence-based medicine were included, medical literature searching through medical databases, critical appraisal of randomized controlled trials and systematic reviews, framing of research question and development of protocols. After the enrolment of the participants for the online course, the completion and registration of a systematic review protocol was considered necessary in order to get the certificate for the course. **Result:** During this period (April 2019 to July 2020), considerable progress has been made in attaining the objectives of the project. The ECHO model utilizes video conferencing softwares to connect the mentors from PGIMER to the participants in remote areas in the North East over the internet. The Scientists involved in conducting these sessions received a 2 day training in New Delhi on how to use the ECHO Model and trouble-shooting. The sessions were started online with real time transmission to the North East Region Participants from 3-4 pm Wednesdays fortnightly. The number of Participants enrolled for the online mentoring program is 49. Total 27 sessions were conducted during this period with 25-35 (Average) participants per session. One workshop was conducted onsite during this period in Guwahati, Assam, with title "National Workshop of Skill building in Systematic reviews in the North East Region" on 26th and 27th of September, 2019. **Conclusion:** Due to this project, more and more people are taking interest in evidence based medicine. The participants trained through these capacity-building courses also help in developing systematic review questions and thereby help in policy guidance at various levels. The case based discussion in these sessions also help the medical professionals in the remote regions in getting important inputs from experts in the host institute.

Centre of Advanced Research (CAR) in Pediatric Emergency Care at PGIMER Chandigarh

Objectives: To establish a Centre for Advanced Research (CAR) in Pediatric Emergency Care at the Postgraduate Institute of Medical Education and Research, Chandigarh so as to provide a state of art facility for research in the field of Pediatric Emergency care and to impart training to other participating academic medical centres in the country. Following projects were conducted by the CAR during the reporting period:

Project 1: Development and Maintenance of a Data Base, 2. Constitution and Evaluation of a Rapid Response System (RRS) for dealing with 'in- hospital emergencies'; 3. Evaluation of effectiveness of a 'Triage' system in streamlining and prioritizing pediatric emergency care.

Conclusion: Pediatric emergency department (ED) of our tertiary referral hospital faces a significant burden of overcrowding as shown by increased boarders and prolonged ED stay. Overcrowding was associated with increased frequency of care discontinuation and mortality. This data lays the foundation for policy and systemic changes to decrease overcrowding. This data has been submitted to Indian Pediatrics for publication. Appropriate triage was associated with significantly higher proportion of children receiving intervention in less than 30 min and lesser mortality. However, the time interval between registration and intervention remained unaffected between both groups. A well-documented triage system in a busy ER is important to streamline patient assessment and management.

Impact Evaluation of "Screen and Treat" Approach for Anemia Reduction: a Cluster Randomized Trial in Rural Telangana"

Objective: To assess the effectiveness of population level screening followed by targeted IFA supplementation according to the grade of anaemia for increasing the mean population level hemoglobin and reducing the prevalence of anaemia as compared to the existing anaemia control

program. **Methodology:** This cluster randomized trial would be conducted in 38 villages of Telangana and would enrol all the village residents (approximately 38000) in the study. Half of the villages would be randomized into intervention arm and half to the control. Intervention would include screening for haemoglobin estimation using a portable autoanalyzer and providing treatment with iron folate tablets to those who would be diagnosed to have mild or moderate anemia. Severe anemia cases would be referred to health facilities for treatment. In the control villages, there would be no intervention by the researchers and the usual anemia control program activities would go on. At the end of 6 months, anemia prevalence would be estimated in all study participants from the intervention as well as control villages to assess the difference in anemia prevalence in the two arms. **Work done during April 2019 to March 2020 and Brief Results:** A formative research in the study area was conducted in 2019. The transcription and translation of the scripts (N=111) have been completed. The leads from the formative research were used to develop the intervention protocol with 6 components A pilot study to evaluate the 'screen and treat' approach was conducted among 411 young girls residing in two social welfare hostels in Hyderabad. Data on haemoglobin and biomarkers of iron status were collected at baseline and at 45 days, 90 days, 120 days and one year post-iron supplementation. The treatment dose conformed to the Intensive National iron plus guidelines (I-NIPI, 60 mg iron and 500 µg folic acid). A mean increment of 1.58± 1.73g/dl was observed 90 days post supplementation using the validated capillary blood-autoanalyzer method. Anemia reduced to 30.7 % at 90 days from 66 % at baseline. The increment in hemoglobin was sustained 90 days post-IFA supplementation suggesting that the treatment regimen planned for the community trial is effective. There was a concurrent increment in ferritin (iron stores) in the participants.

Effect of Biweekly Preventive Supplementation with Multiple Micronutrients and Iron Folic Acid compared to Iron Folic Acid alone in Children aged 6 to 59 Months on Haemoglobin Concentration and Anaemia Prevalence: A Randomized controlled trial in Rural Haryana

Objective: To determine the effect of biweekly supplementation of erythropoiesis relevant multiple micronutrients along with iron (20 mg) and folic acid (100 mcg) for 100 doses in a year on hemoglobin concentration and anaemia prevalence in children aged 6-59 months, compared to biweekly supplementation with iron (20 mg) with folic acid (100 mcg) alone. Study design: This is an individually randomized controlled open-label efficacy trial. Study Participants: Children aged 6-59 months, residing in rural areas of Palwal district, irrespective of their baseline anaemia status, will form the study population. Interventions: Children in the intervention group will be given 1 ml of IFA syrup (containing 20 mg elemental iron and 100 mcg folic acid) and erythropoiesis relevant micronutrients biweekly for 100 doses in a year. In the control group, children will receive 1 ml of IFA syrup (20 mg elemental iron and 100 mcg folic acid) biweekly for 100 doses in a year (as in the current national program). Outcome measure(s): Outcomes will be assessed after the supplementation period for 100 doses is over. **Primary outcomes**: Mean hemoglobin, Proportion of children with anemia (Hb <11g /dL)

The TAG has approved the study to be conducted as an open label trial. **Developing Tools for Data Collection and SOPs**: Draft versions of study forms and their filling guidelines have been developed. A draft of Manual of Operations has also been prepared for the study.

Descriptive Epidemiology of Unintentional Childhood Injuries In India: An ICMR Task Force Multisite Study

Children are more prone to injuries because of their physical and psychological characteristics. Small body size and the softness of tissues make them vulnerable to the impact of injury. **Objectives:** To study the prevalence of unintentional injuries among children aged 6 months to 18 years (i.e. 17 years 11 months 30/31days)**.** To determine

the factors associated with unintentional injuries among children 6 months to 18 years (i.e. 17 years 11 months 30/31 days) of age. **Methodology:** This Multi-centric ICMR Task Force study is being conducted at 11 different sites across 8 states in India. **Study design:** This is a Cross sectional Study. **Sampling Procedure:** Two stage cluster randomized sampling procedure with Probability Proportional to the sample size. **Results:** Total Population covered under the study 108356. The present study covered around 31020 children of which 4208 children were injured. The overall prevalence of unintentional childhood injuries from all the participating was found to be 14.5%. The prevalence of injuries in urban areas was found to be 12.3% , as compared to 16.5 in the rural areas. Among all the type of injuries the most prevalent type of unintentional injury was found to be fall i.e. 8.4% . On analysis some of the factors such as age, area of residence, activity of the victim at the time injury, place where the injury occurred was found to be significant in univariate analysis but on logistic regression we could justify that the contribution of these risk factors were less than 5%.

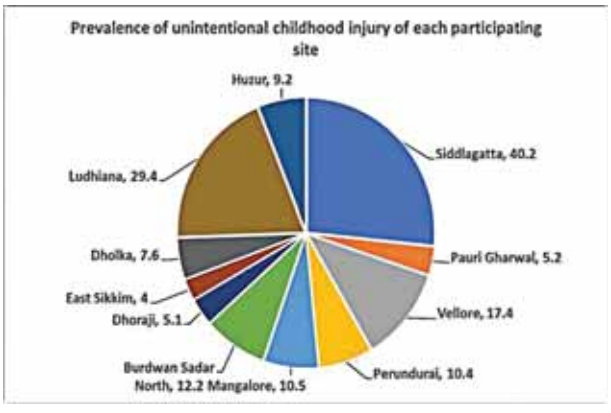


Fig. 14: Prevalence of unintentional childhood injury.

Fig. 15: Data collection by Field investigators.

Phase III, Multicentre, Randomized, Double-blind, Placebo-controlled Study to Evaluate Efficacy of Probiotic Supplementation for Prevention of Neonatal Sepsis in 0-2 Months old Low Birth Weight Infants in India

Neonatal infections (pneumonia, septicaemia, meningitis) are responsible for more than a quarter of the 1 million neonatal deaths every year in India. Low Birth Weight (LBW) is an important indirect cause of death in neonates, accounting for 40% to 80% of neonatal deaths. These neonates have poor cognitive function and compromised immune functions. In LBW infants infections are known to spread rapidly leading to severe disease and death. Prevention of infection in low birth weight babies would directly decrease the neonatal morbidity and mortality. Currently there are no preventive interventions available for neonatal sepsis other than general measures of hand-washing, exclusive breastfeeding etc. Management of neonatal sepsis with antibiotics faces the problem of drug resistance, attributed to availability over the counter, indiscriminate use and incomplete courses in India. Immune-modulation/immune-potentiation with the use of probiotics may prove to be an option. The proposal for this study has been granted award of funding under MRC/NIHR/DFID/Wellcome Trust, Joint Global Health Trials. During the reporting period activities of the preparatory phase are being completed. A tripartite agreement between the sponsor and the pharmaceutical companies for supplies of investigational products (IPs) has been signed and a clinical trial agreement between the sponsor and the participating sites is being signed. Staff recruitment at Collaborating sites is under process. The study protocol has been reviewed by the Research Ethics Committee of the LSTM, UK as suggested by MRC. The Trial has been registered at CTRI. The CT-NOC from CDSCO has been obtained.

EMF HEALTH

Effect of Non-ionizing Electro Magnetic Field (EMF) on Human Health

Based on the recommendation of Parliamentary Standing Committee, ICMR is conducting a multi-centric, multi-disciplinary, prospective cohort study. Salient findings of this study is given under following heads:

CELL PHONE STUDY

Under the prospective multi-disciplinary cohort study of cell phone, 3995 male and female subjects (age 18 to 45 years) have been enrolled after fulfilling exclusion and inclusion criteria's under various study groups. These subjects have been followed for their clinical and laboratory examinations. The major observations of the study are given below:

- Decrease in semen volume, sperm count, sperm motility, percentage of live sperm and serum levels of testosterone were noticed both in highly and moderately exposed male subjects in comparison to control group and this decrease is progressively increasing with duration of exposure. ($p = <0.001$)
- Increase in liquefication time, percentage of non-progressive sperm & percentage of abnormal sperm were noticed both in highly and moderately exposed male subjects in comparison to control group and this is increasing progressively with duration of exposure. ($p = <0.001$)
- High agglutination, liquification time and high alkaline pH was recorded in Group 1, Enrollment No. 0620.
- Decrease in sexual activities, increase in problem in ejaculation before the partner is ready were reported both in highly and moderately exposed male subjects in comparison to control group and there is progressive decrease and increase in sexual activity and problem in ejaculation with duration of exposure. ($p = <0.001$)
- Increase incidence of miscarriage, preterm birth, irregular menstrual cycle and decrease in sexual desire and frequency in female subjects of highly exposed group were noticed in comparison to control group and there is progressive increase and decrease in miscarriage, preterm birth, irregular menstrual cycle and sexual desire & frequency respectively with duration of exposure. ($p = <0.001$)
- Decrease levels of prolactin, cortisol, T-4 and increase levels of TSH were noticed both in male and female subject in highly exposed group in comparison to moderate and control group and there is progressive decrease and increase in prolactin, cortisol, T-4 and TSH respectively with duration of exposure. ($p = <0.05$)
- Increase in air conduction, bone conduction in right ear at various frequencies and speech recognition threshold observed both in highly and moderately exposed male and female subjects in comparison to control group and there is progressive increase in air conduction, bone conduction and speech recognition threshold with duration of exposure. ($p = <0.05$)
- Significant changes in extremely important cognitive domains such as memory, learning, attention, fluency and other higher mental functions both in highly and moderately exposed male and female subjects in comparison to control group. ($p = <0.05$)
- Though no significant difference was found in terms of clinical parameters received from department of cardiology but significant changes in frequency of snoring and Levels of Cholesterol, LDL and Triglyceride in exposed group needs to be followed for long duration to draw a meaningful conclusion.
- Since the decline in levels of testosterone have been noticed in exposed group therefore majority of androgen dependent parameters are decreasing in male subjects of exposed group. This trend needs to be followed to draw a meaningful conclusion.
- The increase incidence of presence of sores and white patches in mouth were noticed both in male and female subjects of exposed group.
- The percentage of apoptosis in lymphocyte and

levels of malondialdehyde were increasing in male and female subjects of exposed group.

- The levels of superoxide dismutase (SOD) were decreasing both in male and female subjects of exposed group.
- The decreasing trend in leukocytes counts and increasing trend in monocytes counts were noticed both in male subjects of exposed group.
- The nodules in breast were observed at (Group 5, Enrollment No. 0075,), excessive bleeding during menstrual cycle (Group 5, Enrollment no. 0020, subject under treatment)
- The pituitary tumors were observed (Group 1, Enrollment No. 0469 IIIrd Visit), high prolectine hormone was observed high in ~126 subjects and Group 2, Enrollment No. 0859 is under treatment. Neuro Cystic Sarcosis was found in Group 1, Enrollment No. 0253.

These results indicated that biological changes are well evident in both male and female subjects of exposed group in comparison to control group. But to find out when these biological changes will result into health hazard/disorder, the subjects need to be followed for longer duration.

Health survey of the people residing near cell phone tower

Health survey based on the prescribed proforma was under taken of 1000 people (700 male, 300 females; age 18 – 45 years) residing at various distances from the cell phone tower in all the five zones of Delhi where the PD was above the prescribed limit.

- A population of 1000 subjects (both male and female), residing at various distance from cell phone towers were surveyed for their health complaints.
- The complaints were recorded through a prescribed proforma.
- Total 32 health symptoms/complaints were recorded.
- Out of 32 health symptoms, in male subjects, 16 symptoms were significantly higher in the subjects residing near cell phone tower i.e. 10 to 100m in comparison to the subjects residing at 300m or beyond 300m. These male subjects reported complaints of Migraine Disability assessment Score, Epworth Sleepiness Scale, Depression, stress, Ear Discharge, Fever, Fatigue, Giddiness, Dark Skin, Yellowish skin, Presence of blood clots, change in size of stool, white patches inside the mouth, White spot on tongue, Cardiac symptoms and involved in sexual activity.
- Similarly, out of 32 health symptoms recorded in female subjects, 14 symptoms were significantly higher in female subjects residing near cell phone tower i.e. 10 to 100m in comparison to the female subjects residing at 300m or beyond 300m. these female subjects reported complaints of Migraine Disability assessment Score, Stress, Fever, Reddened Skin, Etching, Excessive hair growth, Presence of blood clots, Long term constipation, Diarrhea, Change in size of stool, Long lasting sore in mouth, White patches inside the mouth, White spots on tongue and Involved in sexual activity.

NUTRITION

The ICMR continues to be instrumental in developing public health activities with many significant contributions in the country in the field of nutrition. It has been made possible by undertaking the laboratory and hospital based research with community based participation. The salient features of various research activities undertaken during 2019-2020 are given below.

INTRAMURAL RESEARCH

ICMR – NATIONAL INSTITUTE OF NUTRITION, HYDERABAD (ICMR-NIN)

Establishment of Nutrition Surveillance System in Six States of India

In pursuance of goals of National Nutrition policy, sustainable developmental goals, WHO Nutrition Framework and India's developmental plans 'Nutrition Surveillance System (NSS) was established to provide early warning signs of malnutrition among vulnerable population groups to take immediate actions to mitigate the problem of malnutrition. NSS has been established in 6 select states (Kerala, Maharashtra, Madhya Pradesh, Meghalaya, Odisha and Telangana) in India on a pilot basis. Through tabs enabled real-time recording of the data by Anganwadi Workers, vulnerable population's nutritional status is monitored at micro and macro levels on a regular basis. This will enable administrators to take immediate remedial actions for prevention and control of malnutrition.

Prevalence and Predictors of Vitamin B12 Deficiency - Genetic Associations for Low Vitamin B12 Levels – A Multi-Center Pan India Study

Iron – folic acid fortification without considering B_{12} level in the individuals may cause adverse events and this could perhaps be one of the rate-limiting factors in national iron folic acid supplementation programme. The current study was taken up to map the B12 deficiency in India, to estimate the contribution of B12 deficiency to the burden of anemia.

Improving Health and Nutritional Status of Vulnerable Segment of Population by Implementing Multi-component Health and Nutrition Education Intervention as a Sustainable Model of Intervention – Andhra Pradesh, Gujarat, Jharkhand and Telangana

Nutrition status data were collected from 14 districts in 4 states, and based on the baseline, formative research findings district specific multi-component health and nutrition education intervention strategies were developed and implemented in 3 phases in 7 Districts of Gujarat, 5 districts of Jharkhand, one district each in Andhra Pradesh and Telangana. Education materials such as posters, flip charts, table calendars, banners, which were developed and finalized after pre-testing were used for creating nutrition awareness to the adolescent girls, pregnant women and lactating mothers. The mode of education was person-to-person, focus group meetings and counselling. The project staff

contact with each of the beneficiary in the target areas was about 7-10 for counselling. There was significant improvement in all nutrition indicators and IYCF practices. The number of children with stunting, wasting and undernutrition decreased in all districts except one.

Nutritional Status of Women Living with HIV/AIDS and Impact of Food-Based Approach on Disease Progression

To improve nutritional status of women living with HIV/AIDS special full meal supplementation program was implemented for a period of 12 months. A significant improvement was observed in their body weight, BMI and CD4 count.

Impact Evaluation of "screen and treat" approach for anaemia reduction: a cluster randomized trial in rural Telangana", Funder: ICMR Task Force study

Developed and validated a method of measuring Hb in capillary blood by a portable analyser for population level screening of anaemia in cross sectional and longitudinal studies. Pilot tested the 'screen and treat' approach in college girls which showed anaemia reduction by 40% in three months (from 70% at baseline to 30% at endline); and developed behaviour change communication (BCC) materials (videos, calendars) to address the barriers for program uptake and a Customized software for the study.

UKRI-GCRF 'Action against Stunting Hub' (Multi-Country Project)

Project inception meeting was held in Hyderabad in Feb 2019 involving the multi-country partners. A number of capacity building workshops were held in virtual mode to develop safe guarding policies, project management, development of SOP's, digital data collection and data management.

A Community-Based Intervention on Maternal and New-Born Care Among the migrant urban poor living in non-notified slums through Janani Suraksha Yojana (JSY) and Home-based New Born Scheme in Hyderabad city

The survey was done as a case control study with those mothers who delivered under JSY program compared to those who were under the new KCR-kit program. It was observed that KCR-kit increased the awareness of the government services leading to increased uptake and improved maternal and child health indicators.

Comprehensive National Nutrition and Health Survey (CNHS)– district level survey (Pilot study)

This survey was carried out in the district of Nalgonda in Telangana to explore the possibility of conducting a comprehensive data collection, including essential biomarkers on health and nutritional status of the population by establishing a field lab. It is feasible to conduct similar trials and will be cost-effective if done simultaneously in many districts, and more so, if periodic monitoring of health and nutrition status has to be done to study the effectiveness of national programs and reduction in disease burden, as well as to suggest mid-course corrections in program implementation.

Correlation of Prakruti (ayurgenomics) with dietary patterns, HLA-DRB1 genes and disease severity in rheumatoid arthritis (RA) patients

Vata prakriti was associated with Rheumatoid arthritis patients whereas Pitta and Pitta kapha prakriti were protective for RApatients. Vata prakriti subjects had more severity in terms of anti CCP titres, disease duration and DAS sores than other prakriti subjects. HLA-DRB1 *04 gene was associated whereas HLA-DRB1*07 and 14 genes were protective for RA patients. High consumption of red and organ meat, plain rice and less consumption of green leafy vegetables, fruits in RA cases were observed. Consumption of a healthy balanced diet has beneficial effect on development as well as progression of RA.

Situation analysis on Investigation of beriberi cases in Assam

ICMR-NIN team conducted a quick situation analysis in the community and hospital where

cases of suspected beriberi were reported. The case records of beriberi at the hospital showed that in the past one year, 110 cases of Infant deaths have occurred and 6 cases of them were suspected to have died of beriberi. At the field, verbal autopsies carried out in two villages found that of the three infant deaths that occurred in the last one year, two were due to suspected beriberi. The food habits of the mother included consumption of polished rice, fermented fish, betel nut, betel leaves and tea all of which are known to induce thiamine deficiency. Pulses were less frequently consumed.

Fig. 1: ICMR-NIN team conducting verbal autopsy of infant deaths with the help of translator in the nearby village of the local hospital at Karimganj, Barak Valley, Assam.

Developing Micro-greens (MG) Start-ups for Promoting Livelihood and Nutritional Security in Urban Areas

National workshop on Benefits of MGs was organized with different stakeholders to sensitize the importance of MGs and their nutritional significance at the household level and role of women in addressing them were conducted in association with MANAGE-ICAR.

Dose response of Salmonella survival and infection in an in-vitro model of the human intestinal tract as a proxy for foodborne pathogens

Studies on Salmonella survival in stimulated gastric fluid (SGF) showed reduction (0.3 log) after 30 min of incubation time while studies on Salmonella survival in stimulated intestinal fluid (SIF) showed increase in (0.8 log) Salmonella population after 2h of incubation time.

Impact of Salmonella killing lytic bacteriophages on probiotic microflora

Initiated in January 2019, in which no spots and inhibition zone were observed both in the test assay and the agar well diffusion assays while results of turbidometric assay showed that even after incubation up to 24h the growth of probiotic microflora remained unaffected.

Vitamin D deficiency induced neurodegeneration - Role of protein homeostasis pathways

The catalytic enzyme activities of the proteasome were observed to be decreased in the vitamin D deficient brains compared to control brains.

Vitamin D deficiency induced cardiomyopathy - Role of ubiquitin proteasome and signal transduction pathways

Total protein degradation [TPD] in heart atrium was found to be significantly [$p<0.05$] higher in the Vitamin D deficient group compared to the control group, while the total protein synthesis [TPS] in heart atrium was found to be significantly [$p<0.05$] decreased in the Vitamin D deficient group compared to the control group.

Ameliorative potential of tamarind fruit extract on the NaF –induced alterations in the bone related parameters in Saos-2 cell line

Tamarind fruit extract treatment showed ameliorative potential and prevented NaF induced alterations in bone related parameters in Saos-2 cell-line.

Prevalence of fluorosis in the community of selected districts of India (Prakasam district from Andhra Pradesh) and development of an appropriate intervention model for prevention and control of fluorosis

Dental fluorosis was 5% among 5-18 years age in category I villages (8 villages; <1.00 ppm fluoride in drinking water), 13.1% in category II

(7 villages; 1.5-3.0 ppm fluoride in drinking water) and 16.2% in category III (9 villages; >3.00 ppm fluoride in drinking water) in Prakasam district, Andhra Pradesh. g). The fluoride levels in the food samples were higher in category II & III compared to category I.

As expected, the urinary fluoride was significantly higher in category III (>3.00 ppm fluoride) as compared to category I (<1.00 ppm fluoride) and category II (1.5-3.0 ppm fluoride in drinking water). The T3 levels significantly increased in the category III as compared to category I and category II. The TSH levels were significantly decreased in the category III and category II compared to category I.

Training of Trainers (TOT) and Laboratory Technicians (LT) training programme under National Programme for Prevention and Control of Fluorosis funded by Ministry of Health and Family Welfare, Government of India

Training of Trainers (TOT) was conducted from 29th-31st January, 2020. A total of 29 participants (Consultants, District Nodal officers and State Nodal Officers) from New Delhi, Karnataka, Haryana, Chhattisgargh, Odisha, Uttar Pradesh, Jharkhand, Andhra Pradesh, Assam, Jammu, Kerala, Punjab, TamilNadu and West Bengal attended the training programme.

Another TOT was conducted from 4th to 6th March, 2020. A total of 23 participants (Consultants, District Nodal officers and State Nodal Officers) from New Delhi, Karnataka, Andhra Pradesh, Jharkhand, Rajasthan, Madhya Pradesh and Uttar Pradesh attended the training programme.

Laboratory Technicians (LT) Training was conducted from 26th to 30th August, 2019. A total of 28 participants (Laboratory Technicians) from Karnataka, Kerala, Maharashtra, Madhya Pradesh, Chhattisgarh, Tamilnadu, Assam, Uttar Pradesh, Haryana and Jharkhand attended the training programme.

Toxicokinetics of common organophosphate compounds in acute poisoning cases

Toxicokinetic study of pesticide showed that monocrotophos and dimethoate were more absorbed and toxic than other pesticides. A negative correlation was obtained between pesticide concentration and the acetylcholinesterase enzyme. The time for treatment to the survival of patients ingested monocrotophos and dimethoate was observed to be less than 12h. However, for pesticides like chlorpyrifos, propanil, triazophos and acephate treatment time was between 36 and 72h.

Evaluation of Chemical contaminants in fresh/ packaged tender coconut water and marketed coconut milk

A method was standardized for the estimation of recommended/non-labelled or non-recommended pesticides for the marketed coconut milk.

Identification and characterization of suitable biomarkers for zinc status using next generation sequencing (NGS) based platforms

Expression of pattern of several genes associated with zinc homeostasis was studied upon depletion with a zinc chelator TPEN and subsequent repletion with $ZnSO_4$. In HepG2 cells (representing liver tissue) expression of MT2, Znt5, ZnT9, Zip6, Zip8, Zip9 increased significantly at about 6 hours post supplementation. No significant change was observed for Zip7, indicating that several genes involved in zinc homeostasis can be used as a marker for zinc status.

Impact on the maternal exposure of Bisphenol A (BPA): implication to developmental programming of glucose homeostasis and insulin resistance in offspring

Pups (30d) born to mothers exposed to BPA during pregnancy showed a significant increase in body weight, body mass, fat mass, fat percentage, and bone mineral content. Exposure during pregnancy, even at very low concentration of 0.4µg/kgbw/day

lead to a significant increase in IGF-1 concentrations in the plasma of the one-month pups

Effects of Curcumin on Bisphenol-A induced insulin resistance and lipid accumulation in hepatocytes and adipocytes

It was found that in both 3T3-L1 and HepG2 cells, BPA exposure significantly increased the expression of *fasn, sqle* and *hmgcr* as compared to the unexposed controls. Curcumin, when used at 5µM concentration, could suppress BPA-induced expression of *fasn, sqle* and *hmgcr* genes. Curcumin also rescued BPA-induced inhibition of *apoa1* gene in these cells.

Combination of therapeutic efficacy of dietary component stigmasterol and MSCs in the management of osteoarthritis – an in vivo and in vitro approach

Mesenchymal stem cells (MSCs) and plant-derived sterol – stigmasterol together effectively ameliorated osteoarthritis (OA) and facilitated cartilage repair and regeneration in OA model system. The beneficial effects can be attributed to the paracrine, anti-inflammatory and antioxidant functions of MSC and Stigmasterol

Studies on protein hydrolysates from safflower seed and validation of their utility in animal nutrition

A Pilot study has been undertaken to compare the protein hydrolysates from safflower seed and casein protein used in the standard rodent chow formulated as per modified AIM 93G. All the three protein hydrolysates showed significant effect in terms of physical, physiological and biochemical indices in the treated animals.

Drug Toxicology Division

ICMR-NIN-*d-c* a traditional formulation is filed for **patent** after characterisation of phytochemical profile and validation of the treatment in chronic menopausal syndrome. Study on the-Effect of vitamin D deficiency on Statin induced myalgia along with polymorphism has been completed.

Targeted Nutrition Communication for Promoting Consumption of Micronutrient Rich Foods among Rural Households by Developing Dietary Diversity Scores (DDS)

Developed a context-specific methodology to assess dimensions of the rural food environment using a novel 5A's (availability, affordability, accessibility, acceptability and accommodation approach). Psychometrically validated a knowledge attitude and practice (KAP) questionnaire on micronutrients. Developed and validated a Diet Diversity Score (DDS) to predict micronutrient adequacy of the diets in rural households.

Promoting Nutrition and Health of Corporate Employees with Workplace Intervention- A Study Using Communication for Behavioral Impact (COMBI) Approach

Developed tools to capture the food and physical activity environment of a workplace (check list); assessed nutritional status and food and physical activity environment of corporate IT firms using different approaches (Biochemical assessment, diet recall, anthropometry, questionnaire) and developed a multi-component, flexible workplace intervention programme model based on COMBI approach.

Development, Validation and Dissemination of Comprehensive Healthy Eating And Living Index For Adolescents

There is a need to constantly monitor the food, consumption and diets and lifestyle of the adolescents to suggest viable corrective measures. However, Diet and nutrition cannot be looked at in isolation. Therefore, this comprehensive healthy eating and living index (CHELI) was developed not only focusing on the quality of diet consumed but also on physical activity, stress and duration of sleep, screen time among adolescents. The 44-item Score Card has been validated and the study is in the intervention phase

Development of e-learning modules on nutrition and health under *Poshan Abhiyaan* initiative of Government of India

Twelve Nutrition and Health Education (NHE) e-learning modules were developed and uploaded on ICMR-NIN website www.nin.res.in by providing cross-link to ICMR-DHR, MWCD and SWAYAM portals in order to provide access to the community from different parts of the country. The e-learning modules on various nutritional themes are expected to educate general public and girls & boys in adolescent age group and master trainers (paramedics, *Anganwadi* workers, and others). The e-learning module is currently available in Hindi and has had over 60000 registrations and 5.9 lakh certificates have been generated online

A formulation of multiple-micronutrient powder for reducing anaemia and developmental disparities among pre-schoolers in Anganwadi Centers in the state of Telangana - Transition to scale- POSHAN ABHIYAN initiative

A multi-micronutrient formulation was found to be effective in the reduction of anaemia among children in anganwadis. It was through the fortification at the point of care of the SNP meal given at the Anganwadi Centres in the state of Telangana. There was a reduction of over 50%. It is suggested to make the transition to the scale of this strategy in 100 anganwadis of Telangana. This aligns with the goal of Poshan Abhiyaan's *Anemia Mukth Bharath*. In this phase of scale transition, product supply pathway will be established in the current ICDS-SNP supply chain. While evaluating the product's effectiveness through hemoglobin testing, Growth (HAZ) and Childhood development.

Nutraceutical and beneficial effect of 6-Gingerol as an anti-obesity agent to induce generation of beige like cells vis-à-vis browning in white adipocytes – a proof of concept study

6-Gingerol and 6–Shogaol, active principles of Ginger effectively reprogrammed white adipocytes to brown adipocytes in Obesogenic milieu vis-à-vis accelerated energy expenditure, to avert obesity, demonstrated in 3T3 L1 and in WNIN/Gr-Ob obese mutant rats.

Feasibility of mesenchymal stem cells of human perinatal origin to ameliorate type 2 diabetes with insulin resistance in WNIN/GR-Ob mutant rat model system

Human placental - MSCs therapy to Obese -T2D rats was effective (i) to restore glucose homeostasis, (ii) IR, (iii)regulated and modulated cytokine levels, (iv) up-regulated PI3K-Akt signalling, (v) restored Glu 4 translocation and (vi) enhanced glucose utilization.

Regulation of FGF21 in WNIN/Ob and WNIN/GR-Ob mutant rat models

Findings from the current study emphasize the potential role of FGF21 in glucose homeostasis and its attenuation might aggravate glucose impairment during the transition from prediabetes to diabetes in high sucrose diet induced WNIN/GR-Ob rats.

Restoration of reproductive potential by *Ficus racemosa* L. bark extraction in WNIN/GR-Ob rats

The total polyphenols were characterized, and Hesperidin, Chlorogenic acid and Naringenin levels were significantly high compared to other polyphenols. Body wt and body fat reduced significantly in the FRBME treated rats. TG, Glucose and insulin levels decreased and insulin sensitivity improved in FRBME. Administration of FRBME preponed the puberty, and restored regular oestrous cycles in obese rats. The characteristic peak of estrogen and progesterone was restored. Uterine horn length increased in obese rats treated with FRBME. Light microscopy and SEM analysis showed that the treatment of FRBME improved structure and morphology of ovaries, uterine horns. The bark methanolic extracts can be used as therapeutic molecule to treat women suffering with obesity associated PCOS.

Role of free fatty acid receptors in modulating atherosclerosis in WNIN/Ob rats

Short chain fatty acids could attenuate the progression of atherosclerosis in WNIN/Ob rats.

the current study established WNIN/Ob obese rats as a suitable model to study atherosclerosis.

Centre for Advanced Research for Pre-clinical Toxicology

Under the PCT, Reports (safety & efficacy) for regulatory approvals for 'oryzanol rice bran oil' in reducing cholesterol and'Spirulina Nutritional Gummy' as nutritional supplement were submitted. Pre-Clinical efficacy (immune modulatory) and Safety (Regulatory Toxicology) evaluation of Ayush formulation *'Ayush Kwath'* supported by Ministry of AYUSH (EMR Scheme) has been undertaken on priority. Compositional Analysis and Pre clinical safety (Regulatory studies) evaluation of Parboiled Rice enriched with multiple micronutrients supported by Sundar Diabetics Dezire Pvt Ltd, Chennai is in progress.

PUBLIC HEALTH IMPORTANCE

- NSS has been established in 6 select states (Kerala, Maharashtra, Madhya Pradesh, Meghalaya, Odisha and Telangana) in India on a pilot basis. Through tabs enabled real-time recording of the data by Anganwadi Workers, vulnerable population's nutritional status is monitored at micro and macro levels on a regular basis. This will enable administrators to take immediate remedial actions for prevention and control of malnutrition
- Developed a validated point-of-care (POC) method for estimating Hb in capillary blood by a portable analyser for population level screening of anaemia.
- Developed customized software to track treatment delivery as per the I-NIPI guidelines, which can be scaled up to national level.
- Developed E-module to facilitate the training for trainers who are involved in implementation of Anemia Mukt Bharat programme.
- Lytic bacteriophages have great potential as a natural bio-control agent of a foodborne pathogen such as Salmonella enteritidis.
- Developed a precise and accurate method for community screening for anaemia (a portable autoanalyzer) and validated in 620 participants. The 'screen and treat' approach in young women showed substantial reduction in anaemia prevalence.
- KCR kit (for pregnant women, mothers and children) program was found to improve various maternal and child health indicators in non-notified slums of Hyderabad.
- A Comprehensive National Nutrition and Health survey as a pilot study was done in the district of Nalgonda and the study was found feasible and paves way for expansion in other districts in India.
- A quick situational analysis in Assam on investigation of beriberi by NIN found child deaths due to suspected thiamine deficiency.
- As one of the partners of ICAR- Consortium Research Platform on Crop Bio fortification involving numerous crops and nutrients, ICMR-NIN has evaluated several crops and nutrients. Zinc content and bioavailability was high from 'DHAN' rice. Two bio fortified maize lines that provide more than 60% RDA have been identified.
- Studies on trans fatty acids (TFA) in commonly consumed processed foods have revealed that snack items like kachori, samosa, chikodi, potato chips and bakery items contain high level of Elaidic acid, but the levels of TFA within the same foods varies. The use of partially hydrogenated vegetable oil (vanaspati) in the preparation of the foods is the main source of TFA in the diet, although FSSAI imposed upper limit of TFA in PHVO
- Studies on the Meitei community of Manipur have shown that they have much better nutritional status as compared to the national data. Several underutilized indigenous and traditional crops that have high nutritional value have been identified which can increase crops diversity, improve local value chain, and

diversify food system, ultimately resulting in increased household food security.

- Studies on the Particularly Vulnerable Tribal Groups (PVTGs) - Chenchu and Kolam tribes and their food habits - have shown that the resource base of indigenous foods used by the tribe is slowly dwindling and there is a need to conserve and mainstream the important nutritious indigenous foods through policy environment.
- Studies on micro greens showed higher levels of essential nutrients as compared to their counterparts. Scientific evidence on its nutritional and health benefits can bring about their incorporation into mainstream food system.
- A pilot study on Chronic Kidney Disease (CKD) in tribal population revealed high levels of heavy metal content in the food chain in Telangana state.
- Telomere attrition and mitochondrial DNA variations are implicated in the biological aging process and genomic stability can be influenced by nutritional factors. It was found that a decline of Relative telomere length (rTL) and mitochondrial DNA copy number (mtCN) with age in the Indian population and their association suggests that they may co-regulate each other with age. Further, folate and B12 may delay aging by preventing the reduction in rTL length and mtCN.
- Diabetic retinopathy (DR) is a most common complication of diabetes involving microvasculature and neuronal alterations in the retina. In this study, we observed that B12 supplementation to diabetic rats prevented retinal hypoxia, VEGF overexpression, and ER stress-mediated cell death in the retina.
- An animal study was conducted to study the impact of vitamin D insufficiency on muscle metabolism and function. A significant outcome of our work is the deleterious effect of low amounts of circulating vitamin D on functional parameters in muscle such as contraction, energy metabolism and mitochondrial biogenesis; thereby indicating that subclinical deficiency as seen in humans, already impairs muscle function.
- The work physiology group and the Ministry of Youth Affairs (MYAS) supported sports nutrition division extended support to sports academies for evaluating body composition, Energy and nutrient requirements, menu planning, meal timing and hydration for athletes
- Due to rampant use of plastics and epoxy resins, in almost every sphere of life, bisphennol A is widely present in our food chain. BPA is known to mimic estrogen and has been implicated in several pathophysiological disorders. Studies found that curcumin, found in turmeric, a widely used spice in India can abrogate effects of BPA.
- During the year 2019-20, the Animal Facility in NIN met the in-house as well outside demand of quality animals and supplied to various scientific institutions. A total of 12,212 animals were bred, out of which 4,195 animals were supplied to various outside institutions and 1,205 animals were supplied within the institute. An amount of Rs. 16,83,514/- (Rupees Sixteen Lakh Eighty-Three Thousand Five Hundred and Fourteen Only) has been generated as sale proceedings.
- The Animal facility prepared and supplied 9,125 Kgs of feed (Rat & Mouse feed 7,833 Kgs + Guinea pigs and Rabbit feed 1,142Kgs; Gerbil feed 150 Kgs) during the period. Out of this, a total of 1, 278 Kgs of feed was supplied to outside institutions generating an amount of Rs. 5,60,330/-(Rupees Five lakhs sixty thousand and three hundred thirty only). An additional 7,847 Kgs of feed (Rat & Mouse feed 6,555 Kgs + Guinea Pigs & Rabbit feed 1,142 Kgs + 150 Kgs Gerbil feed) was also supplied within the institute. In addition, department also prepared 226 Kgs of custom-

made experimental animal feed and supplied to outside institutions.

- Mesenchymal Stem Cells (MSCs) has potential in treating osteoarthritis (OA), which has wide clinical applications in OA related to Geriatrics, Obese young populations as well as in sports domain.
- Developed a methodology to assess context specific dimensions of the rural food environment using a novel 5A's approach considering availability, affordability, accessibility, acceptability and accommodation of foods
- The nutrition and health education e- modules had overwhelming response from people of different walks of life from across the length and breadth of the country. So far, more than 7,92,137 hits with a rating of 4 stars out of 5 have been recorded on the ICMR-NIN website and around 67,153 candidates (25,186 females and 41,890 males) have registered and downloaded more than 5.8 lakh certificates.

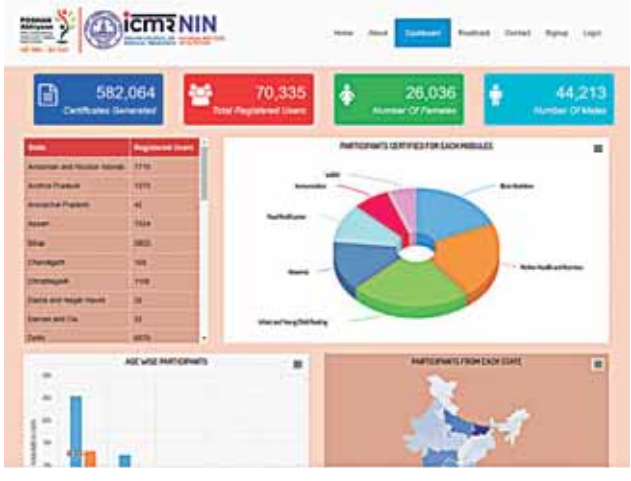


Fig. 2: Poshan Abhiyaan.

- Live interviews cum phone-in programmes (27 episodes) were conducted in Telugu in association with DoordarshanYadagiri (Telangana) TV Channel, wherein common people from across the country interacted with scientists and clarified their doubts on various aspects of diet, nutrition, food safety and health

Fig. 3: Nutrition and Health e-modules.

EXTRAMURAL RESEARCH

Consumption pattern of food and food products/items high in fat, salt and sugar

Ongoing at 16 locations in the country (Delhi; Bangalore; Bhopal, Kanpur, Srinagar, Nagpur, Ludhiana, Jaipur, Trivandrum, Rishikesh, Ahmedabad, Bhubaneswar, Jorhat, Dibrugarh, Agartala, Shillong)

Improving health and nutritional status of vulnerable segment of population by implementing multi-component health and nutrition education intervention as a sustainable model of intervention

Currently ongoing in 41 districts of 20 States (including all 8 north-east states).

Assessment of Iodine status among pregnant women in selected districts of India

Being carried out at 10 locations in the country

Prevalence of fluorosis in the community of selected districts of India and development of an appropriate intervention model for prevention and control of fluorosis

Ongoing at 7 locations in the country (covering one district each in Orissa, Madhya Pradesh, Telangana, Chandigarh, Bihar, Rajasthan and Assam)

Prevalence of vitamin A deficiency disorders among children aged 1-5 years in selected districts of India

Initiated recently at 7 locations of the country (Assam, Odisha, Telangana, Bihar, Madhya Pradesh, Rajasthan and Uttar Pradesh)

Constitution of Expert Committee on Global Hunger Index: The Global Hunger Index (GHI) is a tool designed to comprehensively measure and track hunger at global, regional, and national levels. India was ranked 102 out of 117 in 2019. It was felt that it is important to examine the computation of GHI in the Indian context because of media attention leading to misdirected stigma, and advocacy for hunger alleviating policies and hence an Expert Committee was constituted. The committee met on several occasions and is working on the report and *'White Paper'* on Global Hunger Index

Division supported 34 adhoc projects. The studies ranged from community based studies like Evaluation of prevalence, risk factors, consequences of thiamine deficiency among healthy community dwelling Kashmiri population to clinical studies like Vitamin D deficiency induced cardiomyopathy. Approx. 50 fellowship research studies were supported by Division during the year 2019-20.

CENTRE FOR PROMOTION OF NUTRITION RESEARCH AND TRAINING WITH SPECIAL FOCUS ON NORTH-EAST, TRIBAL AND INACCESSIBLE POPULATION

The laboratory at Centre for Promotion of Nutrition Research and Training has been analyzing biological samples collected from the field for various biochemical parameters like lipid profile; Vitamin A, Vitamin E, Thyroid profile etc. During the year 2019-20; a total of approx. 15,000 serum/ plasma/ urine/ salt samples were analyzed for over 50,000 determinants. The laboratory supported the ongoing task force studies as well as researchers/ scholars from different Medical Colleges/ Universities for their thesis/ dissertation work.

PUBLIC HEALTH IMPORTANCE

- The Division is not only conducting research to provide inputs to policy makers and programme managers but is also dealing/ addressing issues of National pride like Global Hunger Index in which our country has been ranked 102 out of 117 in 2019; and the Division had constituted an Expert Committee to review the same.
- The Division had constituted an Expert Committee on alterations in ration scales of troops of Indian Army and the recommendations were communicated to the Ministry of Defence
- Approximately 15,000 human blood and urine samples collected under various task force studies and collaborations were analyzed in NABL accredited clinical biochemistry lab.
- Various Task Force studies of public health importance such as Vitamin A, Foods high in fat, salt and sugar were successfully carried out.

ENVIRONMENTAL & OCCUPATIONAL HEALTH

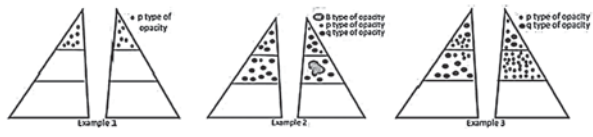
Research in priority areas of occupational and environmental health relevant to national needs for various working groups is actively undertaken by the ICMR-National Institute of Occupational Health, Ahmedabad and the ICMR-National Institute for Research in Environmental Health, Bhopal . Major highlights of various programmes undertaken by the ICMR in the areas of occupational and environmental health during the year 2019- 2020 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF OCCUPATIONAL HEALTH, AHMEDABAD (ICMR-NIOH)

Serum CC16 and its association with degree of lung damage caused by silicosis

Objective of the study was whether serum CC16 was related with amount of lung damage caused by various levels of progression of silicosis. A total of 117 x-ray confirmed silicosis patients were subjected for this study. The subjects were mostly working in sandstone mines, quarry etc. Amount of lung damage was calculated using ILO radiography & NIOH working formula for it as shown in figure-1. Serum CC16 was estimated using ELISA. The result showed that out of total 117 participants, mild lung damage was observed in 8 workers (6.8%), moderate and advanced lung damage were found in 76 workers (65.0%) and 33 workers (28.2%), respectively. Further, significant downfall of serum CC16 values were observed in relation to progressively increasing lung damage (i.e., mild or low, moderate and high), among the subjects (Fig-2). The mean±SD of serum CC16 value in mild lung damage group was 8.4±0.87 ng/ml as compared to 4.0±2.10 ng/ml in moderate lung damage group and 0.7±0.21 ng/ml in high lung damage groups. It was evident that duration of exposure was not associated with the development of silicosis in this study, possibly due to the fact of exposdure of varying quality and quantity of silica content within the dusts. Therefore it supports the view of association of CC16 with severity of silicotic lung damage.



Example	Small (primary / secondary) opacities (X)	Number of zones involved (Y)	Large opacity (Z)	Total = (X*Y)+Z
1	p/p = 1	2	0	(1*2)+0 = 2
2	q/q = 2	4	2	(2*4)+2=10
3	q/p = 1.5	4	0	(1.5*4)+0=6

Fig. 1: Process of calculation of various degree of Lung damage using LDS.

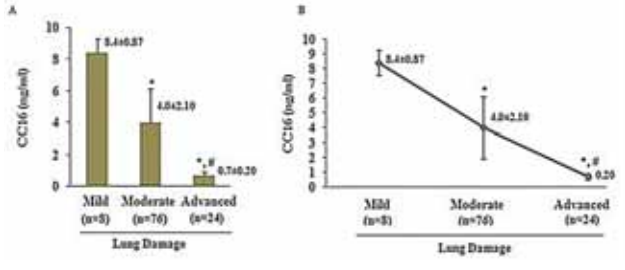


Fig. 2: Serum CC16 values in Mild, Moderate & Advanced lung damage (N=117).

Prevalence & determinants of blood lead levels among lead smelting plant workers

In the traditional smelting process, Lead Sulfide ore (galena) is processed at melting point temperature

in order to obtain lead in its pure form. Lead smelting workers are predominantly exposed to high lead levels and exhibit unacceptable levels of lead in blood (BLL). The objective of the study was to evaluate the blood lead levels (BLL) of all the workers and explore the factors contributing to high blood lead levels in this population. The study recruited 800 occupationally exposed subjects working in different sections of smelting unit, thereby exposed to varying levels and forms of environmental lead. The BLLs were determined as per standard NIOSH method using graphite furnace atomic absorption spectroscopy (GF-AAS). Haemoglobin levels were determined using hemoque tool. Blood pressure was measured using digital sphygmomanometer adhering to American Heart Society guidelines. Statistical analysis was performed using Statistical Package for Social Science version 17.0. Average BLL of the study population was 38.28 ± 13.02 µg/dL (mean ± SE). About 47.7% exhibited high BLL (i.e.>40 µg/dL) and 52.3% had BLL within permissible limits (<40 µg/dL) as per occupational standard and guideline recommended by OSHA. BLL diversity was observed in the study population as per their socio-demographic status, employment elements and clinical symptoms. Higher BLL (i.e.>40 µg/dL) was observed among study participants who were employed in close proximity to the smelting process, possibly as a result of exposure to high levels of lead (like furnace and electrochemical refining sections) as compared to the other sections (Fig. 3). Workers with high BLL complained more often of clinical symptoms.

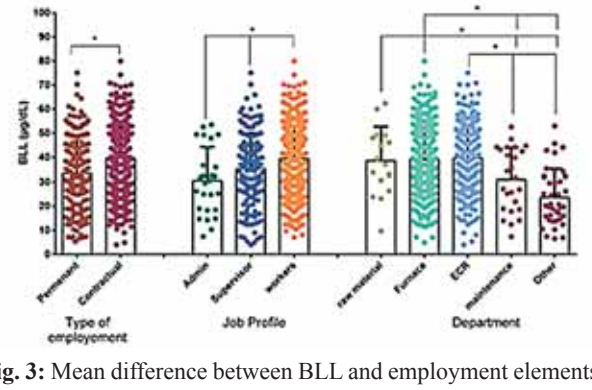


Fig. 3: Mean difference between BLL and employment elements. *P<0.005.

Assessment of environmental pollution exposure and cardio respiratory morbidities among AMTS bus drivers

Present cross sectional study was executed among Ahmedabad metropolitan transport service (AMTS) bus drivers of Ahmedabad city with the aim to evaluate the prevalence of cardiorespiratory morbidities among this population, and determine the possible contributing occupational / environmental hazards. The study evaluated the cardiorespiratory health of 238 drivers in addition to the air pollutants exposed during the duty hours. Average $PM_{2.5}$ and PM_{10} exposure during the 2 working (shift) hours (8-hour Time weighted Average - TWA) were 970.9 (258-1340) µg/m^3 and 1111.7(298-1480) µg/m^3, which were substantially higher than Central Pollution Control Board (CPCB) ambient air quality standards. The study included 73 administrative staff employed at AMTS as control participants. The prevalence of respiratory symptoms like cough and dyspnea were significantly higher among AMTS drivers as compared to control participants. Further a significant fraction (25%) of AMTS drivers exhibited abnormal Pulmonary Function Test (PFT) as compared to control group (8.5%) and mean FEV_1/FVC and $FEF_{25\%-75\%}$ were significantly lower among drivers as compared to control subjects ($p<$ 0.001) suggesting restricted air flow through the large and small airways, respectively. With respect to cardiovascular morbidity, about 65% of the drivers exhibited higher BMI, further 14% & 9 % of the drivers respectively were identified as hypertension for the first time or had their blood pressure poorly controlled. The 10-Year Cardiovascular disease risk score (WHO ischemia 10-year risk score) was substantial higher (>10%) among drivers (27%) compared to controls (17%).Overall, study documented higher cardio-respiratory morbidity attributable to the higher exposure to air pollutant dust ($PM_{2.5}$& PM_{10}).

The role of cattle in transmission of leptospirosis in villages of South Gujarat

Leptospira is a zoonotic disease of public health importance worldwide especially in tropical

countries. The severity of disease in India increase due to various risk factors such as overcrowding, lack of proper sanitation, occupational aspects and socioeconomic class. Transmission of leptospira infection is through direct or indirect contact with urine of infected animals. Although leptospires can infect a wide variety of animals, outcome of an infection is not equal across animal species. Maintenance hosts (wild rodent and cattle) serve as a reservoir for infection to other livestock, domestic animals and wildlife species and human (incidental hosts).To explore seroprevalence and the role of both maintenance host (wild rodent and cattle) in transmission of leptospirosis among human in South Gujarat an epidemiological study was carried out. To study the association of serovars of different hosts (three) of *Leptospira* species, two villages were selected on the basis of death and of illness of human cases in South Gujarat, which is known as endemic for leptospirosis. Seroprevalence of leptospirosis IgM antibodies was detected through ELISA among villagers of South Gujarat (n=153) and was found to be 24.18%. Whereas Microscopic Agglutination Test (MAT), which is gold standard in diagnosis of *Leptospira* and it's seroprevalence was found to be 38.56% with different serovars of *Leptospira* pathogenic Species with serum dilution at 1:50.Diagnosis of *Leptospira* infection in human cases through MAT as per serovars revealed that Australis (27.11%), Hurstbridge (27.11%), Javanica (27.11%) Pyrogens (16.94%), Copenhageni (10.16%) and Bankinang (6.77%).Cattle are considered as maintenance host for *Leptospira* species and it was found that out of 153 serum samples of cattle 12 samples were reacted with different serovars of *Leptospira* pathogenic species (7.84% seroprevalence) with serum dilution as 1:100.Both Human and cattle serum samples from selected villages were tested for serovars through MAT. It was found that some of the serovars (out of 18 serovars used) Australis, Hurstbridge, Javanica, Pyrogens, Copenhageni and Bankinang are common in both human and cattle. There may be chances of transmission of serovars from cattle to human as animal husbandry is their main occupation, hence human cases were found positive for *leptospira* infection. The work is in progress.

Fig. 4: The role of cattle in transmission of leptospirosis in villages of South Gujarat

A study on occupational injuries and evaluation of pollutants among non-traditional tribal community fisherman in coastal area of Tamil Nadu

This study evaluated the health risk associated with fishing and associated activities among tribal fishing community (n=170) in the Pichavaram mangrove in Chidambaram, Tamil Nadu. Demographic data such as life-style characters, socioeconomic status, personal habits, work nature and health illnesses & blood samples for evaluating hematological and biochemical parameters collected during the month of February-2020 after obtaining informed consent. Almost equal number of male (n=82) and female (n=88) subjects were involved in fishing activity. The mean age of the subject was 38.8±15.5 yrs (male 34.8±12; female 39.9±7.8 yrs). Majority of them were illiterate (52%) and few (6%) were graduates. While no female subjects reported of either alcohol or tobacco consumption, male subject had the habits of smoking (12%) and alcohol consumption (23%). Working duration of these workers varied from 12-24 hour per day, commonly spent with their fishing partner. About 69% workers were involved in fishing activity alone, 19% were engaged in selling fish and construction of boats, while remaining 12 % were occupied with the associated / supporting jobs. About 10% of the subjects used personal protective equipment's (PPE). The study population were predominantly from lower socio-economic

status and lower literacy, exaggerating their poor hygiene and dietary practices. Majority of them had injuries related to fishing activities i.e.72% were fish related and 42% related to Oysters (42%). The prevalence of subjective pain in wrist, leg, knee and other joints was high. Abnormal haematological parameters were observed among female (84%) and male (50%) subjects. The population were exposed to the health hazards of high salinity and other contaminants, which is being further explored.

Fig. 5: Occupational injuries and evaluation of pollutants among non-traditional tribal community fisherman in coastal area of Tamilnadu

Study on effect of diesel exhaust fine particulate matter (DPM) containing c-PAHs among the school children in heavy traffic area

Fig. 6: Effect of diesel exhaust fine particulate matter (DPM) containing c-PAHs among the school children in heavy traffic area

A total of 42 indoor and outdoor air samples (< $PM_{2.5}$ fractions) were collected on the PTFE filter paper (37 & 25mm) from the school premises, during work hours, using legacy and personal pumps operated at a flow rate of 9.0 L/min & 2 L/min respectively. The filter papers which were collected through personal pump were assessed for total dust particles (up to PM_{10}) present in the inside and outside of the class rooms. The total dust concentration (863±403 µg/m3) indoors were higher than outdoor premises (562±300 µg/m3). The air samples were collected using legacy pump five stage Sioutas cascade impactor. The concentration of dust in the range of 2.5-10µm, 1.0-2.5µm, 0.5-1.0µm, 0.25-0.5µm and <0.25µm were 26±11 µg/m3, 14±13 µg/m^3, 35±24 µg/m^3, 49±43 µg/m^3 and 26±8 µg/m^3 respectively. The analysis of toxic PAHs compounds by the TQ-GC-MS is under progress. Bangalore schools located proximalto heavy traffic area will be evaluated in the future.

Evaluation of occupational health hazards of coffee plantation workers

About 130 coffee plantation workers residing at Ballehonnur, Chikmagalur district in Karnataka were cross-sectionally evaluated using questionnaire based survey. The study aimed to assess the lifestyle, working conditions, magnitude of health problem and associated risk factors, disease, injuries among coffee plantation workers and develop appropriate intervention strategy based on their felt needs. Their wages were below Rs.10,000/- per month. Majority of them (>90%) were non-smokers and non-alcoholic. Snakebites, insect and mite bites and skin rashes were the most commonly reported complaints. Significantly higher prevalence of irritation, wheezing, stomach ache, lower back ache and joint pain were observed in these workers ($p<0.05$). The other common hazards were physically strenuous work, repeated shouldering of heavy loads, falls and adverse weather conditions.

Fig. 7: Occupational health hazards of coffee plantation workers

Role of noise exposure on Serum magnesium, Ceramide synthase & Platelet Activating Factor (PAF) among professional bus drivers of Bangalore City

The study aimed to evaluate the effects of occupational noise exposure on decreased serum Mg levels and its subsequent effect on platelet activating factor and development of hypertension among bus drivers. Noise levels at 6 sites were measured and the mean time weighted average noise exposures ranged from 69.3 to 77.9 dBA. Ionized and corrected magnesium levels among drivers with hypertension was lower as compared to those with normotension. However, the difference was statistically insignificant, probably due to smaller sample size. Further, in depth study is required towards the problem of low magnesium in hypertensive subjects with Noise Induced Hearing Loss (NIHL).

Scaling up of the implementation of essential interventions for occupational health inBasie Occupational Health Services (BOHS) through Primary Health Care system

This feasibility of BOHS through primary health care system in India was studied. The information collected will serve as baseline data from a pilot project in PHCs of Gujarat State. A structured proforma dealing with the information regarding facilities available at the PHCs and the basic aspects of BOHS was applied, focused on surveillance of work environment and risk assessment, health surveillance and health examinations, advice on preventive and control measures, health education, health promotion, & promotion of work ability, maintaining preparedness for first aid and participation in emergency preparedness, diagnosis of occupational diseases and record keeping. A total of 82 PHCs from 21 districts of Gujarat were surveyed namely Ahmedabad, Gandhinagar, Kheda, Bharuch, Vadodara, Anand, Surendranagar, Bharuch, Mahisagar, Rajkot, Jamnagar, Morbi, Kutch, Mehsana, Patan, Dwarka, Porbandar, Bhavnagar, Amreli, Junagadh and Somnath. Information was collected from 167 medical officers, 782 health professionals, including staff nurses and pharmacists and health workers working in the PHCs and their sub-centres. Overall, the data revealed that all the respondents were in favour of catering the occupational health needs at the grassroot level. However, the findings are a trend of limited knowledge and expertise on occupational health issues among the health professionals at PHCs. It is noteworthy to mention that strengthening of physical resources to cater the occupational health needs may be reviewed along with suitable training facilities to the concerned.

Ergonomics study of Indian ship recycling industry for improvement in occupational health and safety

The aim of this ongoing study is to assess the work stressors in ship recycling process and conceptualize a comprehensive ergonomics surveillance tool for the workers through integrating work life information and ergonomical determinants. A total of 50 workers working in the ship breaking process within the plant area participated in the study. The demographic profile of the workers was recorded, which shows the average age and job tenure of workers were 36.7±9.9 years and 11.1±7.3, implicating experienced workforce in ship recycling work. Most of the workers reported of working more than 10 hours. The average BMI of the studied participants is 21.7 kg/m2 which is normal. The average systolic and diastolic blood pressure are 134.1±19.6 and 88.2±11.0 respectively. As per JNC 7 criteria, the studied group fall under the pre-hypertension category, indicating workers are at risk of developing hypertension in future. Mild conversational hearing loss found in workers whose age is >25 years and having working experience of greater than 5 years. Gas cutting and Jodi work is found to be affecting worker with mild conversational hearing loss as compared to other job. Moderate or severe conversational speech hearing loss was not found in the audiometric data.

Mild and moderate noise induced hearing loss (NIHL) was found in workers with age >25 years, experience greater than 15 years and engaged with gas cutting, jodi and begari work. The data from this project would bring out the health status and morbidities during work among ship recycling workers. This project will be a compilation of ergonomical characteristics and work related health dimensions, work risk assessment, musculoskeletal pain and discomforts of the workers among various ship recycling occupations. Further, workplace noise and environmental warmth, as well as audiometric profile and heat stress surveillance of the workers, would be useful in classification of hearing conservation techniques and heat-related illness. This would aid in designing an effective work-rest schedule protecting the productivity of the organization and the health of the workers, in the long run.

Occupational health study in PakriBarwadih Coal Project with special reference to respiratory health and hearing impairment assessment (TSM)

Occupational health study to evaluate the respiratory health and hearing ability among coal mining workers was executed. The participants of this study were subjected to questionnaire survey, clinical examination, pulmonary function test and audiometry. This study included 250 workers actively involved in mining activity as well as allied activity (having exposure to coal dust). Mean age of the workers was 29.68 ± 7.10 years. Mean height of study subjects was 163.94 ± 5.79 cm and mean weight was 61.23 ± 10.63 kg. Mean job experience was 5.53 ± 5.02 years. Most common symptom complained by study subjects was musculoskeletal pain (16.8%). Other complaints were cough, difficulty in breathing, chest pain, and soreness of mouth. About 10% subjects had systolic blood pressure >140 as well as diastolic blood pressure > 90 mm of mercury. As far as pulmonary function status of study subjects is concerned, about 7% subjects had restrictive type of abnormality (FVC/PFVC < 80%). Obstructive type of abnormality was also present in similar number of subjects. A good number of subjects (17.6%) had $FEV_{1\%}$ values between 70% and 80%. The team examined dust concentration in different workplaces to understand the relationship with lung function problems, if any. The team found that the dust levels ranged from 212 µg/m^3 to 421 µg/m^3**.** As far as hearing efficiency of the study subjects is concerned, most of the subjects were within normal range of hearing. However, six persons had moderate level hearing loss. So far as chest radiographic findings are concerned, opacities suggestive of interstitial lung fibrosis were found in 6% study subjects.

Assessment of health hazards among flour mill workers in Gujarat

Fig. 8: Respiratory health and hearing ability among coal mining workers.

Astudy was carried out at flour mills in Ahmedabad district for health risk assessment of flour mill workers due to bio-aerosols which leads to respiratory morbidities among workers. A total of 152 subjects were participated in this study. Among them 88 were exposed and 64 were non- exposed subjects. Questionnaire based findings showed high prevalence of respiratory symptoms (cough 36.36%, phlegm 26.13% and dyspnea 34.09% among the flour mill respondents compared to the unexposed group (cough 7.81%, phlegm 4.68% and dyspnea 7.81%). The flour mill workers were having significantly higher allergic and asthma complained as compared to control. Exposed workers were significantly more underweight 27 (30.68%) and overweight 11 (12.50%) as compared to control. The

higher value of diastolic 17 (19.32%) and Systolic blood pressure were reported in 13 (14.77%) in exposed workers. In 1999 the American conference of governmental industrial hygienists (ACGIH) proposed a threshold limit value (TLV) of 0.5 mg/$m^3$for flour dust with a sensitization notation. As part of this study, a relationship between flour dust concentrations and units were examined. Total 25 dust sample were collected from 14 flour mills with a range of 1.94 to 472.3 mg/m^3 at different units of flour mill. Dust concentration was significantly greater at processing, packaging and grinding units in comparison to the control reference sites. The dust levels exceed the occupational exposure limit (OEL) of 0.5 mg/m^3 for flour dust. Dust exposure in the working environment affects the lung function values and increased the respiratory symptoms among the flour mill workers. The long term exposure to flour dust and continuous inhalation of flour dust can leads to symptoms of lower respiratory tract inhalation such as cough and shortness of breath. Environment monitoring results showed that airborne bacterial counts were present with a range between 12.35 to 27.26 cfu/m^3 and 1.23 to 2.79 cfu/m^3 on nutrient agar and Mac Conkey agar media by Andersen 6-six stage viable sampler in different units of flour mill, similarly airborne fungal count were varied from 20.46 to 44.03 cfu/m^3. The counts of airborne bacteria and fungi were significantly greater at the processing and packaging units in comparison to the outdoor reference sites. *Pseudomonas* spp., *Enterobacter* spp. were the predominant Gram negative species while *Bacillus* and *Staphylococcus* spp. were the major species of gram positive bacteria were observed. *Aspergillus, Fusarium, Penicillium* and C*ladosporium* spp. were the predominant fungal colonies at flour mill units as compared to outdoor reference sites. Study showed processing and packaging unit workers are more at risk due to concentration of dust was observed significantly higher in these unit as comparison to the control reference sites which may leads development of respiratory impairment.

Fig. 9: Health hazards among flour mill workers in Gujarat.

Hospital Based Surveillance Using Worker's Registry for Occupational Diseases and Injury

Fig. 10: Hospital-based surveillance for disease and injuries pattern among admitted workers at ESIC hospital.

The study involves hospital-based surveillance for disease and injuries pattern among admitted workers at ESIC hospital. The information of 527 under treatment workers were collected from Employees' State Insurance Corporation (ESIC) Model Hospital, Ahmedabad which is a multispecialty center to provide health benefits to worker population along with socio-economic protection. Maximum hospitalizations of workers were related to respiratory (36.20%) and cardiovascular (12.50%) illnesses. Further, nearly 6% workers reported with problems related to musculoskeletal disorders(MSD), among whom

lower back pain was the highly prevalent problem. Injury(non-fatal) at the workplace was recorded as 5.30% among hospitalized workers. Most of the injuries were in the form of bone fractures (35.71%) and burn (28.57%) while performing duties at workplace. Data revealed that compliance and knowledge of safety measure was very less among injured workers, sixty percent of injured workers were not using safety gears or had proper knowledge of preventive measures. These workers were engaged in work continuously for more than 8 hours before injury. A large number of hospitalized workers reported a noisy environment (63.2%) at workplace, and nearly 75.0% workers reported the presence of dust /odour /smoke, and excessive heat at work environment.

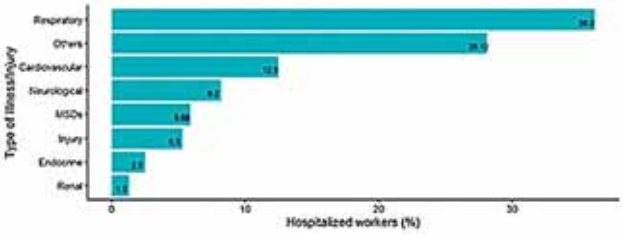


Fig. 11: Reported Illness and Injuries among hospitalized workers.

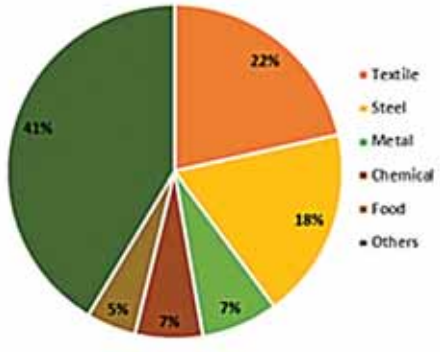


Fig. 12: Distribution of workers from various Industries.

Development of Novel Non-Invasive, Low cost and, rapid detection system for lead in biological sample

ICMR-NIOH have developed and fabricated a transdermal patch system/device for qualitative detection of lead (Pb^{2+}) in clear biological system. The in-vitro validation studies suggested that it has very high sensitivity for lead as the spot test based reaction can detect Pb^{2+} to the level of 10 ppb. When evaluated against other inorganic salt it showed very high specificity towards Pb^{2+} only. The devices is primarily a transdermal patch which collect the sweat sample and a single step colour development reaction confirm presence or absence of lead in the collected sweat sample. The device was also validated among lead-acid battery recyclers and when compared with the gold standard analytical test such as ICP-MS the sensitivity and specificity of the device was found to be > 75% and >95%, respectively. The initial laboratory fabrication was done in the ICMR-NIOH which suggested for readily low cost of the device. It can be useful as point-of-event detection system for lead exposure and considering its non-invasiveness it may also be usable by less trained personnel for detection of the presence/ absence of lead in their sweat. The color reaction developed can also be very useful for detection of lead in environmental monitoring studies for detection of lead in water samples.

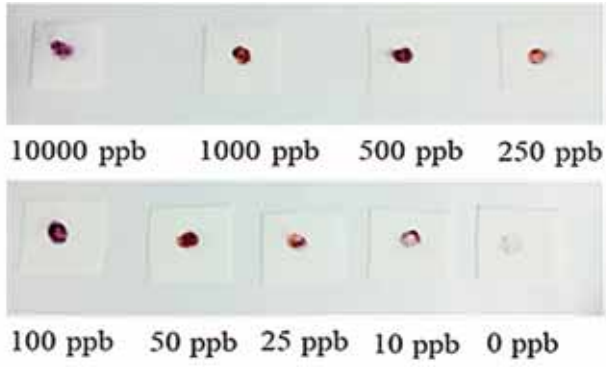


Fig. 13: In-vitro sensitivity testing of the colour reaction

Fig. 14: The developed patch system applied on a worker.

Occupational Health Program: Care and Compliance of Unorganized Sector Workers

Perspective for the Primary Health Care Professionals (OHP-CAPH)

India has a strong workforce of over 500 million, however,>90% of them are in unorganized sector without required minimum socio-economic security. To improve their occupational health services, it is proposed that the existing health care delivery services and through Primary Health Centres (PHCs) would be the most appropriate to deliver occupational health care services to them. Hence it was realized that primary health care physicians need to be trained on Basic Occupational Health Services (BOHS) throughout the country so that they can deliver the required occupational health services for the unorganized sector workers. With that idea a training material on BOHS was developed by ICMR-NIOH in association with Public Health Foundation of India (PHFI) involving national occupational health experts of the country, WHO, and ILO. This was the first of its kind of module. On completion of its development of training material, the first batch of the workshop on Basic Occupational Health & Safety among primary health care physicians was held on 6-8 March 2020 in which Gujarat, Maharashtra &Madhya Pradesh participated. This is the beginning of the programme. Similar kind of workshop will be conducted for primary health care physicians of the country in batches so that they will be able to deliver the required occupational health services for the unorganized sector workers for the control of common occupational diseases specially silicosis and silico-tuberculosis as country is committed to eliminate TB by 2025 and unless silicosis is controlled, TB will never be possible to be eliminated. Hence, training of PHC physicians on BOHS is the need of the country at present.

Multicentre Task Force Entitled "Study to Assess the Exposure and Health Effect of Pesticides"

A total 22 pesticides and their metabolites were targeted in the study.Standard solutions were prepared and spiked into blood and serum samples for accuracy, precision, linearity and recovery determination. Samples were extracted with QuEChERS method for UPLC-QTOF-MS analysis.Biological samples were received from Maharashtra (n=540) and Telangana (n=245) centres May, 2019 onwards (total n=785 samples). Out of which (n=353) biological samples were extracted and analysed using UPLC-QTOF-MS for pesticide residues, which includes blood (n=176) and serum (n=177) samples.The overall result showed that, out of 176 blood samples analysed pesticide residue was found in 8 samples (4.54%) and out of 177 serum samples analysed pesticide residue was found in 18 samples (10.16%). The concentration range of detected pesticide in blood sample was 27 to 154 µg L^{-1} and serum sample was 23 to 346 µg L^{-1}. Pesticide residues of Profenophos, Dichlorvos and Cartap Hydrochloride were found in blood and serum samples. The concentration ranges of Dichlorvos and Profenophos were 124 to 154 µg $L^{-1}$and 27 to 60 µg L^{-1}in blood sample whereas the concentration range of Dichlorvos, Profenophos and Cartap Hydrochloride were 23 to 248 µg L^{-1}, 43 to 51 µg $L^{-1}$and 66 to 346 µg L^{-1} in serum sample.

Monitoring of Pesticide Residues at National Level

A total 829 samples including vegetables (n=686), fruits (n=93), milk (n=30) and water (n=20) were collected from different regions of Gujarat, extracted with QuEChERS method and analysed using UPLC-QTOF-MS and GC-MS for pesticide residues. Overall, monitoring programmeshowed that, Methomyl, Imidacloprid, Thiamethoxam, Acephate, Monocrotophos, Acetamiprid, Cartap Hydrochloride, Chlorantraniliprol, Melaoxon, and Acetamiprid commonly found in the fruit and vegetable samples. The maximum residues were found in Bitter guard, Brinjal, Okra, Bottle gourd, Cluster Beans, Cowpea beans, Green chili and Pomegranate. Moreover, this data can also be used to understand the quality of food and to evaluate the possible health risk associated with their consumption. The pesticide concentration in the majority of samples analysed were well within

the pesticides prescribed limits (MRL) set by Prevention of Food Adulteration (Govt. of India). 0.20% of the samples were found above MRL. However, majority of the food samples were safe for human consumption.

Investigation of availability of the specific antidotes

ICMR-NIOH Poison Information Centre (PIC) investigated the availability of specific antidotes in government and private hospitals from Delhi, Punjab, Haryana, Himachal Pradesh, Uttarakhand, Chandigrah, and Uttar Pradesh, states of India during the year 2019. The study centre has received total 35 responses (some institutes sent department wise response, total institutes responded were 24) from 115 inquiries sent to various institutes. Out of 35 responses received from 24 institutes/ hospitals, 21 were government organizations, 03 were private. All institutes and hospitals were from Urban area and Metro cities. We designed Questionnaire for all the respondent hospitals asking their knowledge about poison information Centre and availability of 41 specific antidotes. Antidote availability was assessed in four categories viz. immediate available, within 24 hrs., within 2-3 days available or not available. Specific antidotes list includes 1. Atropine sulfate 2. Pralidoxime 3. Cholestyramine 4. Vitamin K1 5. D-Penicillamine 6. Calcium disodium edetate 7. Calcium chloride 8. Calcium gluconate 9. Medicated Ethanol 10. Folic acid/Folinic acid 11. Leucovorin 12. Thiamine 13. Amyl nitrite, Sodium thiosulfate (Cyanide antidote kit) 14. Hydroxocobalamin 15. Methylene blue 16. Prussian blue 17. Oxygen, Hyperbaric oxygen 18. Activated charcoal 19. Glucagon 20. Intralipid 21. Fomepizole 22. Dantrolene 23. Cyproheptadine 24. Octreotide 25. Polyethylene glycol 26. Succimer 27. Unithiol 28. N-Acetylcysteine 29. Desferoxamine 30. Flumazenil 31. Naloxone 32. Pyridoxine 33. Digoxin specific antibodies 34. Physostigmine 35. Polyvalant ASV (anti-snake venom) 36. Anti-rabies vaccine 37. Botulinum antitoxin 38. Anti Rabies Serum 39. sodium nitrite 40. Dimercaprol (BAL) 41. Dicobalt edetate. As per response given by participants, common poisoning in their setup is Organophosphorus poisoning, Snake bite, aluminum phosphide poisoning and others. 5 participants told Flumazenil, ASV, Naloxone, Anti Rabies Serum are few of the costlier antidotes. In Immediate antidote availability category majority of participant told Atropine Sulphate, Pralidoxime, Vit K, Calcium Chloride, Calcium gluconate, Folic acid, Thiamine, Leucoverin, Antirabies vaccine, Anti snake venom. In Not available category of antidote, responses were cyanide antidote kit, sodium nitrite, Dicobaltecetate, Dantrolene, Fomepizole, Uninthol, Succimer, Digoxin Specific antibodies, Botulinum antitoxin, Prussian blue, Physostigmine. Rest of antidotes could be available in few hrs. to few days but urgent cases who requires specific antidote will suffer in such situation. 18 participants said they have issue in availability of antidotes. In brief there is genuine issue in getting antidotes in hospitals more common in smaller towns and rural areas. Specifically, Anti Rabies Serum, Anti Snake Venom, Flumazenil, Physostigmine. Most of the time antidotes are out of stock in government as well as private setup.

Interaction between Nrf2 signaling and BDNF-Dopaminergic Circuit in Brain: Molecular Mechanism for Development of Nicotine-Induced Addictive Neurobehavioral Disorders in Rats

The clinical and experimental literatures implicate learned responses evoked by environmental stimuli are associated with subjective actions of drugs of abuse (nicotine, smoking) by means of classical conditioning. Although nicotine and tobacco smoking affect diverse neurotransmitter systems in brain, how these systems may predispose to alter neurobehavioral responses involving specific area of brain is not fully known. Therefore, in the present study, the study centre wishes to highlight dopamine, BDNF, and nicotinic acetylcholine system through receptor-mediated pharmacological modifications in adult rats' neurobehavioral disorders, and underlying molecular mechanism in the cerebral cortex. During 1st year study (2019-2020), the dopamine receptor blocker models were established, where doses mimic human smoking scenario; hence

our experimental model closely resembles to human real life situation. The result showed differential expression of dopamine in the cytosolic fraction of the pooled cerebral cortex homogenates in the adult rats upon treatment with dopamine receptor blockers prior to cigarette smoking and nicotine exposure. Further, serum cotinine, the biomarker of nicotine exposure, increased significantly upon nicotine exposure, which was reversed by pre-treatment of dopamine receptor blockers. The result also showed the modulation of nicotine/smoking-induced stress, or depressive behavior; and cognitive interference due to pre-treatment of the receptor blockers as compared to cigarette smoking/nicotine exposure alone. On completion, our data might be useful in studying the similar scenario of cigarette smoking/nicotine exposure cases in human and strengthening the case for discouraging nicotine replacement therapy as a safe alternative in human. Presently work is continuing with nicotine acetylcholine receptor blocker.

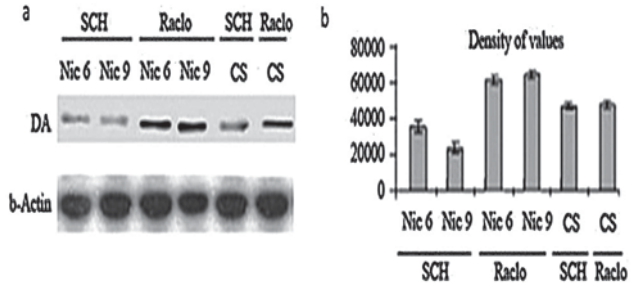


Fig. 15: (a). Western blotting; and (b). Densitometry analysis of dopamine (DA) in adult rat cerebral cortex. CS, Cigarette smoking; Nic 6 & Nic 9, Nicotine dose 6 & 9 mg/kg body weight; SCH &Raclo, Dopamine receptor blockers.

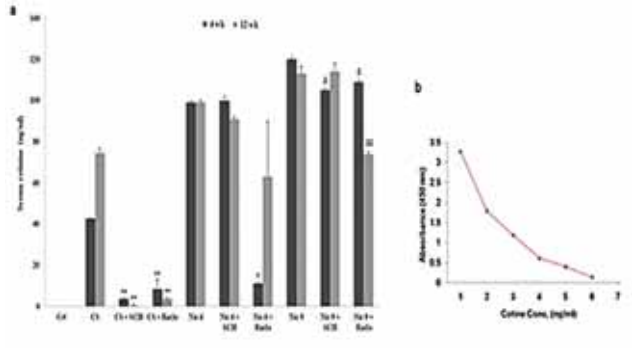


Fig. 16: (a). Serum cotinine (ng/ml) of adult rats; and (b). Cotinine standard curve. Crt, Control; CS, Cigarette smoking; Nic 6 & Nic 9, Nicotine dose 6 & 9 mg/kg body weight; SCH &Raclo, Dopamine receptor blockers. Crt showed '0' as no nicotine/cigarette smoking exposure. $^{**}p<0.01$ vs. CS (4 and 12 week); $^{\dagger}p<0.01$ vs. Nic 6 (4 week); $^{\delta}p<0.05$ vs. Nic 9 (4 week); $^{\delta\delta}p<0.01$ vs. Nic 9 (12 week).

Respiratory morbidities in school children of critically polluted industrial area of Gujarat

A prospective longitudinal study was carried out to assess the respiratory health of school children of the critically polluted industrial area of Ankleshwar, Gujarat. Students (n=736) of class 5th to 7th standard were enrolled in the study.Indoor air sampling revealed that PM_{10} and $PM_{2.5}$concentrations were higher in study area (PM_{10} - 587 and $PM_{2.5}$ -450 µg/m^3 at Andada school; PM_{10} - 334 and $PM_{2.5}$ -302µg/m^3 at Sardarnagar school) as well as control area (PM_{10} - 760 and $PM_{2.5}$ - 696 µg/m^3) as compared to NAAQS/EPA guideline limit (PM_{10} - 150 µg/m^3; $PM_{2.5}$ - 35 µg/m^3 for 24 hrs). VOCs concentrations of study area were found within the ACGIH guideline permissible limits. Ambient Respirable Particulate Matter (RPM) concentration in study area (921 & 411 µg/m^3 at Andada school; 965 & 359 µg/m^3 at Sardarnagar school) were observed 9 times higher than the NAAQS prescribed limit (100 µg/m^3). Oxides of nitrogen (NOx), oxides of sulphur (SOx) and ozone (O_3) though observed higher in study area as compared to control area yet found within the NAAQS guideline limit (NOx- 80 µg/m^3, SOx- 80 µg/m^3, O_3- 180 µg/m^3). Incidence of Upper Respiratory Tract Infection (URTI) episodes were observed significantly higher in the students of study area as compared to the control. Results of PFT of study area student showed that 12% students were found obstructive type abnormality, while 7.2% students ware suffering from restrictive type abnormality. Combined type abnormality found only in 2 students of control area. The result showed that school children of critically polluted area of Ankleshwar are more vulnerable to air pollutants as compared of control area. Chronic exposure may affect the physiological development, learning performance and long lasting health problems which may impose a great economic burden to the society.

Socio behavioural assessment of miners in Gujarat

The study was carried out in different mines in Gujarat (n=76) to assess the magnitude of psychosocial morbidity of workers, to identify the

possible factors associated with the morbidities and to develop intervention strategies to help them cope with the problems. Majority of the workers were on contractual basis. Men workers (66%) were more than women. Many workers, 43.4% had more than 10 years of experience in mining. The workers are exposed to extreme temperatures, dust and noise, 26.3 % complained of high temperatures, 71% complained of dust and 76.3 % complained of noise. The Subjects were screened using General Health questionnaire GHQ-5 to identify minor psychiatric symptoms. The assessment revealed that 43.4% indicated difficulty in their current state. The assessment of social esteem using Rosenberg self esteem scale indicated that 11.8% subjects reported low self esteem. The modified MINI screen indicated that 4% of them needed professional help. WHOQOL-BREF assessment on quality of life scores suggested that the average QOL scores in psychological domain and environment domain (74.6 and 54.5) were comparatively lower than the physical (83.6) and social domain (86). Many of the workers stay away from their families and the contractual nature of their jobs leave them insecure. These may be the reasons for their lower scores. Follow up studies and Professional counselling is recommended which would certainly help those in need to improving their mental health.

Fig. 17: Socio behavioural assessment of miners in Gujarat

PUBLIC HEALTH IMPORTANCE

- **National Survey for State Wise Prevalence of Microbiologically Confirmed Pulmonary Tuberculosis in India"** -As part of the national survey, Gujarat team approached 5240 potential participants and recruited 2656 consenting volunteers across Ahmedabad and Gandhinagar districts. Eight participants were diagnosed Tuberculosis and referred to RNTCP for further management

- **Prepared OHS guidelines** for Copper refinery project: "Occupational Health Assessment and Monitoring Plan for proposed Copper Refinery Project"

- **ICMR-NIOH Poison Information Centre** - In the year 2019, a total of 559 poisoning cases were referred to PIC-NIOH. The male to female ratio was almost 2:1 (Males-362 and females-197) indicating that males are more prone to poisoning compared to females. 22.2% cases (124 cases) were admitted in severe clinical condition. 48.7% of the cases (272 cases) were moderately severe and 24% (134 cases) were with mild severity. 4.3% cases (24 cases) were not severe at all. 0.8% (05 cases) had no history of severity. The team investigated cholinesterase activity in blood samples by testing the plasma as well as RBC cholinesterase activity which are the most reliable markers for acute organophosphorus poisoning. Out of 559 cases tested, 22.7% (127 cases) were known to use of organophosphorus/carbamate pesticides for poisoning, 16.5% (92) cases from antitermite poisoning, 5% (28 cases) from phenyl poisoning, 6.1% (34 cases) from rodenticide and in 5.7% (32 cases) some medications were used for poisoning. The chemicals used for poisoning was not known in 25.4% cases (142 cases). However, various household chemicals, Mosquito repellent, alcohol, and bleaching powder were found to be used in 18.6% cases (104 cases). The exposure to poison was through oral route in 90.5 % cases (506 cases), followed by inhalation in 2.5% (14 cases) cases, dermal exposure in four cases, parental in 01 cases and 6.1% with not known history. The circumstances of poisoning were suicidal in majority of cases (81.4%) whereas accidental

poisoning accounts for 8.4% cases and 01 cases were homicidal. The poisoning cases were categorized according to the occupation of subject who consumed poison. 21.3% were house wives (119 cases) this was followed by unskilled workers 20% (112 cases) and farming allied (8.2%, 46 cases). and 7% (39 cases) were students. A significant number (12.2%, 68 cases) were from people with government/ pvt job. 8.6% cases (48 cases) were drivers. The highest level of incidence was observed in the age group of 21-30 years (38.6%) and found to decline thereafter. Very less incidence was observed in those patients of the age 1-10 years (less than 0.2%). Educational status of patients was found to be inversely related to incidence of poisoning. In 57.6% of the cases, the patient had education up to primary level. The number of poisoning cases were very less (0.7%) among those patients with educational qualification of post-graduation. A significant number of poisoning cases (17.7%) were from uneducated population. The education status of 17 patients was not known. Among all cases main reason for committing suicide is financial issue, around 17.7% (99 cases), followed by family problem 16.5% (92 cases), were mental problem or depression in 10% (56 cases) and love affair or extra marital affairs in 4.7% (26 cases) and exam fear in 0.4% (2 cases). Out of 559 cases 338(60%) says that they will not do it in future if similar situation happens and around 11% (60 cases) says that may be he or she can do it again in future. In short, poisoning with suicidal tendencies with the use of pesticide/insecticide in young population is very common in India and it is mainly due to financial or family problem.

- **Study on perceived morbidity, health seeking behaviour and health care utilization patterns among construction workers of India**"–The study recruited 1250 construction workers and evaluated their perceived morbidity and health seeking behavior, data is being analyzed

- **Study workplace factors associated with burnout symptoms in workers from Gujarat state**" - Designed and developed a culturally appropriate tool to evaluate the occupational mental health and workplace factors of the workers

- **Monitoring of pesticide residues** in food products helps to assess the potential health risk and regulate the maximum residue limits (MRLs) for safe human consumption.

- **Assessment of pesticide related morbidity** profile in the selected populations, burden of pesticide and their metabolites in general population and possible health effects.

- **Study on CKDu among industrial workers** explored occurrence of stage-3 CKDu in workers with increase of age, BMI, experience, presence of risk factors such as hypertension, diabetes, smoking and alcohol consumption habit. Preventive measures were suggested to control/minimize the existing risk factors for further progression of CKDu.

- **Feasibility study of BOHS** through primary health care (PHC) system in India revealed that catering the occupational health needs at the grassroots level is the need of the hour. However, expertise on occupational health issues among the health professionals at PHCs as well as strengthening of physical resources needs upgradation.

- Study on flour mill workers concludes that workers are vulnerable to respiratory impairment due to flour dust exposure in the workplace environment which leads to adverse health effect with work duration in the same profession which may be prevented by using PPE.

- **Evaluation of CC16 as a Reliable Biomarker** for Early Detection of Silicosis in Occupational Set-up: A Pilot Study - conducted a study by enrolling 165 X-ray confirmed silicosis patients (workers from different industries of Gujarat, Rajasthan, Haryana and Delhi NCR); and measured serum club cell protein (CC16) values

along with the extent of lung damage score from their chest x-ray. The result showed that serum CC16 should be a biomarker for early detection of silicosis – higher is the lung damage; lower will be the serum CC16 values among the X-ray confirmed silicosis patients. Based on which a periodic screening of serum CC16, at least once a year along with the occupational history of silica or similar kind of dust exposure is recommended among these workers'/silicosis patients. Further, the periodic screening for serum CC16 will also help to control silico-tuberculosis as silicosis is often associated with silico-tuberculosis.

- **Established a COVID-19** test laboratory with testing by Real time RT-PCR at ICMR-NIOH to support & increase the Govt. of Gujarat's COVID sample tests capacity. A total 32 staff including 4 scientists are dedicated to run the laboratory functional for 24 hr. x 7 days. Laboratory staff were trained from BJ Medical College, Ahmedabad, before initiating its activities.
- **Running Associate Fellow of Industrial Health (AFIH)** course at NIOH along with its regional centres at Kolkata and Bangalore. Associate Fellow of Industrial Health (AFIH) is a three months full time Post Graduate Certificate course in Industrial Health approved by Directorate General Factory Advice Service & Labour Institutes (DGFASLI), Ministry of Labour & Employment, Govt. of India.

ICMR-NATIONAL INSTITUTE FOR RESEARCH IN ENVIRONMENTAL HEALTH, BHOPAL (ICMR-NIREH)

Development of a mito-epigenetic carcinogenic risk assessment model for environmental chemical exposures: A pilot study

Based on the knowledge on mitochondrial epigenomics this study is aiming at developing a mito-epigenetic model of carcinogenic risk assessment for environmental chemical exposures in subjects exposed to highly reactive environmental pro-oxidants.An equal number of blood samples (n=30) were collected from the subjects exposed to broad chemical class of moieties at *in utero* stage and age and gender matched healthy controls. The observed higher levels of pro-inflammatory cytokines (TNF-α, IL-6 and IFN-γ) along with the altered expression profile of transcriptional factors (NF-κβ and NRF-2) in exposed group indicated inflammation existing at a sub-clinical level. Higher frequency of oxidative damages in the mtDNA and complex nature of lesions were observed at fragment 14898-155 bp, 1404-3946 bp and 3734-6739 bp regions of the mitochondrial genome that suggested deficit of an active repair machinery. Moreover, alterations in the expression of mitochondrial fission (Drp1, Fis1 and Mff) and fusion genes (MFN1, MFN2, and OPA1) and higher DNMT1 expression, indicated the possible recruitment to the damaged sites. Variations in mitochondrial respiratory chain complexes and expression of mitochondrial genes (MT-CO1, MT-ND6, MT-ATPase 6 and MT-ATPase8), mitomiRs and their respective targets were also observed. The epigenetic modifiers (HDAC1, HDAC7, EZH2, G9a, KDM6a and P300), methylation of nuclear DNA (LINE1 and % 5mC) and post-translational modifications in histone H3 and H4 also showed variations with respect to controls. The study is ongoing as per schedule.

Aberrant circulating epigenomic signatures: Development and validation of minimal-invasive biomarkers for trans-generational monitoring of air pollution associated cancers

The present study funded under IMPRINT-India Initiative programme by Ministry of Human Resource Development (MHRD) and Ministry of Health and Family Welfare (MoHFW), Government of India, is a collaborative work with Indian Institute of Technology, Kharagpur (IIT-KGP). The study aimed to develop a less-expensive and less-invasive "liquid biopsy" test for screening of high-risk population from air pollution zones of our country. Samples from 220 individuals

residing in high-risk (Delhi, Raipur, Gwalior), mid-risk (Bhopal, Bhubaneswar, Jaipur) and low-risk (Sagar, Nayagarh, Mandla) air-pollution zones of India were collected as per the protocol. Our findings demonstrate that air pollution exposure triggers significant epigenomic alterations, which are reflected in the circulation. Semi-conductor based nanocrystals with controlled excitation for a novel; prompt; "mix and measure" cytometric-based nano-biosensing system was synthesized that offers direct quantification of cell-free circulating (ccf) signatures (methylated ccf-DNA, tri-methylated histone H3 at lysine {4, 9, 27 & 36} and argonaute2 protein-bound ccf-miRNAs). The proposed novel nano-assembly based detection system has a considerable potential of emerging as a minimal invasive easy-to-use method that could possibly permit real-time, rapid and reproducible monitoring of epigenomic markers in clinical and field settings. The work is in progress.

Development of quantum dots based nano–biosensors for detection of circulating cell free miRNAs in environmental associated lung carcinogenesis

In the Indo-Russian joint collaborative project, a novel flow cytometry based immunoassay comprising of semi-conducting quantum dots integrated with antibodies via using copper free site click and carbodiimide coupling chemistries was developed and validated for the detection of differentially expressed AGO2-bound miRNAs in circulation. The work involved amalgamation of fluorescent attributes of the quantum dots (QDs) with the specific targeting properties of the antibodies. The developed point-of-care assay exhibited high selectivity for precise identification of AGO2-bound ccf-miRs, highlighting the translational potential of the nano-biosensor. The study is in progress.

An exploratory study on the potential of circulating microRNAs as minimally invasive effect biomarkers of polycyclic aromatic hydrocarbons exposure

This recently initiated study aims to evaluate a subset of circulating microRNAs as minimally invasive early-warning effect biomarkers of environmental PAHs exposure**.** A total of 100 subjects from heavy vehicular traffic areas in Bhopal has been recruited. Using an interviewer-administered structured questionnaire Information information on potential confounding factors from the recruited subjects was collected along with collection of urine samples from them for the assessment of the internal exposure to polycyclic aromatic hydrocarbons through analysis of their urinary metabolites such as 1-hydroxypyrene, 2-hydroxyphenanthrene, 3-hydroxybenzo[a]pyrene, and 3-hydroxybenz[a] anthracene using gas chromatography-coupled with mass spectroscopy. Expression profiling of a selected subset of microRNAs has been standardized. The study is continuing.

A pilot study on health effects of simultaneous exposure to multiple heavy metals in two different settings of Bhopal. Phase I: Assessment of heavy metals in the ground water from a solid waste disposal site and an industrial area in Bhopal

This pilot study was undertaken during the year to capture the levels of heavy metals *viz.* Cd, As, Hg and Pb pollution in groundwater of a solid waste landfill area, operational for the last 25 years, and an industrial zone in Bhopal and any observable health issues arising from drinking supposedly metal-contaminated water among the residents inhabiting nearby areas. A total of 208 water samples were collected covering all seasons. The recorded seasonally or yearly median concentrations of all the metals were found well within the permissible limits as per Indian Standards in both the areas. The questionnaire-based survey to ascertain health problems that may arise from drinking water contaminated with Pb, Cd, As and Hg was conducted among 285 individuals. No evidence of direct health issues arising from metal exposure was noted.

Population based long term epidemiological study on health effects of Bhopal toxic gas exposure

This long term epidemiological study has been continuing since 1985 (1985-1994 by ICMR under BGDRC; 1996-2010 under Centre for Rehabilitation Studies, Government of M.P; 2011 onwards under NIREH) wherein the available persons belonging to the originally assembled cohort of toxic gas exposed and unexposed persons in 1985, are being surveyed for morbidities and mortalities following the original protocol. During the reporting year 56th round of survey was completed (Jan-Dec 2019). In this round data was collected for a total of 13,962 individuals which included 3,653, 4,074, 3,531 and 2,704 individuals from severely affected, moderately affected, mildly affected and control areas respectively. Out of 13,962 a total of 3,300 (23.6%) individuals reported at least one morbidity. Distribution of morbid individuals (n=2,987; 26.5%) in affected areas was – 25.9% severely exposed, 24.2% moderately exposed, 29.9% mildly exposed and 11.6% unexposed control.

A cross-sectional study on current Health status of gas affected individuals of Bhopal: Phase II Clinical examination of gas exposed survivors

In this new study during the reporting year a total of 500 gas exposed survivors belonging to severely exposed cohort were clinically examined. Of the clinically evaluated subjects, 494 subjects (98.8%) were found suffering from 1 or more acute or chronic morbidities. Of the chronic 494 patients as few as 39 (7.9%) had a single morbidity whereas 455 subjects (92.1%) had multi-morbidity for 7 chronic conditions. As many as 31% subjects were multi-morbid for 3 chronic conditions (triads) and 26.2% subjects were multi-morbid for 4 chronic conditions (tetrads). Of the 72 types of morbidities recorded so far hypertension (47.6%), osteoarthritis (43.6%), refractive errors (29.6%), anemia (18.4%) and cataract (17.4%) emerged as the top 5 individual morbidities. The level of disability in about 87% of the examined subjects, as measured through Barthel Index, was "*mildly ill/near healthy leading near normal life*" (Barthel Index 17-20) followed by 9.2% subjects who were "*chronically ill but able to perform most of the daily activities including employment*" (Barthel Index 13-16).

Cytogenetic profiling of patients with chronic kidney disease : Evaluation of genomic Instabilitity

In this ongoing study cytogenetic profiling of gas exposed and unexposed individuals with chronic kidney disease is being done through conventional and molecular cytogenetic techniques. So far, blood samples from 582 study subjects (Group I: MIC exposed CKD patients - 160; Group II: non-exposed CKD patients -106; Group III: Exposed non-CKD patients -158; Group IV: Normal healthy adults-158) have been collected and micronuclei assay and chromosomal aberration assays completed. Analysis so far showed no significant variation in frequencies of micronuclei (MN) and chromosomal aberration between non exposed CKD group (Group II) and exposed CKD group (Group I). Data is under analysis.

Characterization of prevailing chronic respiratory morbidities among severely gas exposed population of Bhopal

This completed cross-sectional study characterized the respiratory morbidities in severely exposed cohort members of the ongoing Long term population based epidemiological study of NIREH using validated INSEARCH questionnaire followed by evaluation of lung function by spirometry and Forced Oscillation Technique (FOT). The study found a high prevalence of self-reported respiratory symptoms especially breathlessness on exertion in the severe exposed cohort of Bhopal gas disaster. It demonstrated a significantly higher association of breathlessness with abnormality in both spirometry and FOT and confirmed the presence of abnormality in the small airway, independent of spirometry abnormality. This study was carried out more than thirty years after the gas disaster and the cohort population was also exposed to occupational, indoor and outdoor air pollution in subsequent years. In the absence of longitudinal lung function studies, the observed lung function abnormality cannot be attributable by the disaster only.

NON COMMUNICABLE DISEASES

In the area of non-communicable diseases, ICMR's National Institute of Cytology and Preventive Oncology, Noida continues to carry out research studies for prevention and early detection of cancer. The National Centre for Disease Informatics and Research, Bangalore focuses on the National Cancer Registry Programme and related activities like software module for cancer registration, patterns of cancer patient care and survival studies. Desert Medicine Research Centre (DMRC), upgraded and re-named as National Institute for Implementation Research on Non Communicable Diseases (NIIRNCD) on 7th Dec 2019, by Dr. Harsh Vardhan, Hon'ble Minister of Science and Technology, Minister of Health and Family Welfare. This ICMR Institute has been working in the following major research areas during the reported period viz. Early detection of breast cancer, Sickle cell anemia and other studies mainly on IDD, tuberculosis, H1N1, silicosis, snake bite, etc.

Major highlights of various programmes undertaken by ICMR in the area of non-communicable diseases during the year 2019-20 are given below.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF CANCER PREVENTION AND RESEARCH, NOIDA (ICMR-NICPR)

National survey for state-wise prevalence of microbiologically confirmed pulmonary tuberculosis in India (ICMR & WHO Collaborative project)

Carried out in nine clusters of Delhi, a total of 6520 persons were enrolled and 900 sputum samples were tested. Of these, 21 tested positive by CBNAAT, 10 were positive on microscopy and 18 were culture positive.

Fig. 1: NICPR Team for National survey for state-wise prevalence of microbiologically onfirmed pulmonary tuberculosis in India.

Population Based Cancer Registry (PBCR) covering Gautam Budh Nagar covers the rural and urban population of Gautam Budh Nagar (G.B. Nagar) district of Uttar Pradesh. The numbers of incident cases and deaths due to cancer in G. B. Nagar District (UP) for the year 2017 are 1390 and 100 respectively.

Screening and early detection of cervical, breast and oral cancer: A demonstration project in TATA Tea Gardens indicated that increasing awareness among population leading to improved health seeking behaviour, capacity building of

frontline workers and healthcare providers are key components for success.

National Tobacco Testing Laboratory (NTTL) at NICPR

NTTL is a national laboratory providing analytical facilities for tobacco and tobacco products. The Lab analyzed 208 SLT samples for the various parameters such as Nicotine, Moisture, Nitrate-nitrite, Chromium, Total sugars, Ammonia, Volatile Bases, Chloride and pH.

Development DNA vaccine Constructs against India-specific HPV-16 Variant: Enhancement of Immunogenicity of L1construct and characterization of T-cell Epitope-based E6/E7 construct- After multi sequence analysis 12 variations in E6 gene and 8 variations in E7 gene were identified. The previously prepared constructs of HPV 16 L1 (pV16 & pV8) were also evaluated in mice model and pV16 was found to be more immunogenic than pV8.

Role of Ets-1 Transcription Factor in Breast Carcino genesis demonstrated the key role of transcription factor E26 Transformation-Specific-1 (Ets-1) in breast cancer progression in Indian Population. Overexpression of Ets-1 was associated with severity of the cancer lesion and was associated with molecular subtypes of breast cancer.

Identification of Novel phytochemical for Reversal of drug Resistance reversal property in lung cancer cells- 1500 phytochemicals were screened against MRP1 (ABCC1) by in silico methods. Carnosic acid was found to be a potential growth inhibitor of lung cancer stem cells and leads to reduction of the drug resistance by down regulating expression of ABCC1 & ABCG2 and CSC markers CD44 & CD133. Carnosic acid may be a potent molecule against drug resistance in lung cancer.

Existing NICPR web-portal for cancer awareness of general population and level-1 healthcare providers was evaluatedfor face validity, construct validity, tool evaluation using qualitative and quantitative research methods and efficacy check through web analyticsto assist in better outreach of cancer screening activities in the country.

Effective implementation of tax and TAPS measures for prevention and control of smokeless tobacco (SLT) in South East Asia Region -A repository of information on SLT industry and good practices related to SLT policy and regulation was launched "smokelesstobaccocontrolindia.com".

Addressing Smokeless Tobacco Use & Building Research Capacity in South Asia (ASTRA)– A randomised-controlled, feasibility trial for smokeless tobacco cessation

This is a multi-country study being conducted in collaboration with the University of York, United Kingdom to identify the feasibility and effectiveness of behavioural support therapy in enabling quitting use of smokeless tobacco (SLT) among adults.

Capacity building in cancer prevention and early detection throughthe ECHO model at NICPR-ECHO Superhub -566 medical officers, 149 gynaecologists, and 59 dentists from across India were trained successfully as per the mandate of the Ministry of Health & Family Welfare, Government of India.

PUBLIC HEALTH IMPORTANCE

- Spearheaded a Policy Review, *published in* ***The Lancet Oncology*** which describes the policy implementation gaps in smokeless tobacco control, its reasons and recommendations on how to bridge this gap.
- National Tobacco Control Programme (NTCP) website maintained by MoHFW, Govt. of India, has included a dedicated page for WHO FCTC GKHSLT on their website.
- The WHO FCTC Global Knowledge Hub on Smokeless Tobacco at NICPR conducted a 4-month global online course on smokeless tobacco in collaboration with Tobacco Control Research Branch (TCRB) at National Cancer Institute (NCI)to equip the

participants withskills and strategies necessary in supporting effective SLT control policy development, implementation and evaluation. 78 participantsfrom 11 countries were trained successfully.

- Organized an International meeting on Tobacco Advertisement Promotion and Sponsorship Ban for Smokeless Tobacco, 6-7 Nov 2019 for four SEAR countries (Bhutan, Sri Lanka, Bangladesh, Myanmar) and Indian states in collaboration with WHO SEARO .
- The WHO FCTC Global Knowledge Hub on Smokeless Tobacco at NICPR **assisted Myanmar** to identify priorities and key recommendation for framing policies for tobacco control during a meeting held on 19-22 Nov 2019, Nay Pyi Taw, Myanmar,


तंबाकू नियंत्रण की बारीकियां सीखेगा म्यांमार

म्यांमार में आयोजित चार दिवसीय कार्यशाला में दोनों देशों के बीच बनी सहमति

नॉलेज हब से कराया अवगत

Fig. 2: Assisting parties in addressing SLT use and development of relevant policies on WHO FCTC requirements – Nay PyiTaw, Myanmar, 19–22 Nov, 2019.

Organized the National Consultation for regulating Smokeless tobacco, 18- 19 Feb, 2020 in Patna, Bihar in collaboration with The International Union against Tuberculosis and Lung Disease to address Effective implementation of tax and TAPS measures for prevention and control of smokeless tobacco in South East Asia Region. Representatives from 11 high SLT use burden States attended the meeting and shared the challenges and measures adopted by various state governments for control of SLT use.

Fig. 3: National Consultation on "Effective Implementation of Measures for Control of Smokeless Tobacco (SLT) use in India".

- ICMR-NICPR has been designated as **nodal center for training Medical Officers of all States in cancer screening** by MoHFW in May 2019. NICPR has trained 345 Medical Officers, 145 Gynecologists and 112 dentists from Govt sector in cancer screening.

Fig. 4: Training workshops for Medical Officers of all States in cancer screening.

- ICMR-NICPR organized **three workshops under the aegis of ICMR-AU-STRC collaboration for African delegates** on (a) Basic molecular biology techniques relevant to cancer research; (b) Cervical cancer screening for pathologists; (c) Research methodology and biostatistical analysis.

Fig. 5: Microscopy session during the ICMR-AU-STRC Hands-on workshop on cervical cancer screening for pathologists.

- Division of Molecular Diagnostics of ICMR-NICPR is recognized for **Evaluation of In-vitro diagnostic Medical devices for Cancer (Cervical cancer/HPV diagnostics) under the Medical Devices rules 2017, CDSCO** since September 2019
- ICMR-NICPRhas been**accredited as National Training Centre for Colposcopy**by the Indian Society of Colposcopy and Cervical Pathology (ISCCP) in April 2019
- The **NTTL at ICMR-NICPR was notified in the Gazette of India** on 5th September, 2019 by Ministry of Health and Family Welfare, Govt. of India.


भारत का राजपत्र
The Gazette of India

Fig. 6: Gazette notification of NICPR-NTTL.

ICMR-NATIONAL CENTRE FOR DISEASE INFORMATICS AND RESEARCH, BENGALURU (ICMR-NCDIR)

Research Study to Develop Mapping of SNOMED CT to ICD-10 Coding

SNOMED CT is a standard clinical terminology inputs used in Electronic Health Records (EHR), and useful for indexing, storing, retrieving, and aggregating clinical data. Objectives of the study were to identify the gaps in SNOMED to ICD 10 mapping for Non-Communicable Diseases like Malignant Neoplasm, Diabetes and Diseases of the Circulatory system.A prototype to integrate SNOMED CT terms to ICD 10 mapping has been developed in Java and integrated in the e-Mor software application.

Pilot study on a national model to measure burden and map quality of care for type 2 diabetes mellitus rural population in India, involving medical colleges through primary health care setup

A pilot study was conducted between June-August 2019 in three villages of Devanahalli taluk, rural Bengaluru. Prevalence of Diabetes and Prediabetes in three villages were 10.9% and 6.3% respectively. Prevalence of behavioral and metabolic risk factors were inadequate intake of fruits and vegetables (82.3%), inadequate physical activity (46.8%), current tobacco use (32.7%), current alcohol use (9.9%), generalized obesity BMI $\geq$ 30.00 kg/m2 (7.5%), central obesity (46.4%) and Hypertension (24.3%). More than three-fourth (75.8%) of known diabetes individuals were taking treatment from private health sector and 85.5% had controlled blood glucose levels. Based on the pilot study, a larger study is being planned in a multi-centric mode.

ICMR Policy on Research Integrity and Publication Ethics (RIPE)

Fig. 7: The primary aim of the policy is to ensure highest professional and ethical standards for biomedical and health research at all stages right from inception, conduct of research, review, integrity in analysis, reporting and publication and translation for the benefit of population and provide a roadmap to overcome/eliminate any sort of misconduct.

ICMR Consensus Guideline on Do Not Attempt Resuscitation (DNAR)

ICMR drafted a position paper on 'Do Not Attempt Resuscitation (DNAR)' to guide treating physicians to take decision when the patient's chances of survival are extremely low and to preserve the dignity in death by avoiding medically non-beneficial CPR while providing compassionate care.

Fig. 8: Do Not Attempt Resuscitation (DNAR)' meeting.

1. Dissemination Report (2017-2019)

A consolidated report was prepared on dissemination and training programs on ICMR National Ethical Guidelines conducted by ICMR Bioethics Unit, NCDIR, Bengaluru across the country during 2017-2019 to reach out to maximum possible stakeholders.

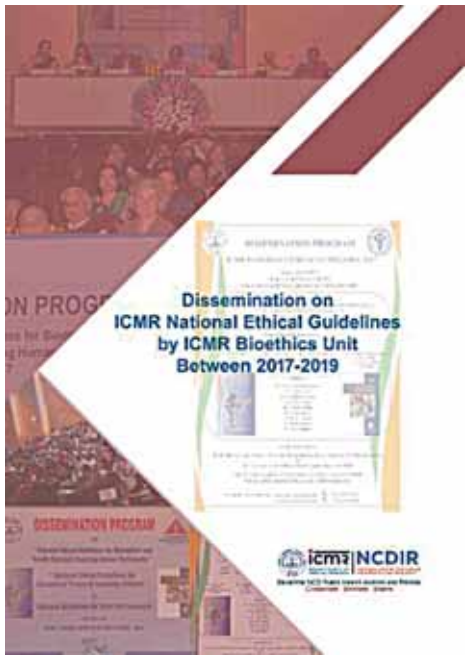


Fig. 9: Dissemination and training programs on ICMR National Ethical Guidelines conducted by ICMR Bioethics Unit, NCDIR, Bengaluru.

2. ICMR Training on Biomedical and Health Research Ethics

Fig. 10: At BRD Medical College, Gorakhpur on 21st-22nd January, 2020.

Fig. 11: ICMR Training on Responsible Conduct of Research and Publication Ethics held on 28th February 2020 at NCDIR, Bengaluru.

Implementation of NCDIR electronic Mortality software (NCDIR e-Mor) in hospitals of the National Cancer Registry Programme (NCRP) network

Aim of the study is to improve the cause of death information using electronic software to record institutional deaths in cancer registry hospitals in the north east states of India. Four centres have implemented NCDIR e-Mor in the sates of Mizoram, Nagaland, Assam and Meghalaya during the year 2019-20 totalling to 17 centres that have implemented the project in North East.Fivecentres registered to implement NCDIR e-Mor in the state of Haryana, Karnataka, Gujarat, Maharashtra and Jharkhand during the year 2019-20 making the total no. of centres seven.

National Guidelines for Ethics Committees Reviewing Biomedical & Health Research during Covid-19 Pandemic, April 2020

Prepared to facilitate easy understanding for the Ethics Committees (ECs) to conduct review in

expedited manner in the current prevailing pandemic situation. It is expected that this guideline will be useful not only for ethics committees but for all stakeholders in research and public.

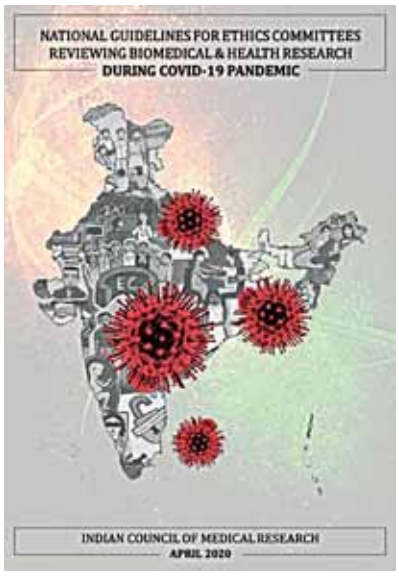


Fig. 12: National Guidelines for Ethics Committees Reviewing Biomedical & Health Research during Covid-19 Pandemic

SOP Template for Ethics Review of Biomedical and Health Research during Covid-19 Pandemic

The Standard Operating Procedure (SOP) template was developed to guide the Ethics Committee for the conduct of ethics review in an emergency situation with restrictions as imposed by social distancing requirements during the COVID-19 outbreak. The SOP can be adopted by EC reviewing biomedical and health research during Covid-19 Pandemic. The SOP template highlights the step by step procedure for submission and initial review of the protocol, virtual EC Meetings and post meeting activities.

ICMR-NATIONAL INSTITUTE FOR IMPLEMENTATION RESEARCH ON NON-COMMUNICABLE DISEASES (ICMR-NIIRNCD)

Desert Medicine Research Centre (DMRC) was upgraded and re-named as National Institute for Implementation Research on Non Communicable Diseases (NIIRNCD) on 7th Dec 2019, by Dr. Harsh Vardhan, Hon'ble Minister of Science and Technology, Minister of Health and Family Welfare and Minister of Earth Sciences and Shri Gajendra Singh Shekhawat, Hon'ble Union Minister of Jal Shakti.

Fig. 13: Desert Medicine Research Centre (DMRC) was upgraded and re-named as National Institute for Implementation Research on Non Communicable Diseases (NIIRNCD) on 7th Dec 2019, by Dr. Harsh Vardhan, Hon'ble Minister of Science and Technology, Minister of Health and Family Welfare

Fig. 14 & 15: Desert Medicine Research Centre (DMRC) was upgraded and re-named as National Institute for Implementation Research on Non Communicable Diseases (NIIRNCD) on 7th Dec 2019

Institute has been working in the following major research areas during the reported period viz. Early detection of breast cancer, Sickle cell anemia and other studies mainly on IDD, tuberculosis, H1N1, silicosis, snake bite, etc.

- Under the breast cancer project, a total of 389 suspect cases of breast cancer were identified by different modes, of which, 122 had undergone Clinical Breast Examination at PHCs and 23 at Private hospitals. 99 cases were referred from PHCs to Govt. Tertiary health centres and 57 cases had visited Tertiary health centres including 87 who had visited directly.

Sickle Cell Anemia – Screening & Counselling

Large scale of screening of tribal populations in Tribal Sub Plan Districts of Rajasthan and implementation of intervention/counseling with treatment to affected population is being carried out.

- 83000+ (6-21 age group) were screened
- The overall prevalence was 11.5% with highest among Garasiya tribe.
- On basis of the recommendation of Institute, the individuals were considered eligible for 'persons with disabilities' under RPWD Act.

Table 1: District wise prevalence of trait and sickle cell diseases

Name of the District	Number of student screened	Positive N (%)	AS N (%)	SS N (%)	Refused
Udaipur	31128	4377 (14.06)	3590 (11.53)	89 (0.29)	698 (2.24)
Banswara	52157	5229 (10.03)	4504 (8.64)	176 (0.34)	549 (1.05)
Total	83285	9606 (11.53)	8094 (9.72)	265 (0.32)	1247 (1.50)

A newborn screening program for Sickle cell anaemia (disease) in tribal populations of TSP areas of state was conducted.

Table 2: Distribution of new born in Kotda and Jhadol block of Udaipur.

BLOCK/ PHC	AS in % (n)	SS in % (n)	% Positive (n)	Number of new born screened (n)
KOTDA	17.04 (114)	1.04 (7)	18.08 (121)	669
JHADOL	9.37 (15)	0.62 (1)	10 (16)	160
Total	15.56 (129)	0.96 (8)	16.52 (137)	829

National TB Prevalence survey is being conducted with primary objectives of estimating point prevalence of microbiologically confirmed pulmonary TB among persons aged ≥15 years in India at National level and also individually for 20 states / state groups. Till the end of Mar 2020, 5 clusters covering 3640 registered participants were completed. 12 cases of active tuberculosis were detected during this survey period.

Early diagnosis & development of a referral system for silicosis among sandstone miners Project has so far screened about 350 miners; and 12% of them have respiratory symptoms. An interesting observation of the project so far is that 10% of those with no symptoms have pulse oxymetery readings below 95%; especially the ones who are above the age of 30 years and have been working for last 10 years or so.

The objective of the setting up of **Model Rural Health Research Unit, Bhanpur Kala, Jaipur** (MRHRU) was to create infrastructure at the periphery for transfer of technology to the rural areas for improving the quality of health services of rural population and to ensure the much needed geographical spread of health research infrastructure in the rural areas.

i. **Point of Care:** Use of point of care technology Cardiotocography in MRHRU and its interpretation from experts of SMS Medical College, Jaipur through WhatsApp has been executed and found to be effective and life saving for rural population. Use of point care technology for the detection and treatment of H1N1 and TB has been found to be effective in rural setup.

ii. **Mapping of Sickle Cell Anemia, β-thalassemia**: A total of 686 individuals were screened for beta- thalasemmia and sickle cell disorder and out of them 67 were found to be sickle positive and prevalence was found to be 9.76%. No sickle cell disorder case has been reported from the study area.

iii. **Consumption pattern of food and food products/ items high in fat, salt and sugar among selected cities/ towns and rural population of India.** Each of 30 villages of Chomu block and Jamwaramgarh has been surveyed and blood collection has been done for biochemical analysis. The report has been distributed to study participants. Study participants of Chomu block were having more serum Cholesterol , Glucose and Triglyceride than the study participants of Jamwa Ramgarh. A total of 2060 household were assessed for the consumption pattern of Jamwa Ramgarh block of Jaipur district. A total of 2052 household were assessed the consumption pattern of Chomu block of Jaipur district. The anthropometric parameters of the individuals residing in the study houses have been taken. The 24 hour dietary recalls have been taken.

Tribal Health Research Unit

This is one of the five units of ICMR and was established in 2015 in this Institute. The objectives of the unit were to establish a data bank and knowledge centre on Tribals of Rajasthan. Tribal population of Rajasthan consists of 13.5% of the total population. A total of 4175 tribe individuals were screened for sickle cell anemia, out of which 405 individuals were found sickle cell positive. The overall prevalence of the disease was 9.75%. When the prevalence was compared between the tribes, highest prevalence of 9.07% was recorded among the Garasia tribes and the among the Bhils, it was 0.18%. A total of 951 cases were screened for beta-thalassemia and 69 individuals were found beta-thalassemia positive with a prevalence of 7.25%. A total of 465 individuals were screened for glucose 6 phosphate dehydrogenase deficiency test and 13 individuals were found glucose 6 phosphate dehydrogenase deficient with prevalence of 2.79%.

EXTRAMURAL RESEARCH

In the division of Noncommunicable diseases, 24areas are covered and a total of 11 Centres for Advanced Research and Excellence were ongoing during the year 2019-20. In addition there were 102 Task Force projects, many of which were multicentric, and 180 adhoc projects and 251 Fellowship projects. The division spent a collective of 90.84 crores during the year. A brief description of some of these is as follows:

CARE

Centre for Advanced Research and Excellence in Heart Failure

CARE in HF at the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), initiated on 20.03.2019, is undertaking following activities:

i. A national database of heart failure including all heart failure databases in country (e.g. the one in Himachal Pradesh)

ii. ICMR – National HF Biobank

iii. Task sharing and mHealth interventions by trained nurses and family care givers for management of HF in India (TIME-HF)

iv. Micro-economic impact of HF. Assessing Quality of Life (QOL) in Indian patients with HF

v. Development of point-of-care (POC) device for measuring plasma NT-proBNP (N-terminal fragment of Pro-Brain Natriuretic Peptide

vi. Heart failure rehabilitation and genetic studies.

Centre for Advanced Research & Excellence in Young Diabetes

The Centre for Advanced Research (CARE) in young diabetes has four independent research projects.

- It is proposed to develop and test a paediatric to adult management transition intervention for T1DM.
- A family based intervention to reduce cardiovascular risk factors among women with history of gestational diabetes will be tested.
- The longitudinal studies and GDM mother-offspring cohort are designed to understand the pathways of long term outcomes of YOD and GDM, with an aim to develop preventive and management strategies.
- It is also proposed to establish a national young diabetes information warehouse to translate the evidence to be generated through the CARE in young diabetes.

Centre for Advanced Research & Excellence on Acute Myeloid Leukemia

Acute Myeloid Leukemia (AML) in India has a disease burden of 2.5 cases per 100,000 and is distinct from the west. The main focus of the project is to characterize LSC in AML to identify deranged pathways or factors which may then be used to develop appropriate therapeutic approach against them. Work has been initiated primarily on detection, identification and quantification of Leukemic Stem Cells (LSC) and Hematopoietic Stem Cells (HSC). The protocol for characterization of HSC and LSC has been standardized in AML as well as controls. Eighty patients with a diagnosis of AML and five controls have also been analyzed for frequency of HSC and LSC. Out of the 80 AML cases, 18 with paired bone marrow at the time of diagnosis and post-induction have been compared for the frequency of HSC and LSC.

CARE- ON KIDNEY DISEASE: BIOMARKER & NEWER THERAPEUTICS

To establish urinary-exosome biomarkers for early prediction of incident CKD in the highrisk population

For this, subjects from Lucknow and Puducherry Area have been recruited. Nearly , 340 subjects who fulfilled the inclusion criterion have been recruited. Gender, BMI and Age of these subjects have been noted besides isolating Urinary Exosomes for bio-marker analysis besides 1100 non-diabetic subjects.

Establish a non-invasive approach for diagnosis of non-diabetic kidney disease (NDKD) or superimposed NDKD, in CKD patients with DM

Progress: To date, renal biopsies and urine samples from 260 kidney failure cases have been collected. The samples from these biopsy-proven cases are processed for analysis; Besides performing data mining and plan to use bioinformatics approaches to build a biomarker panel (of around 20 genes) with the potential for specific diagnosis of DKD and NDKD in subjects with diabetes

Test the therapeutic potential of exosomes in diabetic kidney disease

Under this project, isolation and characterization of kidney derived exosomes, and then test their therapeutic potential in rodent models with kidney disease is being undertaken. Exosomes from two different sources have been collected, and characterized these by miR-profiling. In the first trial experiment, Kidney disease was successfully developed and validated in three Wistar rats. The PI has tracked the bio-distribution of the injected exosomes and found their successful homing in kidney tissue . The animal experiment is underway.

Centre For Advanced Research (CAR) In Paediatric Uropathies & CKD

Centre of Excellence aimed at studying pathways for finding out pathophysiology and pathogenesis of various uropathies and kidney diseases among children at its inception was initiated in December 2017 . The specific objectives of the Centre are

To study the alteration in the status of mRNA (up-regulation) as an early indicator for inception of renal damage. ***In Blood:*** Plasma renin activity (PRA), Transforming growth factor ß1 (TGF-ß1), Tumour necrosis factor α (TNF-α), Soluble TNF receptor-1 (sTNFr-1), Interleukin-6 (IL-6), Microalbuminuria & Angiotensin II. ***In Urine:***Urinary lysosomal enzyme N-acetyl-beta-D-glucosaminidase (NAG), and brush border enzymes alkaline phosphatase (ALP) & gamma-glutamyl transferase (GGT) before and after anti-reflux procedure AND before & after spontaneous resolution of reflux.

Messenger RNA (mRNA) upregulation in urine was studied with respect to the distribution of following polymorphisms in, both, subjects & controls PAX2, BMP-4, ACE & AT2R . Besides, these additional four urinary biomarkers (TFF1, TFF3, NGAL and microalbumin) are found to be raised in the setting of early & late stages of CKD. NGAL and TFF3 are strong predictors of early (stage 1 and 2) and late (stage 3 and above) stages of CKD respectively, therefore can be considered as point of care tests.

The significantly higher concentrations of urinary biomarkers in children with polymorphisms of RAS candidate genes (AT2R and ACE) provides a clear image about children at-risk for progressive renal injury. Serial measurement of urinary biomarkers in these children, even before surgery, can serve as a great prognostic tool.

CARE on Neuro-assistive technologies for Stroke Recovery

Primary objectives of the Centre will be (four verticals)i.e.tooptimizetherobotichandexoskeleton for upper limb rehabilitation in stroke patients; to design a piezoelectric hand glove (robotic glove) with machine interface for hand biomechanics and function; to explore the potential of virtual reality (VR) and /or its integration to robotic exoskeleton for neuro-rehabilitation; and to study the efficacy of these on upper limb hand function in stroke on clinical scales and functional MR imaging. Secondary objectives will be to develop the module for cloud based tele-rehabilitation monitoring for robotic exoskeleton, which include to improvise the device to include proximal joints exercise in the device, to take patient feedback and optimize the robotic device accordingly; to use the device in different operational mode and evaluate if any enhancement is required in the capability of device; to provide real time feedback of robotic hand glove for neuro-quantitative assessments like muscle and joint torque, angular displacements, and hand position; and to explore the role of non-invasive brain stimulation (TMS &tDCS) and robotic glove for upper limb function in stroke.

ONCOLOGY

Cancer Management Guidelines

Cancers are an important disease entity in India, accounting for about 17, 00,000 new cases in the country as per recent data of National Cancer Registry Programme (2012-2014). While survival after treatment in certain sites of cancer is good, the response in many other common sites (like lung, oesophagus, stomach, etc.) is extremely poor. As per recent publication on Patterns of Care and Survival Studies; the chances of survival vary depending upon treatment being followed. A total of 20 documents have been published so far (Buccal Mucosa, Gastric, Colorectal, Gall Bladder, Tongue, Non Hodgkin'sLymphome –HG, Soft Tissue Sarcoma, Multiple Myeloma, Breast, Oesophagus, Paediatric and Soft Tissue Tumors and Lymphomas; Cervix, Larynx and Hypopharynx Cancers, Pancreas, Hepatocellular Carcinoma, Neuroendocrine Tumours). Out of which, 07 are published during period. The summary is available at ICMR website (www.icmr.nic.in) and is also published in journals.

Screening and Early Detection of Cervical, Breast and Oral cancer in Cachar, Assam: a pilot project

The proposal is aimed at (i) capacity building i.e. to train the master trainers in screening of cervical,

breast and oral cancer and work up of screen positive cases for referral and treatment; (ii) initiate a systematic population based cancer screening at Cachar district and link the screening services to appropriate evaluation and treatment facilities and (iii) assess the prevalence and incidence of cancers specially three common cancers viz. cervix, breast and oral cavity and their premalignant conditions. During phase I, the training of the master trainers on screening and early diagnosis of common cancers was undertaken by NICPR, Noida. These master trainers, in turn train the frontline workers. During phase II, the front-line workers trained by master trainers implemented the screening program in the community. A mobile application had been developed based on this proforma, which can be used for data collection online as well as offline. Cachar staff and Medical Social Workers were trained using ECHO (Extension of Community Health Outcomes).

Strengthening State Non-Communicable Disease Programme for early detection of Breast Cancer involving strategic education and awareness among the women: a joint programme of State Government and ICMR-Desert Medicine Research Centre, Jodhpur

The study is aimed to strengthen state breast cancer screening programme and develop a referral system for diagnosis and treatment of suspected cases at state medical colleges/ district hospitals. The proposal is aimed to create awareness amongst women aged 30+ in the state about the disease and practice of breast self-examination, train para- medical staff to create awareness and locate the suspects and develop referral system for diagnosis and treatment of suspected cases.A total of 57,241 women have been interviewed and 68,197 women have been taught breast self examination technique. Further, training was also imparted to 17,833 women on breast self examination (BSE) for early detection of breast cancer. A total of 8,281 telephonic communication have been made with women motivating them for breast self examination. Around 229 suspect cases of breast cancer were identified at community level and through referral system via Primary Health Centre (PHC), The suspected cases of breast cancer reached the medical college. A feasibility study has been undertaken for screening of three common cancers (oral, breast and cervix) in one PHC area of Jalore district of Rajasthan.

Concurrent evaluation of Human Papilloma Virus (HPV) vaccine program and vaccine acceptance among adolescent girls in Punjab, 2017

It is aimed to review the HPV vaccination program in terms of various inputs (material and human resources etc.), implementation processes and coverage in four program districts in Punjab. The study was primarily aimed to review the implementation of the program in first phase and to understand the acceptance of the program at the community level. Cross sectional survey was conducted in Bhatinda and Mansa districts among girls who received one dose of HPV vaccine in government/private schools and among girls who received second dose in government schools in 2017. The acceptance was above 98% in all the groups. Among parents of unvaccinated children, acceptance was above 96% in both the districts. Overall, 4-8% of the girls reported minor side effects such as pain at the injection site, fever and giddiness. Awareness that HPV vaccine prevents cervical cancer ranged from 7% - 21.8% in various groups. There was high acceptance of HPV vaccine and low prevalence of minor side effects among girls in two districts in Punjab.

Cancers in North East Region

The proposal on "Comprehensive microbiome characterization in esophageal, stomach and nasopharyngeal cancers of North Eastern India by Cachar Cancer Hospital and Research Centre, Silchar, Assam," was initiated with aim of undertaking comprehensive microbiome profiling of esophagus, stomach and nasopharyngeal cancers and validate microbiome microarray findings with

targeted NGS and qPCR based testing. It is also proposed to correlate microbiome data with tumor stage, treatment response, prognosis, ethnicity and other clinic- pathological factors.

India Cancer Research Consortium (ICRC)

India Cancer Research Consortium (ICRC) was established (in July 2019) under aegis of ICMR-DHR with aim to bring all the stakeholders working in cancer research under one umbrella that include researchers, health-care professionals, public health representatives/policy makers, international agencies, academic institutions about working together to conquer cancer. It is expected that research would be accelerated, especially in areas and programmes relevant for policy makers. The purpose of cancer consortium is to identify, prioritize and respond to the research needs of the country for prevention, control and management of cancer in India. The Thematic Working Groups are constituted based on the strategic areas and draw upon a diverse set of competencies and knowledge. Seven Thematic Working Groups identified are: (i) Prevention and Epidemiology; (ii) Diagnostics; (iii) Therapeutics; (iv) Palliative Care; (v) Innovation and (vi) Clinical Trial. Technical Advisory Group is mandated to provide technical guidance and prioritize research topics with Director General, ICMR as chairperson. The TAG also oversees establishment of ICRC and periodically review its activities vis-à-vis action plans. The TAG would also inform the Leadership Group (LG) periodically about the progress, achievements and challenges, if any and assist the LG in decision-making. The TAG facilitates the development and support of trans-institutional efforts and ensure research is tuned to address programme gaps & challenges. Government agencies (MOHFW, DGHS, ICMR institutes, PGI Chandigarh, AIIMS, Delhi); academic institutions (Indian Institute of Science, Bangalore, Institute of Bioresource and Sustainbility Development, Assam); international agencies (WHO, National Cancer Institute, USA), industries (Biocon, Pfizer, Thermofisher), etc are part of various comittteees thus constituted. A high-level Leadership Group (LG) with the Hon'ble Union Minister for Health & Family Welfare as Chair would be constituted to provide the overall advice and direction to ICRC. Following call for proposals; the project review committees were constituted to review proposals and 13 proposals are being funded.

DIABETES

Registry of People with Diabetes in India with Young Age at Onset

Young Diabetes Registry (YDR) was started in the year 2006. By end of phase II, around 20,000 young diabetes patients in the registry were enrolled. Apart from the routine data collection exercises, annual training workshops were organized at all the collaborating centres. Data entry software was developed in-house. So far data of 20785 subjects (phase I-5546 and phase II-155239 and follow up proformae 11780) has been entered. Two publications have been brought out viz: *Registry of Youth Onset Diabetes in India (YDR): Rationale, Recruitment and Current Status; Diabetes Science and Technology; 1-8; DOI: 10.1177/1932296816645121*) and second paper (*Demographic and clinical profile of youth onset diabetes patients in India- Results from the baseline data of a clinic based registry of people with diabetes in India with young age at onset (YDR) - [YDR-02]*. Pradeep A Praveen, S V Madhu, Viswanathan Mohan , Siddhartha Das , Sanjeeb Kakati, Nalini Shah, Manoj Chadha , Sanjay Kumar Bhadada, Tanvir Kaur, R S Dhaliwal, Ashok Kumar Das, C S Yajnik, Nikhil Tandon. Pediatric Diabetes, 2020; 1–7; DOI: https://doi.org/10.1111/pedi.12973.

The work being undertaken in Indo US project is aimed to harmonize the Indian YDR and the SEARCH registry in the U.S; compare phenotypic, clinical and demographic characteristics by type of diabetes between YDR and SEARCH. Preliminary comparative analysis of clinical features of SEARCH and YDR suggests higher DKA prevalence at onset

amongst SEARCH registry while the HbA1c is overall high amongst YDR in type 1 diabetics.

ICMR-India National Diabetes Study (ICMR-INDIAB)-Rest of India

Until now, 26 states/UT have completed the survey and approximately 99,600 individuals have been studied so far. During 2018-2019, the survey was completed in 5 states viz., Goa, Haryana, Chhattisgarh, Kerala and Puducherry. The final phase of the INDIAB study is currently ongoing in Himachal Pradesh, Odisha, Uttrakhand and West Bengal.

Out of data generated from 26 states/UT; the weighted prevalence of diabetes is 9.4% and significantly high in urban areas (12.9%) compared to rural areas (7.5%) while that of pre-diabetes is 14.0% (Urban-14% vs. Rural-7.5%). Overall, weighted prevalence of diabetes varies from 4% in Uttar Pradesh to 23.6% in Kerala whereas pre-diabetes varies from 6% in Mizoram to 31.8% in the state of Sikkim. The prevalence of general obesity varies from 11.8% in Jharkhand to 45.9% in Puducherry, while prevalence of abdominal obesity varies from 16.9% (Jharkhand) to 58.2% in Kerala. Hypertension prevalence varies from 22.2% (Madhya Pradesh) to 44.4% (Sikkim). Dyslipidemia varies from 66% in Gujarat to 90.3% in Kerala

Consolidated data of 15 states (which completed survey initially including six north east states) was published previously (The Lancet Diabetes & Endocrinology, (ICMR–INDIAB-9); DOI 10.1016/ S2213-8587 (17) 30174-2; 2017). From this study, ten publications have come out so far including the 15 states/UT data published in Lancet Endocrinology in 2017.

Impact of Yoga on Chronic Care

As per recommendations of meeting held in PM office; the ICMR constituted Expert Group on the subject; the three proposals were initiated after review of Expert Group: (i) "A pilot multicentre open label parallel arm RCT evaluating whether yoga can delay initiation of insulin therapy in patients with type 2 diabetes mellitus with suboptimal glycemic control on near maximal oral drugs and/or who may require insulin therapy in near future.; (ii) Impact of yoga on stress, metabolic parameters and cognition of Indian adolescents and (iii) Adoption of healthy lifestyle behaviors focusing on improving dietary habits, physical activity levels and attention span and concentration using a cognitive psychometric test called the Letter Cancellation Test (LCT).

ICMR-INSERM Workshop on Metabolic Diseases

The workshop was held on 29th-30th January 2020 at ICMR Headquarters, New Delhi under chairmanship of Dr Balram Bhargava and Dr JF Gautieu. Memorandum of Understanding was signed in 2018 between ICMR and inserm. Two day meeting was spanned in 5 scientific sessions viz: New Paradigms in β Cell Loss and Regeneration; Clinical Phenotypes; Genomics, Epigenomics and Genetics and Diabetes and End Organ Complications. The participants were informed about the two modalities of collaboration as mentioned in ICMR-INSERM Memorandum of Understanding viz: International Association Lab (IAL) and joint call for proposals. For IAL; the scientific coordinators from India and France need to be identified who would develop an IAL project. Based on deliberations; the recommended areas for collaboration are: Omics Study-genetics and epigenetics in early gestational diabetes mellitus, Atypical diabetes including lean diabetes

CARDIOVASCULAR DISEASES

Risk Factor Control Initiative

India Hypertension Control Initiative (IHCI)

India has almost 20 crore adults with hypertension. However, only 25% of the people with hypertension are aware of their condition, and only approximately 10-15% of those with hypertension have their blood pressure controlled. In order to meet the

Government of India target of a 25% relative reduction in the prevalence of raised blood pressure by 2025, it is estimated that approximately 5 crore additional people will need to have their blood pressure effectively treated.

The primary goal of IHCI is to reduce cardiovascular disease, particularly by improving the control of high blood pressure, a leading risk factor, among adults in India. The implementation partners include Ministry of Health and Family Welfare, WHO, ICMR, Academic institutions and state governments. The project initially was piloted in 25 districts across five states- Punjab, Kerala, Madhya Pradesh, Telangana and Maharashtra. It now aims to strengthen the hypertension management in 100 districts where National Program for Prevention and Control of Cancer, Diabetes, CVD and Stroke (NPCDCS) is ongoing.

Fig. 16: Crucial components of effective hypertensive care.

The strategies used in the project include (i) use of standard drug- and dose-specific algorithms for hypertension management; (ii) ensured availability of drugs in the algorithm in all facilities either through the state or NPCDCS (National Health Mission) funds; (iii) building capacity of program managers at state and district level for effective applied epidemiology and programme management and of all levels of staff for management of hypertension as appropriate at each level; (iv) ensuring high-quality service delivery in all health. Implementation science to promote continuous quality improvement at patient level and health facility level is being undertaken.

Activities related to decentralization of hypertension management is done by involving AYUSH practitioners and Nurses for screening, referring to higher facilities and regular monitoring and maintaining treatment of blood pressure. Auxiliary Nurse Midwives/ ASHA are trained to educate the patient and drug refills at the sub-centre level/ Health and Wellness Centers for patients diagnosed and initiated on hypertension treatment. Monitoring systems with standard indicators and documentation mechanisms that ensure collection of data for the key monitoring indicators, mainly control rates are being used.

A team based care and task sharing approach has been developed to provide healthcare to patient. NCD corners/stations have been set up in some facilities to promote opportunistic screening and streamline patient flow.

A digital information system, **Simple App**, an android based phone app was developed and field-tested with the help of health care providers and patients in Punjab to assist in storage and retrieval of patient information. **Simple** allows medical staff to use their time more effectively and efficiently when treating patients with hypertension

Highest proportion of estimated hypertensive was registered in Maharashtra (23.5%), followed by Kerala (16%), Telangana (14%), Punjab (11%) and Madhya Pradesh (8%). The quarterly blood pressure control varied between 21% and 63% in different quarters in these states.

Table 3: Implementation status of IHCI March 2020

State	Number of districts	Number of health care facilities
Madhya Pradesh	6	352
Punjab	5	497
Telangana	10	201
Maharashtra	5	495
Kerala	4	360
Chhattisgarh	1	48
Total	31	1953

A community-based survey of hypertension control is also being conducted to estimate the change in hypertension awareness, treatment and control among adults with hypertension

in the selected districts where IHCI is being implemented. Prevalence of hypertension ranged from 18% - 33% in various districts. Awareness (previously diagnosed with hypertension) ranged from 25% in Madhya Pradesh to 68% in Kerala. Treatment coverage was highest in Kerala (52% - 56%). Screening respondents for hypertension at the household-level provides a cost-efficient model for rapid district-level surveys to estimate the population level hypertension indicators and understand the treatment seeking behaviour.

HEART ATTACK INITIATIVE

A Web Based National Network of Management of Acute Coronary Events (MACE) Registry

To improve the understanding of Acute Coronary syndrome (ACS) patient characteristics, management practices and to gather information on long term outcomes in these patients, a prospective multicentre registry was established for Management of Acute Coronary Events (MACE) at 32 hospitals across India. Twenty-four sites were PCI enabled hospitals while 8 sites were PCI not enabled. A total of 17,388 patients were enrolled in the study. Of the total cases, 57% were STEMI cases of which 80% were males and 27% were less than 50 years. Tobacco use the single most important risk factor in half of the patients. Mortality in patients not receiving any kind of revascularization was 15% as compared to 4 % in angioplasty group and 12.5% in thrombolytic alone group. The higher mortality in these patients suggest the need of improving quality of care of these patients as well as raising awareness in the community.

Delhi Emergency Life Heart- Attack Initiative: MISSION DELHI

To avoid delays in care arising due to patient not being able to reach emergency care in time, this project has been initiated with an aim to develop, test and implement a 24-hour emergency response system for a pre-hospital thrombolysis service, using bolus-dose of thrombolytic agent for the treatment of acute myocardial infarction in a geographically defined area of Delhi. The project uses **Nurses on motor cycle** as '**First Responders**'. On receiving a call from patient with chest pain, a nurse team on motor cycle is dispatched. This team makes assessment for Acute Coronary Syndrome (ACS) and monitor vital signs. ECG recording is transmitted to consultant at AIIMS. Thrombolytic therapy is initiated on advice of Consultant and patient is shifted to AIIMS in an ambulance for further management.

Fig. 17: Delhi Emergency Life Heart- Attack Initiative: MISSION DELHI.

This project is now being implemented in the geographic area of radius 5 km around AIIMS as a pilot project. The RWA's, shopkeepers, school teachers, private practitioners and government doctors in field area have been contacted and made aware. Twenty four hour operations commenced from 1st May 2019. Since then 59 calls of chest pain, breathlessness and related issues have been received. Most of the calls are non-cardiac calls. In remaining 20 cases, motorcycles nurse responders were sent immediately. The medical nurses took ECG and successfully transmitted to AIIMS where the consultant provided diagnosis and initiated appropriate treatment. A STEMI case was provided thrombolytic therapy, three had to be shifted for primary PCI as thrombolytic therapy was not advisable and in one CABG was done.

ICMR STEMI ACT

ST elevated myocardial infarction (STEMI) is the commonest form of acute coronary syndrome (ACS) in low income countries and is a major cause of morbidity and mortality. Timely initiation of thrombolysis based reperfusion has been demonstrated to be effective in lowering mortality. The project has been initiated in 6 districts of 5 States with AIIMS, New Delhi as coordinating Centre. Improvement in thrombolytic rate through innovative approaches to reduce prehospital delay; through creating awareness about symptoms of ACS in the community, identifying hospitals in the given block for strengthening through training and TELE ECG based decision support system to deliver thrombolytic to eligible STEMI patients.

HEART FAILURE PROGRAM

National Heart Failure Registry

ICMR initiated National Heart Failure Registry (NHFR) with objectives (i) to establish a representative national HF registry in India and study the demographic characteristics, aetiology and modes of presentation of patients admitted with acute decompensated heart failure,(ii) to study the current practices in management of HF including diagnostic and treatment patterns, and (iii) to assess the short-term and long-term mortality outcomes of HF in India and (iv) to develop a risk prediction/ stratification algorithm for survival of HF patients in India.

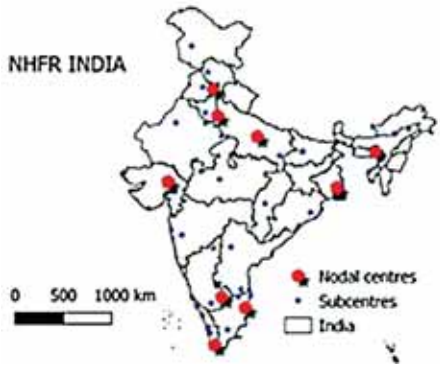


Fig. 18: NHFR India.

NHFR is a registry of acute decompensated heart failure patients admitted in 53 participating hospitals from 24 states and 2 union territories. The nine Nodal centres and the five participating centres under each one of them have recruited 8000 patients and 4000 patients have completed their follow up for at three months.

The mean age of HF patients was 59.9 years, 69.2% were male and median years of education as 8 years. Sixty three percent of patients were Heart failure with reduced ejection fraction (HFrEF). Only 13.2% of patients were Heart failure with preserved ejection fraction (HFprEF). The most common cause of Heart Failure in these patients was ischemic heart disease (72.3%) followed by dilated cardiomyopathy (17.8%) and RHD (6.7%). Hypertension (8.1%) , diabetes (41.6%), tobacco use (34.8%), alcohol (18.6%) , atrial arrhythmias (10.4%) were observed in these patients. In hospital mortality was 5.7%.

NEUROSCIENCES

STROKE INITIATIVE

Stroke Care Pathways in Northeast

The stroke Care Pathway is planned to be developed through Stroke unit at Hospital level and Mobile Stroke Unit at community level. The aim is to decrease response time of stroke victim through establishment of 24-hour Stroke Emergency Helpline, a 6-7 bedded stroke care unit at a Stroke Care Facility, an ambulance with mobile CT scanner and thrombolytic therapy through telemedicine for patients residing in remote areas. Two projects for establishing Clinical Stroke Care Pathway using Mobile Stroke Unit have been started in Tezpur and Dibrugarh involving Assam Medical College (AMC), Dibrugarh, Baptist Christian Hospital (BCH), Tezpur in association with Tezpur Medical College (TMC).

Establishment of Clinical Stroke Care Pathway using Mobile Stroke Unit in Tezpur, Assam

BCH, Tezpur set up a 24-hour stroke emergency helpline 9126091260 and the operator has been trained to identify the Stroke symptoms and

coordinate with MSU to reach the patient. A mobile stroke unit was assembled. Staff of the MSU has been trained in all aspects of Stroke Care. A multi-disciplinary team of doctors has been formed to provide consultancy through Telemetry. Training manuals and IEC material has been developed.

Fig. 19: Mobile Stroke Ambulance.

Establishment of Population Based Stroke Registry and Clinical Stroke Care Pathway using Mobile Stroke Unit in Dibrugarh, Assam

The study was initiated in March 2019. The population based stroke registry is developing an integrated network system for registering stroke cases in two blocks of Dibrugarh district (Barbaruah and Lahowal) by utilizing the support of ASHA workers, ANMs, MOs of health facilities, general practitioners and specialist of Assam Medical College and private hospitals/nursing homes in the area. IEC material was prepared for ASHA workers, ANMs Nurses and Medical Officers and trainings done. Networking with 15 hospitals including Government hospitals, private hospitals, scan centers, tea garden hospitals and municipality offices has been done.

STROKE REGISTRIES AND SURVEILLANCE SYSTEMS

Population Based Rural Stroke Registry at Ludhiana

The 'Rural population based stroke registry at Ludhiana' includes all 70 villages in Pakhowal block and 94 villages in Sidhwan Bet block. The project utilizes 260 ASHA workers trained. Utilization of ASHA workers and ANS was demonstrated as an innovation in NHM Innovation Workshop and won a prize. Project has a toll free number 1800-270-8585 for stroke related enquires and notification of stroke cases by general public and ASHAs. In this rural belt of Punjab, stroke was more prevalent in lower socioeconomic status - 93% of cases from lower and lower middle class; 47% of stroke cases not educated. Age standardized incidence was 218.5 per lakh in this population aged above 18 years. Age specific incidence of stroke was 281 per 100,000 in age group 50-54 years and increased to 861 per 100000 in age group 70-74 years. Importantly, the registry observed that the **first medical contact was an unqualified person in 52 to 56 %** of the cases. Ischemic strokes were present in 26.4% of cases whereas hemorrhagic were seen in 9.5 and unspecified in 64.6% of cases. Three Apps have been developed in collaboration with Tiatech – TIA Care for general population for early case detection, TIA Tele Cart for stroke ready hospitals and TIA Tele Doctor for treating consultants. In TIA Tele Cart, CMC Ludhiana has been attached for any consultation.

Study of Feasibility in Establishing a Stroke Surveillance and Management System through Community involvement and Technology Use in Rural Tirunelveli (MRHRU Field Practice Area)"

The primary objective of this study isto assess the feasibility of establishing a stroke surveillance and management system in rural Tirunelveli under the MRHRU field Practice area.

Women Self Help Groups (WSHGs) were identified as key informants. A total of 266 stroke patients' data were registered out of which 218 were first stroke patients. Incidence of stroke is 50/10,00,000. Ischaemic stroke is most common (83.9%). Only one-fourth of the patients could reach the hospital in less than 3 hours. The Mobile App - Tamil Nadu Accident Emergency Initiative – Stroke Mobilization Assessment and Rapid Treatment" (TAEI SMART) has been developed and a Stroke care pathway is being developed after consultation with local neurologists.

Development and validation of a comprehensive clinical and neuropsychological test battery for use in the Indian context for patients with Vascular Cognitive Impairment Background

A multidisciplinary research group, for the first time in India, developed a comprehensive neuropsychological and behavioral test battery, **the ICMR Neuro Cognitive Tool box (ICMR-NTB),** in six different Indian languages that can be used to assess cognitive impairment due to stroke and other dementias in different populations within India. The ICMR NTB meets diverse needs: a short version for the busy OPD to a comprehensive version for more in-depth testing or research purposes. A pilot project developed and validated cognitive test protocol for an illiterate population in four centres. The ICMR NCTB is being used in DBT's "Dementia Science program" and four hospital based dementia registries. The **ICMR Neuro Cognitive Tool Box** is planned to be made available free of cost for use both within the country and by other developing countries.

Indian Stroke Clinical Trial Network (INSTRuCT)

The Indian Stroke Clinical Trial Network (INSTRuCT) was setup by ICMR.A total of 25 stroke centres across the country have been included in INSTRuCT. India is the only developing country with a Government sponsored Stroke network.

To build the capacity of country in undertaking Clinical Trials in this area, ICMR-NIH Stroke Clinical Trial Development Workshop was conducted in September 2019. Following trials are being conducted under INSTRucT network.

Secondary Prevention By Structured Semi-Interactive Stroke Prevention Package in INDIA (SPRINT INDIA) Trial

SPRINT is a multicenter, randomized, parallel-design, adaptive and blinded end-point clinical trial of sub-acute stroke patients. The hypothesis of the study is "A structured semi-interactive stroke prevention package will reduce the risk of Recurrent Strokes, Coronary Artery Syndrome and Death in patients with sub-acute stroke after one year."

Twenty five centres are participating. Study material/Intervention was developed in the form of Stroke Prevention Workbook in 11 languages namely, English, Hindi, Punjabi, Malyalam, Tamil, Telugu, Kannada, Bengali, Assamese, Gujarati and Marathi.

A total of 3484 patients have been screened of which 2724 patients (1312 in each arm) have been randomized. Six month follow-up of 1587 (80.2%) patients has been completed and dropout rates are around 2% only. One year follow-up of 510 (62.3%) patients has been completed and the drop-out rate remains close to 4%. The study protocol for SPRINT India has been published in International Journal of Stroke

Ayurvedic Treatment in the Rehabilitation of Ischemic Stroke patients in India: A Randomized controlled trial (RESTORE)

Ayurveda has certain beneficial effects in the rehabilitation of stroke patients. It was planned to study the safety and efficacy of ayurveda in improving the motor functions of stroke patients in a randomized trial. One hundred and forty consecutive hemodynamically stable adult patients with first ischemic stroke, 1 month to 3 months from stroke onset were proposed to be recruited in the study.

Enhanced Control of Hypertension and Thrombolysis Stroke study (ENCHANTED)

The trial was conducted in 15 countries worldwide including India, UK and China in 110 centers. Although intensive blood pressure lowering is safe, the observed reduction in intracranial haemorrhage did not lead to improved clinical outcome compared with guideline treatment. ENCHANTED Trial results have been published in the Lancet 2019.

MENTAL HEALTH

Implementation Research under National Mental Health Programme (NMHP)

Pregnancy and Perinatal Depression Group ("BIND-P" project)

This group completed cross sectional survey in 400 pregnant women coming to ANC OPD. The prevalence of depression among this sample was found to be 35%. Manuals for training of nurses and self help skills have been developed under this project.

Manuals Prepared

1. ICMR BIND-P Project: Facilitators Guide Manual for training of nurses in identifying depression and providing psychological intervention
2. ICMR BIND-P Project Flipchart: Understanding depression in pregnancy and self-help skills

Tribal Survey Group

This group is performing a survey about the use of alcohol among the tribal adolescence in the three locations. The group is also evaluating the 'Life Skill Training' to prevent the alcohol addiction among the tribal youth. A Survey of 542 subjects was completed using MINI, MINI kids and ASSIST v3, and the recruitment of participants was concluded for the administration of the NIMHANS Life Skill Training. A qualitative process evaluation component was used to measure feasibility and process evaluation to understand the effectiveness of this intervention. Which indicates that the tribal youth who received the Life skill training has fewer tendencies towards alcohol addiction than in control arms

Evaluation of District Mental Health Programme (DMHP) psychiatric services to the severely mentally ill in their old age

This project is exploring and evaluating the services of DMHP towards the serious mental illness among the old population. Out of 14 districts, the PI selected 3 DMHP implemented districts, 20 Panchayats from each district, to recruit 759 severe and persistently mentally ill old age people for the study. Data obtained from pilot testing of one Panchayat: 70% - symptoms of Psychosis, BPD or Severe depression, 49% - symptoms of Dementia, 16% - bedridden, 84% under treatment, 58% of them receiving it from government facilities.

Development and Validation of the Screening Version of Indian Scale for Assessment of Autism

This project comes up with a new version of Indian scale for assessment of autism and performs a validation study against the standard version of autism assessment scales. The newly developed scale shortens the assessment question to only 15 and analysis and sensitivity of positive predictive values is completed.

ENVIRONMENT

ICMR's task force project on Effects of air pollution on acute respiratory symptoms in Delhi: A multisite study

The objectives of the study are to study the association of acute respiratory symptoms with changes in outdoor air quality and weather variables. Total number of screening and enrolment in the emergency room of participating hospitals was 263764 and 33221 from1st June 17 to 28th Feb 2019. Cluster analysis was done. According to air pollutants the days were divided into higher (cluster 1), moderate (cluster 2) and lower (cluster 3) pollutant days. Lower levels of pollutants cluster was chosen as the reference. No statistically significant association was observed between the total daily number of enrolled cases and pollutant driven clusters from the air quality monitoring stations. There was a statistically significant association seen with PM 2.5 & NO2 with increase in level being associated with higher percentage of enrolled patients.

ICMR's task force project to assess the exposure and Health effects of pesticides

ICMR has initiated this study on the health effects of pesticides with following objectives: (i) To

assess the health status of the population in areas with high and low pesticide usage.(ii) To estimate the levels of pesticide residues in blood and urine

Global Climate Change and Health

Under the High-Powered Committee on Global Climate Change and Health; the research activities under three task force projects viz: "vector borne diseases," "eye health" and respiratory diseases are ongoing. Based on data obtained in phase I; project on "**Multi centric Study of the Impact of Exposure to Ultraviolet Radiation (UVR) and aerosols exposure on Ocular Health "** under "task force on eye health," and two projects viz: "**Epidemological Study of Foci of Visceral Leishmaniasis in Himachal Pradesh"** and "**Vulnerability Assessment and Adaptation Measures Towards Potential Impacts of Climate Change on Malaria in Hot spots of India" under "task force on** vector borne diseases" are ongoing. Under "task force on respiratory diseases," project on "**Impact of Meteorological Changes and Air Pollution on Respiratory Health and Morbidity,"** is ongoing.

Epidemological Study of Foci of Visceral Leishmaniasis in Himachal Pradesh

Reduction in Kala-azar in Bihar is being observed since 2011, yet the states like Himachal Pradesh, Uttarakhand and eastern Uttar Pradesh are reporting cases since last three decades. The study is aimed to understand the transmission dynamics of Visceral Leishmaniasis in Himachal Pradesh and delimit the focus and climatic and ecological determinants of VL. It appears that the CL in Himachal is atypical leishmaniasis (close to dermal leishmanoid) as the detected parasites from patients were *Ldonovani*, *L.tropica* as well *L. major*. Rattus rattus collected from study area were found negative for Leishmania parasite.

Vulnerability Assessment and Adaptation Measures Towards Potential Impacts of Climate Change on Malaria in Hot spots of India

The findings of phase I data revealed that the Himalayan region in India is most vulnerable as new foci for malaria due to increase in temperature. On the other hand, states like Orissa may witness reduction in malaria due to extreme temperatures and vectors may develop Heat Shock Proteins (HSPs). The findings provide evidence that in-spite of climatic suitability and availability of vector species, the vulnerability of Kangra district for malaria transmission is very low. In Uttarakhand, on the basis of temperature and availability of vectors, transmission windows were suitable for 10 months in study villages. However, based on the entomological data generated from the study villages of Tehri and Pauri Garhwal. Blood slides (66) were found negative for malaria parasite, however, evidence of malaria parasite was detected in 18 *An. culicifacies* collected from cattle shed. Expression of HSP-70 and HSP-90 proteins was detected in *An. culicifacies* exposed to temperatures (38-40°C) indicating that mosquitoes can adapt to high temperature.

Multi centric Study of the Impact of Exposure to Ultraviolet Radiation (UVR) and aerosols exposure on Ocular Health in India

The findings of phase I showed significant association of cataract, dry eye and pterygium with sun exposure. All these 3 diseases namely cataract, dry eye and pterygium were found more in people with exposure to unsafe kitchen fuels more than 15 years in Gurgaon but in Guwahati there was a significant association of sun exposure with cataract but not with dry eye and pterygium. Phase II was initiated based on findings obtained in phase I.

OTORHINOLARYNGOLOGY

ICMR National Task Force Project - prevalence and etiology of hearing impairment

This project was initiated with the objective of estimating the prevalence and etiology of hearing impairment in six representative regions of India viz.. South region (Bengaluru),West region (Bhavnagar),East region (Bhubneshwar),Central

region (Raipur), North region (Shimla), North East region (Shillong). A general rising trend in disabling hearing loss was noted with age and a very sharp rise after the age of 50. In the 46-60 year age group- the prevalence of HL is 16.6% and DHL is 3.8% In the > 60 year population – the prevalence of HL is 51.2% and DHL is 21.1% Contrary to the previous studies , Only 1/3 of the hearing loss was Conductive Hearing loss, and 2/3 was either sensorineural or mixed. The four commonest causes of Disabling Hearing loss noted was i) Presbycusis ii) Infectious Ear disease iii) Early onset Presbycusis iv) Wax Presbyacusis at Age > 60 years. - 44.1% suffer from Presbycusis. In 20.1% it was above the threshold of DHL Early onset Presbycusis in Age 46-60 years- 7.1% suffer from Early Onset Presbycusis. Oral Tobacco Consumption was strongly associated with SN hearing loss.

GERIATRICS

In the area of Geriatrics as an offshoot study of the muticentric Task Force project on Assessment of Nutritional and morbidity status and utilization of health care facilities in the elderly population aged 60 years and above was initiated at AIIMS Delhi to use the dried blood spots to test and validate the viability of using these vis-à-vis fresh samples. The study is continuing.

The Division had also initiated ICMR-FORTE (Sweden) collaboration in geriatrics. Under this umbrella, five projects were initiated for joint support. The projects have developed telemedicine hub and spoke model and is testing the use of time assistive devices for elderlies in Indian settings besides sharing the rich Indian positive effects of Yoga with the Swedish collaborators.

MUSCULOSKELETAL DISORDERS

Peptide based diagnosis of osteoarticular tuberculosis using immunodominant B-cell epitopes of secretory RD antigens of *Mycobacterium tuberculosis*

The project was initiated with the aim to develop highly sensitive Immuno-PCR for diagnosis of osteoarticular tuberculosis using the multi-epitope cocktail of the immunodominant peptides of RD proteins using bioinformatics identification of secretory RD proteins of *Mycobacterium tuberculosis* known to be absent in BCG and environmental mycobacteria. The study has identified the proteins and peptides having potential for diagnosing Osteo-articular TB, and is in the process of validating it in new patients.

Comparative evaluation of genetic and cytokines profile in age matched Indian subjects with and without knee Osteoarthritis

This project was sanctioned with the aim to study the baseline genetic association by exome sequencing of Indian patients with and without knee osteoarthritis followed by validating the candidate gene list in bigger by RT PCR and also to validate the related cytokines which will be correlated to first phase candidate genes .The project has been able to identify the most common susceptibility genes of OA in north Indian Population. The study is continuing.

Overuse injuries among school-going children in Manipur

This project has identified the spectrum & type of overuse injuries among school-going children (7-15 years) in valley and hill districts of Manipur

Comparative evaluation of genetic and cytokines profile in age matched Indian subjects with and without Osteoporosis

This project has been sanctioned for initiation in 2019 with the aim to study the baseline genetic association by exome sequencing of Indian patients with and without OP followed by validating the candidate gene list in bigger by RT PCR and also to validate the related cytokines which will be correlated to first phase candidate genes.The project has been able to recruit the target sample for identify the most common susceptibility genes.

Human Skeletal Disease Bio-Bank

The Bio Bank was established in march 2017 at NIMHANS. During the year under report ,a

total number of 914 muscle tissue samples (405 NIMHANS cases, 509 – referral cases) of patients diagnosed as skeletal muscle disorders were collected and banked along with 689 blood samples from which DNA has been isolated and 697 of serum samples have been separated and banked. The muscle tissues banked comprised of 290 cases with no diagnostic pathology (unclassified histologically), 328 cases of Neurogenic disorders, 247 cases of Muscular dystrophies, 112 cases of inflammatory, 147 cases of miscellaneous , 25 cases of mitochondrial myopathies , 17 cases of congenital myopathies, 11 cases of metabolic myopathies, seven cases of distal myopathies, two cases of myotonic dystrophy/ myasthenic disorder and drug induced myopathy each.

Mitochondrial Respiratory Chain Disorders (MRCD) – Proteomic analysis of Complex I and IV deficiencies

The project has been initiated with the aim at establishing laboratory control for blood and muscle respiratory enzyme activity so to compare the enzyme activity in blood and muscle-so that blood can be used as screening tool. deficiency. The respiratory chain assay is now offered as a diagnostic test on a self sustaining model

Dysferlinopathies– Biochemical, Morphological and Proteomic analysis

Molecular differences between two phenotypes (MM and LGMD2B) are unclear and Proteomic analysis of dysferlinopathy is yet to be undertaken in Indian patients. Therefore the present study has been initiated with the aim to Characterize molecular (synaptotagmin, caveolin3 and calpain I and II) and ultrastructural features of dysferlinopathies.

Impact of multidisciplinary care on the quality of life of Duchenne Muscular Dystrophy(DMD) affected Children:A prospective study

The project was sanctioned in November 2018. It aims to provide multidisciplinary clinical model for care to patients with DMD as per International guidelines and to evaluate the influence on the progressive deterioration of children with DMD selected at different stages. It involved 100 children from the age group of 3 to 15 years at different stages of ambulation. The subjects were recruited and work to standardise the protocols along with their motor functions was undertaken.

Genotypes underlying Duchenne and Becker Muscular Dystrophy phenotypes:Aprospective follow up study of selected mutations

This project sanctioned in November 2018, aims to determine the phenotype heterogeneity in Duchenne and Becker Muscular Dystrophy with select mutations and to identify relationships between genotypes and motor function outcomes of patients with select mutations.

KIDNEY DISEASES

In the area of CKD, an NTF project was initiated which will provide estimates of CKD in the community setting across seven centres of the country. The estimates from the study will provide the actual burden and likely need of Dialysis facilities required for the country. The project on CKDu will try to unravel the causes of CKDu in Srikakulam, Prakasam district of AP and Supbeda village of Chattisgarh. The CAR for Paediatric uropathies will decipher the pathways for PUV,,PUJO and VUR-the leading causes of CKD in children. The Centre will also develop management protocols for these conditions . It is also expected that the project on gene environment interaction as a cause for various pediatric uropathies will provide leads for the pathways resulting into these conditions.

Chronic kidney Disease

A study was initiated across seven sites- Delhi, Mumbai, Jaipur, Hyderabad, Bhubneshwar, Kolkatta, Guwahati. A total of 15,372 subjects were enrolled in the study. History of CKD and acute kidney injury was reported in 0.2% and 0.05% respectively. Of the study population, 17.4% subjects were known hypertensive, of whom, only 47.9% were controlled on medical treatment. Another 12.4% were found to have hypertension

on examination. So, total hypertension in subject population was 29.7%. Reported diabetes in study population was 11.6%, of whom only 41.9% was controlled on medical treatment. In addition, 10.1% subjects were diagnosed to have diabetes for the first time, making diabetes in total of 21.7%. Kidney disease on first visit was found in 11.4% subjects. Prevalence of CKD in present study was total-9.4%. Of the total CKD, sate-1 to stage-5 were 16.9%, 23.5%, 51.5%, 5.9% and 2.3% respectively.

Registry for Assessing the Determinants of Dialysis Outcomes in India

The study was sanctioned to establish a pragmatic approach that utilizes web enabled data collection mechanisms. This information will be useful for patients, clinicians, hospitals, funding agencies and governments to identify populations in greatest need and how existing social and economic resources can be capitalized upon in meeting challenges of ensuring equitable access to dialysis care in India. The study has developed a template which has been tried across 14 centres in India.

Grand Challenge Scheme on CKDu in Srikakulam

The ICMR in collaboration with Govt. of A.P launched this scheme where in one project was selected for initiation-The STOP CKDu study. This project has conducted survey of sample population aimed at addressing all aspects of the problem – estimate the disease burden using rigorous scientific methodology and sociological tools, undertake an environment mapping and additional investigations as needed. The study also aims to establish the etiology, economic consequences of chronic kidney disease of uncertain etiology (CKDu) and develop evidence guided interventions for general improvement of health conditions in the high CKDu incidence areas of Andhra Pradesh. The initial data revealed very high prevalence of CKD in Uddanam area of AP.

A longitudinal study of risk factors associated with decline in eGFR in Prakasam district, Andhra Pradesh, India

The study was initiated with the objectives of determining the risk factors associated with decline of eGFR in a rural cohort in•Prakasam district, Andhra Pradesh, India. And to describe the trends in the eGFR distribution over 3 years in a rural cohort in Prakasam• district, Andhra Pradesh, India. Five resurveys at 6, 12, 18, 24 and 30 months in the age group of 18- 60 years are to be done.

Prevalence estimation of Chronic Kidney Disease in Supebeda Panchayat of Chattisgarh

A cross- sectional study was conducted in Supebeda village. Entire Population was surveyed and a total of 588 subjects. The prevalence of CKD was estimated to be 12.07%. The prevalence of diabetes and hypertension in subjects with CKD was found to be 15% and 40% and it was 5% and 12% in non-CKD group. Mean eGFR was found to be 50.23±28.7.

As per NKF-K/DOQI stage-wise classification of CKD, 43.85, 17.54, 22.8 and 15.78% of CKD patients were found in stages IIIA, IIIB, IV and V respectively. Proteinuria alone (CKD stages I and II) without decreased GFR was seen in 18 (24%) subjects. Univariate analysis of biochemical and demography of characteristics of subject population demonstrated significant predictors of CKD baseline including age, education, tobacco smoking, alcohol consumption, diabetes, hypertension and Proteinuria.

Gene Environment Interaction In Congenital Uropathies

Genetic basis underlying congenital uropathies follows Mendelian inheritance. Host and environment factors are implicated in the pathogenesis of aberrant renal development. It is proposed to validate the 'two-hit' hypothesis for renal damage in congenital uropathies as a sequelae of gene-gene interaction between i) pathogenesis of aberrant renal development & ii) ACE I/D induced renal parenchymal injury., besides studying the effect of Nitric Oxide on renal function recovery

as a baseline study for a future role of 'iNOS gene transfer studies' for renal recovery. The project is continuing as a Pilot study for one year.

Task Force project on "Cleft Lip and Palate Anomaly in India: Clinical Profile RiskFactors And Current Status Of Treatment: A Hospital Based Study"

The nationwide multicentric project, has been initiated at four centres namely (i) Delhi, (ii) Hyderabad,(iii) Lucknow and (iv) Guwahati in march 2017 for a period of 3 years. The findings of this study reveal that among the enrolled 909 cases, majority of the cases in the study had UCLP (395 cases/43.5%) 255 cases with UCLP left side and 140 cases with UCLP right side. BCLP was found to be second most prevalent in the study (195 cases/21.5%).131(14.4%) cases had isolated cleft of the palate, 88 cases (9.7%) had cleft of lip alone, 72 cases (7.9%) had cleft lip and alveolus while 28 cases (3.1%) had a submucous type of cleft.

Indicleft tool has also been formulated in this project hosted in ICMR server for centralization of data on cleft in India.

Fig. 20: Indicleft tool for centralization of data on cleft in India.

Gastroenterology

Task Force Project titled " Prevalence of Non-Alcoholic Fatty Liver Disease (NAFLD) and its association with cardio-metabolic disease risk factors in North India" was completed. The study reported higher prevalence in urban area than rural areas. NAFLD was more prevalent in female in urban areas while the converse was observed in rural areas. In both urban and rural areas, higher crude prevalence of NAFLD was reported among the participants with diabetes, hypertension, metabolic syndrome, insulin resistance, overweight, obese and hypercholesterolemia.The pro-inflammatory cytokines- IL-1, IL-6 and leptin were significantly higher in NAFLD without raised liver enzymes than healthy controls. In contrast the adiponectin hormone was significantly lower in NAFLD without raised liver enzymes than healthy controls.

ICMR-PHFI-IHME Collaboration

India State Level Disease Burden Initiative with GBD methodology. After successful completion of the initial study (Phase 1) which has estimated the disease burden at state level with its epidemiological transition from 1990 to 2016. The study has been continued as Phase 2 for further estimation of disease burden at district level with comprehensive of the available data from different sources in the country with WHO, India office also as a technically partner under an MoU till December 31, 2021.

ICMR-NTF for Research on Snakebite

Nationwide study to estimate incidence, mortality, morbidity and economic burden due to snake bite in India has been approved initiated from March 2020. This study includes 13 states, 31 districts and 336 blocks from 5 different regions of the country viz. North, South, East, West and NER (North Eastern region).

ICMR-NTF for Assessment of Impacts of PMUY

Four short term studies (as Pilot study) has been initiated in the 3 different centres (KEM, Pune, RMRC, Bhubaneswar and PGIMER, Chandigarh) to assess the barriers to and facilitators of uptake and sustained use of LPG, challenges faced by LPG distributors in providing LPG connections through PMUY and also health outcomes of adoption and sustained use of LPG and also toward exclusive use by ensuring increased use through a second LPG gas cylinder and reducing availability of the

traditional Chula. The studies at KEM, Pune have been completed and the final reports are in review process.

The preliminary findings: The study was conducted in Junnar block of Pune district comprising 46 tribal villages with a population of approximately 42,000 individuals living in 8,000 households. PMUY has been implemented there for the last three years and about 70% of the households in the area own only one LPG cylinder. 186 household were randomly selected for the study. Most households expressed a desire to own an LPG gas stove and the perceived benefits of using LPG gas stove differ among people, depending on their own experiences, and the commonest ones are ease of use and lesser time spent for cooking and a sales offer for a spare LPG cylinder coupled with the requirement to initially disable the indoor chulha showed a huge effect of about 90% reduction, in indoor biomass use. The major challenges are affordability for sustained usage due to additional 'out of pocket' expenses for purchasing the gas stove and expenses towards building a platform for placing the stove above the cylinder level, difficult-terrain for LPG distribution and difficult to travel to the offices of LPG distributors and get a cylinder and absence of requisite documentation needed to obtain LPG connecting in the PMUY, with many households unable to produce Aadhaar cards and bank accounts in the name of an eligible woman in the household who is the beneficiary in the PMUY.

Public health importance

The "**White Paper on Electronic Nicotine Delivery System**" published in the *Indian Journal of Medical Research,* May, *2019* which was released and disseminated on "World No Tobacco Day 2019". This publication had a significant policy implication on public health towards the ban of e-cigarettes or ENDS or like products in India in September 2019.

Guideline Document formulated "Guidelines for Dental Professionals during Covid-19" which has been released at MoHFW website on 19/5/2020.

DIABETES

Guidelines for Management of Type 2 Diabetes

In 2005, the Indian Council of Medical Research (ICMR) brought out the 'Guidelines for Management of Type 2 Diabetes' as a small book and this has found wide application all over India. As more than a decade has elapsed since the publication of that document, ICMR felt that a revision of the Guidelines for Management of Type 2 Diabetes was indicated. Revised Guidelines for Management of Type II Diabetes were published in 2018 and are also available on ICMR website.

ICMR-Indian National Diabetes Study (ICMR-INDIAB)-North East

The study was aimed to estimate prevalence of pre- diabetes and diabetes among rural and urban population in north eastern region of the country. A sample size of 32,000 individuals covering the North-East regions representing eight states in India namely Sikkim, Assam, Meghalaya, Tripura, Mizoram, Manipur, Nagaland and Arunachal Pradesh has been completed. The prevalence of diabetes is 5.9% (urban: 10.3%; rural: 5.1%) whereas prevalence of pre-diabetes is 13% (urban: 12.3%; rural: 13.3%). Tripura and Sikkim states report high prevalence of Diabetes as 9.4% and 11.8% respectively whereas prevalence of pre-diabetes is reported to be very high (31.8%). The prevalence of General Obesity (39.5%) and hypertension (42.5%) is reported to be very high in Sikkim. The prevalence of hyper-cholesterolemia is high in Nagaland (20.7%); Manipur (22.3%) and Sikkim (26.2%). High consumption of salt in North East may be attributing to high rates of hypertension in North East. In state of Nagaland; the prevalence of diabetes and pre-diabetes was reported to be 5.4% (urban 9.9%; rural 3.6%) and 9.5% (urban 10.2%; rural 9.2%). The prevalence of metabolic syndrome is 36.1% in urban and 23.1% in rural. In Sikkim; the prevalence of diabetes is 11.8% (urban 17.9%; rural 9.6%) and of pre-diabetes is 31.8% (urban 28.9%; rural: 32.8%). The prevalence of hypertension is 40.3% (urban) and 43.4% (rural).

ONCOLOGY

Immunophenotyping of Hematolymphoid Neoplasms

In the recent past, flow cytometer is increasingly being used in diagnosis of haematolymphoid malignancies. However, results differ from laboratory to laboratory, suggesting a need for formulating standardization of procedures (SOPs). The development of an algorithm for use of panel of antibodies as well as their logical interpretation would also help the same. In view of the above a task force on this aspect was initiated. The document incorporating chapters such as (i) indications for FCM in a suspected case of hematolymphoid malignancy; (ii) sample collection, transportation, preparation, processing, procedure (surface, intracytoplasmic / nuclear) and storage; (iii) panel selection, methodology, fluorochrome and antibody clones, multicolor immunophenotyping color combinations, processing; (iv) quality control; (v) testing for viability, adequacy of cell yield, acquiring, gating strategies, analysis of data; (vi) data acquisition, analysis, reporting and interpretation, storage and archival and (vii) safety were drafted. The SOPs are published and also available on ICMR website (www.icmr.nic.in).

Cancer Monograph

Division has compiled cancer research activities undertaken in the form of centrally commissioned projects, important research out puts in adhoc research schemes and major research programmes undertaken by the ICMR institutes engaged in the cancer research. The document has been published and is also available on ICMR website.

Cancer Management Guidelines

A total of 20 documents have been published so far and is available at ICMR website (www.icmr.nic.in) and is also published in journals. 07 documents (uterus, ovary, MDS, AML) were published during period. The documents for other cancer sites are at different stages of preparation.

BASIC MEDICAL SCIENCES

The Basic Medical Science division coordinated intramural research in the field of basic medical sciences at the National Institute of Pathology (NIOP), New Delhi, National Institute of Immunohaematology (NIIH), Mumbai and National Institute of Traditional Medicine (NITM) at Belagavi. The extramural research was undertaken in several areas viz. Nanomedicine, Haematology, Biochemistry, Pharmacology, Physiology, Human genetics, Stem cell research, Genomics, Allergy, Immunology, Translational Neuroscience, Drug development initiative.

INTRAMURAL RESEARCH

ICMR-NATIONAL INSTITUTE OF PATHOLOGY, NEW DELHI (ICMR-NIOP)

TUMOR BIOLOGY

Comparative analysis of Genetic, clinical and epidemiological factors of breast cancer in Indian population

Transcriptome profiling of breast tumor tissue (N=28) was performed on Ion proton. Total 2060 DEGs are observed between tumour and adjacent normal. 946 genes observed to upregulated while 1120 genes are down regulated. List of top 25 pathways enriched by 2060 deregulated genes was presented. PCLO gene was up regulated while OBSCN, RP1L1, and SVEP1 were down regulated. PCLO and OBSCN are part of interactome involving TP53, TTN and PIK3CA, hence might be of interest for further evaluation. Validation will be performed on final analysis of transcriptome data.

In vitro evaluation of effect of PKCε silencing on tumour invasiveness in urothelial cancer

The effect of silencing of PKCε&PKCζ in Urothelial cancer cell lines (T24, 5376, HT-1376 & TCCSUP) was studied. The successful silencing of PKCε and PKCζ were demonstrated by decreased expression of PKCε& ζ RNA and protein expression by RT-PCR and Western blot in silenced bladder cancer cell lines. The effect of silencing PKC isoforms ε & ζ on gene expression of NFκB pathway related genes (NFκB/p65 and AKT1) was studied. NFκB/p65 andAKT1 were both found to be down regulated after treatment with both PKC ε & ζ silencing. Silencing of PRKCε and PRKCζ showed reduction of invasion and proliferation in all bladder cancer cell lines. Hence PRKCε and PRKCζ identified as potential target in bladder cancer which may reduce tumorigenesis by reducing invasion, cell motility and proliferation.

In vitro and *in vivo* anticancer efficacy of combination therapy with alpha linolenic acid, lignans and BCG against urinary bladder cancer

Intravesical BCG therapy after transurethral resection is standard treatment for nonmuscle invasive bladder cancer. A major challenge with the BCG therapy is its severe side effects, such as BCG sepsis, immunosuppression, hematuria, active urinary tract infection, and mild cystitis. To overcome these adverse effects combination therapy, a treatment modality that combines two or

more therapeutic agents, can play important role. The antitumor potential of alpha linolenic acid (ALA), secoisolericiresinoldiglucoside (SDG) and BCG alone and in combinations on three human bladder cancer cell lines: one nonmuscle invasive cell line and two muscle invasive cell lines and one urothelial bladder cell line was investigated to identify potential new therapeutics.

The IC50 of the drugs based on MTT assay and Combination Index (CI) of drugs using Chou and Talalay method was calculated. The drug combinations ALA+ BCG and SDG+ BCG; ALA+ SDG+ BCG showed the CI<1 i.e. synergism or additive effect. Cell viability assay using the drug combinations were also performed. Further studies are continuing.

Molecular profiling of invasive urothelial bladder cancer

Transcriptome profiling was done in 28 samples. Human genome hg28 was used for alignment. The invasive cells revealed 417 upregulated and 737 downregulated genes. BIRC5, MYCN, MMP11, MMP12 and AURKBC2 were upregulated in MIUC in comparison to NMIUC and selected for validation. Result of gene expression showed the significant upregulation of BIRC5 (6.8 fold), MYCN (8 fold) and MMP11 (9 fold) in Muscle invasive bladder cancer whereas AURKBC2 and MMP12 were seen upregulated in MIUC cases but not found statistically significant. BIRC5, MYCN and MMP11 may play a role in invasion of bladder cancer.

Clinical decision support system to identify histogenesis in cases of carcinoma with unknown primary (CUP)

Total 469 samples of primary carcinoma were scanned, uploaded to developed database. Scripts for digital image processing and image stratification between tumour and normal have been developed. The graphical user interface has been developed. An annotated image database of high quality images will be a national resource of educational material and also a source for other morphometric and pattern recognition projects. The pattern recognition based classifier is now being developed.

A pilot study to determine causes of death in under-five children in a tertiary hospital in India using MITS technique

SOPs and forms for various stages of case assessment, sample collection and specimen testing were created and/or optimized according to the local scenarios and complications. Total 159 MITS (including 50 stillborn cases) were performed and found ~ 50% success rate in receiving consent. TaqMan® Array Cards (TACs) technology will be used further to detect the multiple pathogens (up to 48 targets) from MITS cases.

Understanding the effect of crosstalk between microglia and glioblastoma cells on vasculogenic mimicry in Glioblastoma

Clinically suspected gliomas samples were collected and were confirmed as glioma by histopathological parameters. Of these, astrocytic tumours (PA, DA, AA and GBM) were selected for evaluating IDH1 mutation status. IDH1 mutation was mainly associated with Diffuse (DA) and Anaplastic astrocytoma (AA). No association of IDH1 mutation was found with reactive gliosis, pilocytic astrocytoma (PA) and primary GBM.

The blood plasma levels estimation of D2HG using colorimetric assay corroborates with IHC of IDH1. High levels of oncometabolite D2HG were observed in IDH1 positive tumors. Primarily, DA cases were positive for IDH1 and also had high D2HG in blood plasma.

Fig. 1: IDH1 R132H staining in Glioblastoma.

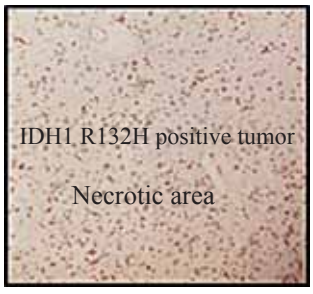


Fig. 2: IDH1 R132H staining in Diffuse astrocytoma.

High levels of D2HG- oncometabolite were also seen in DA in pre-op plasma samples when compared to pre-op plasma from GBM patients. Furthermore, a noticeable decrease in D2HG levels was observed in post-op plasma of DA patients.

Role of IL-8 Signalling in Glioblastoma Progression

Glioblastoma multiforme (GBM) is characterized by robust microvascular proliferation. Previously it was shown that combining anti-IL8/CXCR1/CXCR2 therapy along with TMZ in TMZ resistant cases may confer additional benefit in limiting neovascularization in the form of vascular mimicry.

The team identified several molecules from literature which have been shown to play role in VM formation in various other cancers. Then the study centre utilized the RNA seq data for U87MG and LN-18 cell lines from Cancer cell line encyclopaedia (CCLE) and compared the expression of those molecules between the two cell lines. LN-18 was chosen for comparison because it expresses IL-8 and its receptors but does not exhibit VM in vitro like U-87MG cell lines. From this database, the study centre identified 5 genes which are either downregulated in LN-18 but upregulated in U-87MG or highly upregulated in U-87MG cell line.

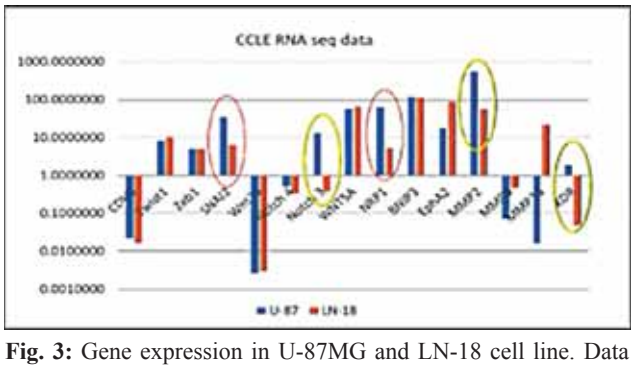


Fig. 3: Gene expression in U-87MG and LN-18 cell line. Data from CCLE data base.

Investigating the Role of Negative Regulators of WNT Signaling Pathway in Prostate Cancer and Exploitation of Their Therapeutic Potential

Gene expression profiling to determine the role and therapeutic potential of negative regulators/inhibitors of WNT signaling pathway in suppression of prostate cancer was performed. RNF43/ZNRF3, NKD2 and APCDD1 expression profiling were analysed. Gene expression studies in prostate cancer tissues by real-time PCR showed RNF43/ZNRF3, NKD2 andAPCDD1mRNA transcripts were down-regulated with highest down-regulation in NKD2 gene.

Role of Long Non-coding RNA MEG3 in Breast Carcinogenesis

The aim of the project is to understand the mechanisms through which MEG3 is functioning in breast cancer cells and contributing to breast carcinogenesis. Earlier, the team found MEG3 to be downregulated in breast cancer cell lines by qPCR. Hence, to restore the expression of MEG3 in breast cancer cell lines we have made stable cell line of T47D with MEG3 lncRNA. Induced expression of MEG3 in breast cancer cell line T47D has resulted in reduced proliferation, colony formation efficiency of the cells, also it reduced the expression cell cycle related genes.

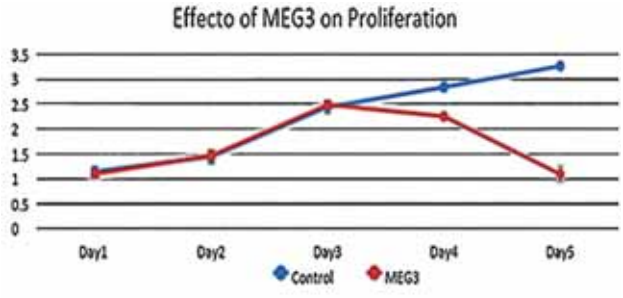


Fig. 4: Effect of MEG3 over expression on T47D breast cancer cell line, MTT assay was performed between T47D-MEG3, stable cells and as a control, native T47D cells were used. Currently we are exploring the downstream targets regulated by MEG3.

Targeted resequencing of breast cancer specific genes in early-onset breast carcinoma

The project is aimed to identify sequence variations and chromosomal rearrangements of deregulated

genes in early onset breast cancers. Earlier we have done whole exome sequencing of 22 breast cancer patients and 4 control samples belonging to early and late onset breast cancers.

In this year, the study centre has identified the genetic variations associated with luminal, basal and Her2 subtypes. In the luminal subtype tumours, 13,855 variants were identified in the coding gene exons among them 12.7% were novel alterations and 87.3% were known (Figure 2 b). Further, analysis to study chromosome wise distribution of the genetic variations shown that highest number of genetic changes were found in chromosome 1 and least in chromosome 21 in luminal subtype patients.

In the basal subtype tumours, 14722 variants were identified in the coding gene exons, among them 15.5% were novel alterations and 84.5% were known alterations. In Her-2 subytpetumors, 10864 variants were identified in the coding gene exons, among them 28.5% were novel alterations and 71.5% were known alterations. These genes identified will be validated in pateinets to study their clinical relavance, and to verify their utility as biomarkers. The team is currently validiating various genetic variations that are assoicated with different subtypes.

Autoantibody Response and Identification of Tumor-Associated Antigens In Gallbladder Carcinoma - Immunoproteomics Approach

Early diagnosis is important for the timely treatment of gallbladder carcinoma (GBC) patients and may lead to increased survival outcomes. Here, the study centre has applied serological proteome analysis (SERPA), an immunoproteomics approach, for detection of 'tumor-associated antigens (TAAs) that elicit humoral response' in early stage GBC patients. Earlier, using 2-D immunoblotting followed bymass spectrometric analysis, the team identified 27 proteins from 08 protein spots showing intense immunoreactivity (based on densitometric analysis) in early stage GBC cases. Some of the identified proteins include ANXA1, HSPD1, CA1, CA2, ALDOA and CTSD. Autoantibody levels for two of the functionally relevant proteins, namely ANXA1 and HSPD1, investigated in individual plasma samples(52 cases and 89 controls) by dot blot assay using recombinant proteins showed a significantly elevated autoantibody levels against ANXA1 in early stage GBC cases in comparison to healthy volunteers or GSD cases (unpaired t-test, p <0.05). Receiver operating characteristic (ROC) curve analysis for ANXA1 showed an Area under the Curve (AUC) of 0.69, with 41.7% sensitivity against a specificity of 89.9% for early stage GBC. The study suggests that the autoantibody levels against ANXA1 may be potentially employed for early stage detection of GBC patients. Other proteins could also be explored and verified in a large cohort of clinical samples.

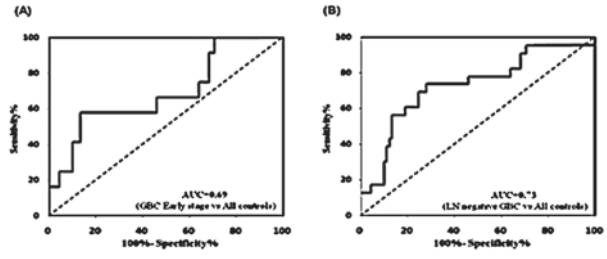


Fig. 5: ROC curve for ANXA1 antibodies in plasma from GBC cases and controls.

Proteomic Analysis of Plasma Extracellular Vesicles to Identify Circulatory Biomarkers for Gallbladder Carcinoma

Extracellular vesicles (EVs) have emerged as a novel source of circulatory biomarkers for cancer. Quantitative proteomic analysis of plasma-derived EV proteins showed a total of 95 proteins with altered levels in GBC in comparison to controls. This includes 19 proteins common to early and advanced stages including ALPL, CRP, NT5E, ANPEP, 38 specific to early stage including MME, SAA1and 38 specific to advanced stage GBC including DPP4, ECM1, SAA2. Clinical verification of MME showed a significant increase in their levels in early stage GBC (p value= 0.0093) while NT5E and ANPEP showed a significant increase in their levels in advanced stage GBC (NT5E, p value= 0.0182;ANPEP, p value=0.0026) in comparison to controls. ROC curve analysis for

MME, early stage GBC vs controls, showed an AUC of 0.6707 with 53% sensitivity and 100% specificity while for NT5E and ANPEP, advanced stage GBC vs controls, showed an AUC of (0.7533 and 0.6929), with sensitivity (40% and 45%) against a specificity of (100% and 97.14%). The results suggest that MME, NT5E and ANPEP may be useful as circulatory markers for detection of GBC and needs to be further explored in larger cohort of clinical samples.

AUC- 0.7533 AUC-0.6929 AUC- 0.6707

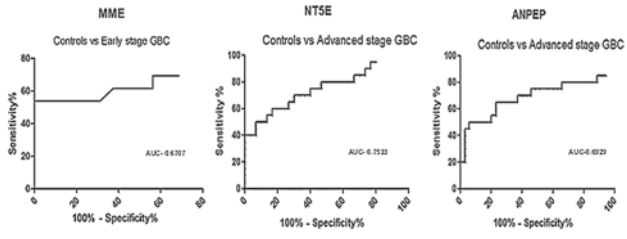


Fig. 6: ROC curve representing sensitivity and specificity of MME, NT5E and ANPEP for detection of early and advanced stage GBC cases.

Non- Communicable diseases- Rheumatic Heart Disease

As Rheumatic heart disease RHD is endemic in INDIA, prevalence of Atrial Fibrillation AF is also high with complications like stroke or thromboembolic events. The incidence of such complications in non-valvular AF is 4% per year as compared to 17–18% per year in patients with rheumatic AF. Despite the fact that paroxysmal AF is frequently asymptomatic, the risk of stroke is the same as in permanent AF. There is an increasing need to identify patients at a significant risk of paroxysmal AF which may help in preventing stroke by starting oral anticoagulation/antiplatelet therapy in the initial phase of the disease.

Identification of metabolic markers in Rheumatic Heart Disease (RHD) with Atrial Fibrillation using untargeted LC/MS based Metabolic Approach

The aim of the study is to understand the difference in pathways leading to stroke in patients of RHD with Atrial Fibrillation (AF) and Normal Sinus Rhythm (NSR). The target sample size for the study is 150 individuals (AF=50 NSR=50 Healthy Control=50). Of these 90 RHD patients (AF=40, NSR=50) and 30 sex and age matched healthy controls (HC) have been recruited. Standardization and data acquisition of untargeted metabolomics for 20 AF, 20 NSR patients and 20 age sex matched healthy controls has been performed at our collaborative Institute THSTI for the identification of metabolites.

The team designing and developing new drugs against cancer by identifying and determining the potent inhibitors against cyclooxygenase and Glutathione-S-transferase using computer aided drug design approach. Five new novel analogues designed and synthesized fromamide and chloride derivatives of proposed compounds by structural modifications which are not yet reported any where and will be evaluated further using invitro studies.

INFECTIOUS DISEASES

Tuberculosis

Role of M.tb signature protein Rv1507A in T cell memory: prospect in generating recombinant BCG expressing Rv1507A exhibiting enhanced memory response

Comparative genomic and proteomic analysis of several mycobacterial species revealed the presence of protein, Rv1507A, that is present only in *M.tb*. Purified Rv1507A protein as well as recombinant *M. smegmatis* expressing Rv1507A (Ms_Rv1507A) led to enhanced pro-inflammatory cytokine production through TLR4 pathway in macrophages. The team observed a Th1 biased response on immunization with Rv1507A protein or recombinant Ms_Rv1507A, with cellular phenotype indicative of an enhanced effector memory (EM) and central memory (CM) response. Apart from evaluation as a novel diagnostic candidate, further studies are being done to engineer recombinant BCG expressing Rv1507A, thereby improving the memory response of recombinant BCG.

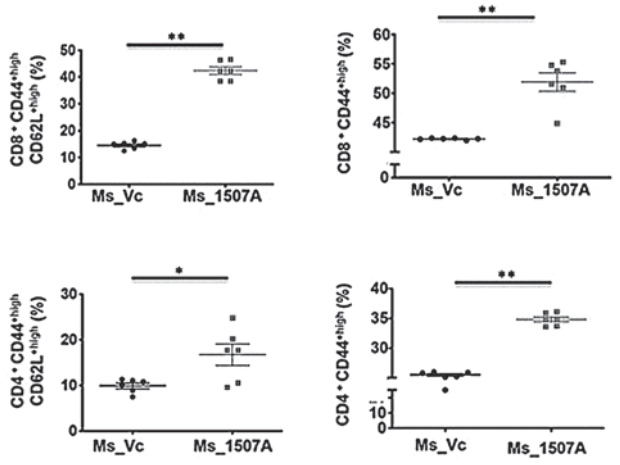


Fig. 7: Rv1507A protein and recombinant Ms_Rv1507A mount a robust effector and central memory response. Representative plots of $CD8^{+}CD44^{high}CD62L^{high}$cells and $CD4^{+}CD44^{high}CD62L^{high}$cells are shown. Percent of $CD8^{+}$ cells expressing $CD44^{high}CD62L^{high}$ and $CD44^{high}$ cells were measured by flow cytometry. Similarly $CD4^{+}$ T_{CM} and T_{EM} were quantified and shown as mean ± SEM. *p < 0.05, **p < 0.01 [Arora et al. (2020) Front Immunol. DOI: 10.3389/fimmu.2020.01199].

NGS analysis of *M.tb* strains in North eastern region of India: Top mutant variants belong to PE-PGRS and PPE family

In a pilot study, the team analyzed clinical samples of *M. tb* obtained from TB patients from North-East regions (NER) of India. The whole genome sequence analysis of the sputum collected in collaboration with Guwahati Medical College and Hospital and RMRC, Dibrugarh showed that Indian Ocean lineage is prominent in the NE region, followed by East Asia strain. SNPs present in the NE region samples showed that most variants belong to PE-PGRS family of proteins, PPE proteins, protein belonging to ESX-1 secretion system and copper transporter protein.

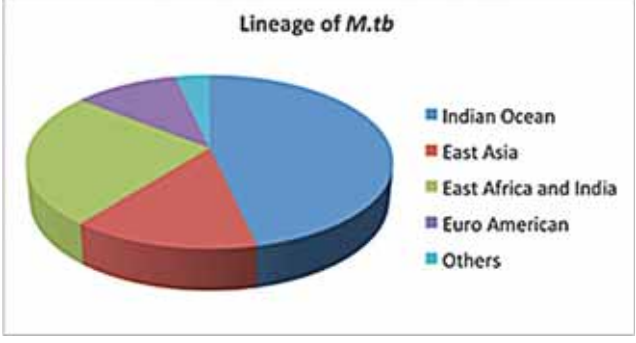


Fig. 8: Lineage distribution of NE region M. tb WGS Samples.

Differential roles of *M.tb* MoxR1 in Virulence: Novel target for repurposed FDA approved drugs

M. tb MoxR1, chaperonic protein acts as transcriptional regulator and are upregulated upto four-fold in persister cells, thus causing drug tolerance. The studies showed that MoxR1 plays a key role in formation of *M. tb* biofilm, harboringpersister cells. MoxR1 inhibits autophagy initiation of macrophage cells. MoxR1 activates pro-inflammatory signaling pathway and elicits secretion of TNF-α, IL-6 and IL-12 through the activation of TLR4, induces macrophage M1 polarization and modulates host-pathogen interplay to alter infection outcome. The multifactorial role played by MoxR1 in *M.tb* physiology makes it a novel drug target.

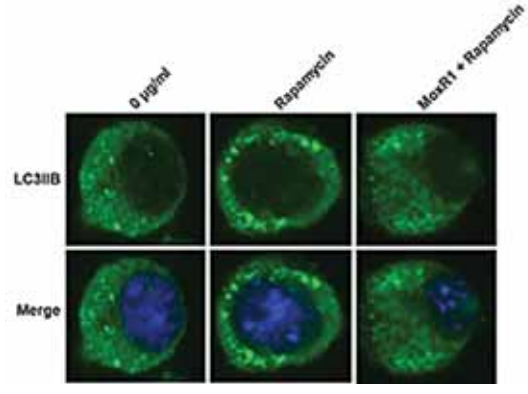


Fig. 9: MoxR1 inhibits autophagy initiation of macrophage cells. Immunofluorescence microscopic pictures demonstrating the LC3 foci in untreated, Rapamycin treated and MoxR1 + Rapamycin treated RAW264.7 cells. DAPI was used to mark the position of the nucleus.

Role of *Mycobacterium tuberculosis* methyltransferases in Pathogenesis and virulence

The previous study showed that*M.tb* signature proteins, SP2, is an essential for survival of *M.tb*, exhibits iron binding activity and possess methyltransferase activity. SP2 knock-in *M smegmatis* showed improper septa formation that lead to increase in length of bacteria by uptoten fold and formed thick outer cell wall. Macrophages fuse together to form multinucleated giant cells (MGC) in granulomas associated with

various pathological conditions. MGC can arise in response to an infection with foreign body such as from tuberculosis, herpes and HIV. The studies highlight the role of *M.tb* SP2 signature proteins in formation of granuloma and points to the role of SP2 in pathophysiology of TB.

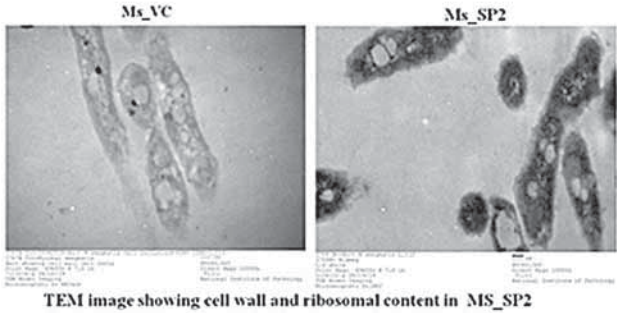


Fig. 10: TEM analysis revealing the outer cell wall modification in Ms_SP2 as compared to control Ms_Vc cells.

LEISHMANIASIS

Evaluation of immune status and parasite load in patients of post kala azar dermal leishmaniasis (PKDL) in response to treatment with miltefosine and amphotericin B

Confined treatment options and substantial increase in relapse rate after miltefosine (MIL) treatment warrant the need to adapt resilient combination therapies for post-kala-azar dermal leishmaniasis (PKDL). An equal number of confirmed cases of PKDL (n = 16) were put on MILmonotherapy (100 mg/day for 90 days) or MIL and LAmB combination for 45 days (3 injectionsofLAmB, 5 mg/kg body weight, and 100 mg/day MIL). Parasite load in slit aspirate was monitored using qPCR. Patients treated with combination therapy demonstrated a rapid declinein parasite load and achieved 100% cure, with no reports of relapse. Those treated with MILmonotherapy attained clinical cure with a gradual decrease in parasite load; however, 25%relapsed within 18 months of follow-up. Liposomal amphotericin B and MIL combination fortreating PKDL was found efficacious and safe, with high tolerability. Furthermore, this study established the utility of minimally invasive slit aspirate method for monitoring of parasite loadand assessment of cure in PKDL.

Comparative study of host cell modulation by miltefosine (MIL) resistant and sensitive Leishmania donovani parasites

This study aimed to investigate the differential capability of miltefosine resistant and sensitive L. donovani parasite in modulating the host cell immune response. The expression level of proinflammatory cytokine TNF-α was significantly downregulated (p<0.05) while the expression level of anti-inflammatory cytokine IL-10 was significantly upregulated (p<0.05) in host macrophages infected with miltefosine resistant LdMIL-R parasits. Thelevel of ROS was significantly lower (1.7 fold, p<0.05) whereas, the level of NO (nitrosativeresponse) was comparable in host cell upon infection with LdMIL-R parasite compared withsensitiveLdMIL-S infected host cell.

Whole genome sequence analysis of drug sensitive and resistant Leishmania isolates originated from patients of kala-azar and post kala-azar dermal leishmaniasis

Present study aims to use the high through put next generation sequencing technology togenerate the whole genome sequence data of clinical isolates of Leishmania. The team has determined the whole genome sequence of a wild type and a drug resistant parasite of L.donovani. The comparative data analysis revealed 240 SNPs, 237 InDels , 616 CNVs (377deletions and 239 duplications) and trisomy in chromosome 12 in case of resistant parasite.

Genomic analysis of virulence and antimicrobial resistance determinants of hypervirulent Klebsiella pneumoniae, an emerging threat to public health

This study will identify genetic factors associated with increased virulence and resistant determinants in K. pneumoniae isolates (hypervirulent hvKp and classical Kp) collected from community or hospital acquired infection The clinical samples collected at OPD and ICU of Safdarjung Hospital and directed to Microbiology Department were screened for

MDR K. pneumoniae. Sequence type (ST) was determined. Virulence associated genes viz. ferric iron uptake system genes (kfu, entB, ybtS), aerobactin (iucA),fimbrial genes (mrkD, fimH) and exopolysaccharides synthesis regulator gene (rmpA, rmpA2) were identified using PCR. The WGS analysis of an extensively drug resistant isolate was determined.

CHLAMYDIASIS

Study on matrix metalloproteinases and their inhibitors in women with *Chlamydia trachomatis*-associated tubal ectopic pregnancy

Ectopic pregnancy (EP) is the major cause of maternal morbidity and mortality in early pregnancy and a pathogenic link between *Chlamydia trachomatis* and tubal EP has been reported, however, persistent chlamydial infection in the fallopian tubes (FT) at the time of EP is still not confirmed. In this regard, chlamydial heat shock protein (chsp) may have a key role in the development of FT scarring. The study reveals the presence of few chsp-60 encoding genes, *viz.*: Ct604, Ct 755 and Ct110 in the FT from patients with tubal EP. Also, early diagnosis is the key to successful clinical management of women with tubal EP and identification of novel markers is needed for an early intervention during *C. trachomatis* infection. Expression of selected matrix metalloproteinases (MMPs) and their inhibitors showed significantly higher mRNA expression level of MMP-2,-9,-14 and significant downregulation of TIMP-1 in the FT tissue of *C. trachomatis*-positive EP patients in comparison with uninfected control women (undergoing mini laparotomy for tubal ligation), thereby suggesting their association with EP.

Immunogenetic study on enzymatic antioxidants in *Chlamydia trachomatis*-associated spontaneous aborters

Capturing gene expression profiles and biological pathways involved in failed pregnancy should be useful in pinpointing novel biomarkers or therapeutic agents potentially applicable in clinical conditions for the benefit of recurrent spontaneous abortion (RSA) patients. In this regard, the pathological mechanism behind *C. trachomatis*-associated RSA and enzymatic antioxidant genes was explored by investigating mRNA expression of two superoxide dismutase (SOD) genes in *C. trachomatis*-positive patients with history of RSA. Also, the role of selected pregnancy-associated micro-RNAs (miRNAs) as potential biomarkers was studied in these patients. Gene expression of SODs in urine showed that SOD1 (Cu-ZnSOD) was significantly downregulated whereas SOD2 (MnSOD) was upregulated significantly in infected RSA patients *versus Chlamydia*-negative aborters. Circulating miRNAs, *viz.*: miR-101-3p, -16, -133a were significantly upregulated while miR-559 showed a significant downregulation in the serum of *C. trachomatis*-positive RSA as compared to uninfected aborters. The study is in progress to understand the role of miRNAs in RSA with *Chlamydia* infection.

Public Health Importance

NIP has been at the forefront in tackling COVID-19 crisis. NIP was designated as depot for COVID-19 kits and distributed more than one lakh kits to various regional testing centers. The team is validating RT-PCR based COVID-19 kits so far validated more than 50 non-USFDA approved, some of which have already been commercialized. Besides, NIP provided technical and infrastructure support in setting up COVID-19 testing facility at STNM hospital, Sikkim.

Liposomal amphotericin B and MIL combination for treating Post kala azar dermal leishmaniasis (PKDL) was found efficacious and safe, with no relapse and high tolerability.

Early detection of gallbladder carcinoma (GBC) may impact long-term survival of the patients. One of the EV proteins, neprilysin (MME), identified from quantitative proteomic analysis of blood plasma-derived EV proteins, showed 53%

sensitivity against 100%specificity and could be a promising marker for early detection of GBC.

Early detection of TB can impact the success outcome of ATT therapy.The prototype of seeTB device (*Sci Rep* 2019), as a cost effective, portable unit for detecting *M.tb* in sputum samples, has been developed in collaboration with IITD. The device will be deployed at MRHRU (Bhunga), Safdarjung Hospital (New Delhi) and Hamdard Institute Medical Sciences and Research Hospital (New Delhi) for field trials.

A novel signature protein Rv1507A of *M.tb,* elicits strong memory response (*Front Immunol* 2020) can be a vaccine candidate with improved memory response for long time protection.

Cancer

- Autoantibody response analysis using immunoproteomics approach followed by clinical verification using dot blot analysis showed significantly increased ANXA1autoantibody levels in early stage GBC cases.
- Quantitative proteomic analysis of blood plasma-derived EV proteins from early and advanced stage GBC cases identified a total of 95 proteins with significantly altered levels.
- Of these, 19 proteins were common to early and advanced stages and 38 proteins were identified only in early stage.
- Clinical verification of three proteins MME (early stage), NT5E and ANPEP (both early and advanced stages) in large cohort of clinical samples showed neprilysin (MME) with an AUC of 0.6707 with 53% sensitivity against 100% specificity and could be a promising marker for early detection of GBC.

ICMR-NATIONAL INSTITUTE OF IMMUNOHAEMATOLOGY, MUMBAI (ICMR-NIIH)

HEMATOGENETICS

Satellite centre for Hemoglobinopathies at Chandrapur

This centre was established in Chandrapur with a high prevalence of hemoglobinopathies to cater to patients of central India. Comprehensive diagnostic facilities, including HPLC and molecular diagnosis, have been established at the centre and it is currently running programs like population screening, antenatal screening, newborn screening, and antenatal diagnosis. A total of 658 sickle cell disease (SCD), 112 Sickle/β thalassemia and 34 β-Thalassemia major cases were enrolled. Intervention and follow up have improved Hb levels and reduced morbidity in both SCD and S b-thal patients.

Under the antenatal screening programme, a total of 12365 pregnant women were screened for various hemoglobinopathies. Of these 496 women were found to be sickle cell trait and 21 were sickle cell anaemia (SS) while 73 were β-thalassemia trait. The antenatal diagnosis was provided to 51 eligible couples. Newborn screening programme has also been initiated, and screening of 1461 cord blood identified 100 sickle cell heterozygous (AS) and ten suspected sickle cell homozygous (SS) babies. Of the 10 SS babies, six babies could be traced out and were confirmed at the age of 28 days

Community awareness, along with screening for hemoglobinopathies, continued medical education (CME) for the local medical fraternity and training programme for laboratory technician and Medical Social Worker (MSW) were also organized.

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and The Effect of Early Intervention in Management of the Disease in Tribal Populations

The study involves a newborn screening program for Sickle cell anaemia (disease) in tribal populations of 7 different states for early detection and providing early comprehensive care to the affected babies. Overall, 5547 newborns were screened. Based on the HPLC reports, 40 newborns showed SS pattern (Disease) (0.72 %). The Sewa Rural hospital centre,

Gujrat, showed the highest incidence of SCD (1.4 %) The other centres RMRC Bhubaneshwar and NIRTC, Jabalpur also showed sickle homozygous newborns of around 1 %. 60 % of the SS newborns were followed up, and the treatment was initiated.

Training of in-service clinicians from Govt Hospitals and outreach programme for Aspirational Districts

This project was initiated in 2019. Under this project, six months training programme is conducted for in-service clinicians aimed at focused training in the diagnosis of various inherited haematological and immunological disorders. The eventual aim is to establish these facilities at different government hospitals and also to establish a smooth referral pattern for these disorders. In the first batch, a total of two clinicians from KEM hospital and AIIMS Bhopal and one Nidan Kendra clinician were trained from September- February 2019.

In the outreach program, Nandurbar was selected as an Aspirational District. A total of 1349 ANC samples was screened. Of these,280 (20.7 %) cases were captured in the first trimester of pregnancy. The overall prevalence of beta-thalassemia was found to be (3.1%), sickle cell trait (12.2%), and sickle cell anaemia was (0.96%). The team also detected 1 case of HbE trait and 7 cases with raised HbF determinant. The study centre offered prenatal diagnosis to 2 couples at risk. The fetuses were found to be unaffected.Newborn screening for the early detection of 5 metabolic disorders and sickle cell disease were initiated. A total of 918 newborns were screened, wherein 1.3% of neonates showed the presence of sickle cell disease. During the screening of 5 metabolic disorders, G6PD deficiency was the most prevalent metabolic defect detected with the incidence of 1.8% (Mutation analysis: G6PD Coimbra Shunde).

Assessing the role of microRNAs in clinical severity of Thalassemia Patients, and in hydroxyurea mediated HbF induction

To elucidate the mechanisms behind hydroxyurea-mediated HbF induction, the team proposes to evaluate the effects of miRNAs expression on HbF expression to hydroxyurea therapy. The functional relevance analysis of 15 miRNA studied identified miR-146a as a γ globin repressor. MiR-155 transcriptionally inhibits *BACH*-1gene, involved in inhibiting RBC phagocytosis. miR-326 miR-374 plays a key role in regulating *EKLF* expression and modifies the HbF level. Altered miRNA expression associated with hydroxyurea is potentially important for the pharmacological induction of HbF.

Prevalence and molecular characterization of NADH-Cytochrome b5 reductase deficiency in India

Recessive congenital methemoglobinemia (RCM) is an autosomal recessive hereditary disorder caused by the deficiency of NADH-cytochrome b5 reductase (NADH-CYB5R). The Analysis of 81 cases of *CYB5R3* variant across India indicated the presence of three potential prevalence pockets, including Uttar Pradesh from whereRCM cases were reported. Methaemoglobin levels and NADH-CYB5R activity of homozygous RCM I / II cases ranged from 23-33% and 12-14 IU/g Hb. The transcription of *CYB5R3* in lymphocytes was higher in heterozygous cases, and RCM I patients expressed higher levels of *CYB5R3* than RCM II. The homozygous p.Arg50Trp, p.Gly76Ser, p.Arg160Pro, p.Ala179Thr, p.Arg192Cys were found to be the most prevalent variants of *CYB5R3* in India. Most cases of Gly76Ser were found in Gujrat, whereas Arg160Pro was only prevalent in Kerala.

Molecular characterization of undiagnosed cases of congenital haemolytic anaemia using a multigene next-generation sequencing panel

Congenital hemolytic anaemia is a diverse group of genetic disorders characterized by mild to life-threatening anaemia (along with physical and mental retardation in fewer cases). The diagnosis could be offered to 137 transfusion dependant anaemia patients out of 169 evaluated using NGS platform. This study highlights the utility of NGS

in providing rapid and accurate diagnosis for early diagnosis and effective management.

Red cell membrane molecular pathology in hereditary spherocytosis (HS) in India

Hereditary Spherocytosis (HS) is the most common inherited anaemia characterized by anaemia, jaundice, and hepatosplenomegaly with the presence of spherocytes on blood smear examination. Comprehensive diagnosis facilities, including EMA binding assay on an imaging flow cytometer (IFC) and molecular diagnosis of HS, have been established at the centre. A total of 457 suspected cases were screened, and of these 108 cases were diagnosed as HS. Total nine novel variants have been identified in Indian patients for the first time in RBC membranopathies such as HS, HPP and HX. Also, 16 cases of HS and distal renal tubular acidosisharbouring the common *SLC4A1* mutation were diagnosed. Apart from HS, nine patients showed *PIEZO1* gene variants causing Hereditary Xerocytosis (HX). This is the first report of HX cases from the Indian population.

PAEDIATRIC IMMUNOLOGY AND LEUKOCYTE BIOLOGY

Centre of Excellence for diagnosis, management, and research of Primary Immune-deficiency disorders

This projectaims at establishing the state of the art facilities for diagnosis of PIDs at NIIH, including simple and cost-effective diagnostic tools, designing algorithms for the diagnosis of different PIDs suitable for the Indian population, increasing our knowledge of complicated diseases and creating trained human resources in the area of PID. 1436 patients from more than 50 centres across have taken benefit of these facilitiesthis year, out of which 116 cases have a confirmed diagnosis. Molecular confirmation was achieved in 100 cases by Sanger sequencing or NGS analysis. Prenatal diagnosis was offered to 5 affected families. A large cohort of PID patients is being generated to understand their immunological characteristics, molecular pathology and genotype-phenotype correlation. Based on the experience of a large cohort of patients, the team has established algorithms for CGD, SCID and HLH suitable for Indian cohort of patients. The team has also prepared a policy brief for free IVIG therapy for patients with PID.

Defining immunological markers for response to therapy in patients with Aplastic Anemia (AA)

Under this project, the study centre plans to comprehensively study the immunological abnormalities in patients with AA and compare them with the age-matched healthy controls to get an immune signature for AA and compare this with the response to IST and known predictive factors. Twenty-six patients with AA recruited so far have shown Reg T cell abnormalities which can predict response to therapy which needs to be validated in larger sample size.

Multi-centric study to understand the pathophysiology of inherited disorders among patients presenting with BCGosis and BCG adenitis

Serious side effects of BCG vaccination may be a manifestation of Primary Immunodeficiency Diseases (PIDs). This study aims at looking at the prevalence of PIDs amongst patients with BCG complications and establish guidelines for the evaluation and management of these patients. Of the total 19 patients presenting with severe complications to BCG vaccination evaluated so far, 40% of patients have an underlying immunodeficiency. This highlights the need for screening children with severe complications to BCG vaccination for underlying PID.

Explicating the role of programmed death 1 (PD-1) expressing CD8 T cells in hemophagocytic lymphohistiocytosis (HLH)

HLH is a rare, life-threatening hyperinflammatory syndrome characterized by excessiveactivation of macrophages and T cells resulting from defective cytotoxicity. It is associated with increased expression of PD1 cells on cytotoxic CD8+ T cells.

However, their role in the pathophysiology of T cells is not clear. The current study is expected to shed light on the proportion of PD-1 expressing CD8 T cells and their possible role in regulating CD8+ T cell responses in the pathophysiology of HLH. Based on the total, 18 patients recruited the high expression of PD-1, TIM-3 and LAG-3 on CD8 T cells signify functional exhaustion of these cells in HLH.

THROMBOSIS AND HAEMOSTASIS

A rapid nanoparticle-based lateral flow immunoassay for the detection of von Willebrand factor and alloantibodies to von Willebrand factor and procoagulant factor FVIII from human plasma samples

A rapid, simple and cost-effective gold nanoparticle-based lateral flow immunoassay based point of care test has been developed for the diagnosis of severe Haemophilia A and von Willebrand disease (International PCT application Number PCT/IN2020/050260- PCT-2014). The test is highly specific and sensitive with the working cost being < Rs 50. Being a qualitative test and with the simplicity of a POC test not requiring any equipment or technical expertise, this kit is likely to find its way even to the remotest parts of the country for the diagnosis of these two common bleeding disorders. The Commercial Collaborator has been identified, and these kits should be available in the market in the next few months.

Development of simple, novel and rapid diagnostic tests for Glanzmann thrombasthenia

The diagnosis of common platelet function defects like Glanzmanns thrombasthenia (GT) requires platelet aggregometer , flow cytometer along with well trained laboratory technical personnel. The POC test has been developed for GT. This qualitative test can offer the diagnosis of a severe GT within 15 minutes of sample application without the requirement of any of these expensive machines. Since GT is due to defects in either or both of GPIIb and GP IIIa receptors , a multiplex LFIA has been established validation of this kit is under process.

Comprehensive genomic and functional evaluation of factors influencing CAD and Myocardial Infarction in young patients

Coronary Artery Disease (CAD) and Acute myocardial infarction (AMI) are rapidly progressing to become leading causes of death in the young Indian population below 40 years of age. The study multi-centric study will recruit young patients below 40 years of age. The aim is to identify possible specific genomic variants that may alter gene expression profiles in the development and progression of cardiovascular diseases. Clinical exome sequencing has been performed on 12 patient samples. 14 Variants were detected in 10 patients. Further functional studies are being planned for understanding the clinical implications of these variants.

TRASFUSION MEDICINE

Centre of Excellence for Advanced Research in Immunohaematology and Transfusion medicine and create a National Rare Donor Registry

COE aims to study different immunohaematological aspects of blood banking in India with a vision to develop the Molecular Immunohaematology reference laboratory. High throughput techniques like NGS will be used for blood group genotyping of all minor blood group antigens in India, which will help ICMR to develop a National Rare donor registry to ensure safe blood transfusion in time. Other molecular strategies will also be developed for noninvasivefetalRhD typing and diagnostic facilities for HNA and HLA typing. The advanced tertiary centre will help in resolving complex problems in blood grouping & cross matching across India and train human resources.

For making a database of blood group antigens at national level four blood banks from are very well

known institutions from different regions of India (north, south, west, and east) have been chosen: 1) Postgraduate Institute of Medical Education and Research, Chandigarh, 2) JIPMER, Pondichery, 3) KEM hospital, Mumbai, 4) Medical College Hospital, Kolkata.

DNA based assays for screening for RHD & RHCE exons have been standardized, and 100 RhD negative samples have been screened by multiplex PCR specific. RHD deletion is the primary cause of D negativity in Indians. More number of samples will be screened to develop a genotyping strategy for correct RhD typing.

The centre has established methods for detecting human neutrophil antigens by genotyping. A panel of typed neutrophils was prepared, and a flow-cytometry based Granulocyte immunofluorescence test was standardized for detecting HNA antibodies. This study will evaluate the incidence of alloimmunization against HLA and HNA antigens in Indian donors and multi transfused patients, which will help ICMR to establish a donor deferral strategy for the prevention of TRALI cases in India.

Centre has also established a method for noninvasivefetalRhD typing by real-time PCR from cell-free DNA isolated from maternal plasma, and this is being validated for noninvasivefetal RHD genotyping.

In-house NGS panel developed will be used to resolve complex cases in blood group serology by predicting the antibody specificity.

CYTOGENETICS

Study of Genotypes, Phenotypes and search for new genes in patients of Fanconi anaemia with no mutations in known genes

During the three years, 95 subjects with FA were studied referred from all over the country. Our study highlights the chromosomal breakage investigation as the gold standard for the diagnosis as 95% of FA were diagnosed using this technique. The frequently occurring complementation groups are FANCA (48.19%), FANCG (14.45%), and FANCL (20.48%). The team has identified 40% novel mutations in different FANC complementation groups.

FANCL complementation group as one of the frequently occurring in our cohort. Worldwide frequency of FANCL is 0.2%, but ICMR's study established FANCL as a third frequent gene in the study.

FANCL c. 1092 G>A variant was identified as a founder mutation in Indian patients with FA. The functional studies confirmed that the FANCL c.109G>A is pathogenic mutation and the haplotype analysis suggested that the mutation is present in the Asian population, particularly all the ethnic populations in India.

The correlation of telomere length with FANC complementation groups showed significantly reduced telomere length in FANCL complementation groups. The telomere length may be considered as one of the markers to assess the response to the treatment in FANCL complementation groups.

Study of splice factor mutations and risk assessment in primary myelodysplastic syndromes

Spliceosomal gene (SF3B1, SRSF2, U2AF1) mutations are common in Indian MDS patients and molecular mechanism in leukemogenesis is not known clearly. The microarray analysis of CD34 positive cells separated from the bone marrow of MDS patients with spliceosomal mutations resulted in an alteration of a total of 4166 genes. Microarray data showed significant upregulation ($p<0.05$) of genes related to the chemokine signalling pathway, the Jak-Stat pathway, CML pathway, and AML pathway in MDS patients. Genes involved in signalling by GPCR were found to be significantly downregulated ($p<0.05$) in MDS patients. The validation of genes in MDS showed aberrant expression of AMPK, MTOR, and ULK1 genes in MDS patients with spliceosomal mutation compared to non-spliceosomal mutant MDS

patients. However large sample size needs to be studied to understand the different pathways.

Incidence of imatinib Resistance and associated BCR-ABL Kinase domain mutations among Chronic Myeloid Leukaemia in North East Indian Populations

The standard operating procedures for the patient recruitment, proforma preparations, and clinical data recording, Cytogenetics methods including GTG banding and fluorescence in-situ hybridization (FISH) and real-time PCR were prepared at collaboration Institute at Department of the Anatomy, Assam Medical College, Dibrugarh, Assam.The project staff and researchers were trained in cytogenetics, FISH, and real-time PCR techniques for the diagnosis and follow up of the CML patients of the North East Region. The molecular study also carried out at NIIH from 43 baseline CML patients. The present study revealed no mutation in the bcrabl kinase domain of newly diagnosed CML patients. However, among 4 follow up patients, two mutations (E255K and E255V) were identified in one IM resistant patient.

TRANSFUSION TRANSMITTED DISEASES

The impact of Pharmacogenomics on HIV-1 Antiretroviral therapy

The study showed the presence of the alleles HLA-DRB1*14, HLA-DQB1*02 and HLA-DQB1*05 predisposing the patients to the rash. Also, alleles HLA-A*11, HLA-B*56:01:01:01, HLA-B*52:01:01:01 and HLA-C*12 may play a protective role in EFV/NVP associated hypersensitivity reaction. MassARRAY PGx 74 analysis identified association of APOE,CYP450 and GLP1R genes with ADRs in TDF combinational therapy whereas COMT and CYP450 genes with toxicities of ZDV based combinational therapy.

Glycosylation of the serum haptoglobin-beta—A potential biomarker for Hepatocellular carcinoma in Hepatitis B virus infection

The present study reported the unique bifucosylated tetra-antennary glycan (7Hex:10HexNAc:2Fuc) at Asn211 of Haptoglobin glycoprotein that was predominantly present in HCC using ESI-Liquid Chromatography-Mass spectrometry. The AUC of three combinational markers AFP+AFP-L3+FucHp was 0.93 for distinguishing HCC cases from controls whereas, AFP+DCP+FucHp had AUC of 0.94. Glycan modification combined with protein expression profiling of haptoglobin may be used for diagnosis, monitoring development and progression of liver diseases.

PUBLIC HEALTH IMPORTANCE

Sanction of "Centre for Research, Management and Control of Hemoglobinopathies" at Chandrapur

The proposal for "Centre for Research, Management, and Control of Hemoglobinopathies" at Chandrapur by ICMR was sanctioned this year. This center will provide diagnostic services including genetic diagnosis and prenatal diagnosis, support State and District administrations for control and management of haemoglobinopathies, carry out basic and translationalresearch in the area of Haemoglobinopathies and strengthen the capabilities of Government Medical Colleges in the region through collaborative research and contribute to human resource development. After completing all the formalities, the construction work was initiated in Nov 2019.

- A rapid, cost-effective and simple gold nanoparticle-based lateral flow immunoassay based point of care test has been developed for the diagnosis of severe Haemophilia A and von Willebrand disease (International PCT application Number PCT/IN2020/050260-PCT-2014). The test is highly specific and sensitive with the working cost being < Rs 50. Being a qualitative test and with the simplicity of a POC test not requiring any equipment or technical expertise, this kit is likely to find its way even to the remotest parts

of the country for the diagnosis of these two common bleeding disorders. The Commercial Collaborator has been identified and these kits should be available in the market in the next few months.

- The diagnosis of common platelet function defects like Glanzmanns thrombasthenia (GT) requires platelet aggregometer, flow cytometer along with well-trained laboratory technical personnel. The POC test has been developed that can offer the diagnosis of a severe GT within 15 minutes of sample application without the requirement of any of these expensive machines. Since GT is due to defects in either or both of GPIIb and GP IIIa receptors, a multiplex LFIA has been established validation of this kit is under process.
- A simple ATP release assay has now been established to diagnose patients with the *RASGRP2* gene, which encodes the Ca^{2+} and DAG-regulated guanine nucleotide exchange factor I which plays a key role in integrin activation in platelets. It is based on lumiaggregometry which can easily diagnose this condition nearly seen in one-third of patients with unexplained platelet defects.
- The team reported a novel prognostic marker i.e. FUT2 in Chronic Granulomatous Disease patients (CGD) patients. *FUT2* gene is responsible for altered susceptibility to different bacterial and viral infections and diseases. Increased susceptibility to infection was seen in secretors compared to non-secretors. Secretors are also prone to Graft versus host disease (GVHD) post HSCT. All secretors who underwent HSCT also showed significant GVHD.
- Simple, cost-effective degranulation assay has been established on NK and Cytotoxic T cells and has been validated as a screening assay for diagnosis of Familial Hemophagocytic Lymphohistiocytosis assay and it can be incorporated in routine diagnostic screening for patients with HLH.
- The team's work in collaboration with NIV/EVRC in 2015 on polio vaccine virus excretion in patients with PIDs has led to an understanding of the importance of polio surveillance in patients with PIDs which is crucial for the success of polio irradiation program. This has led the initiation of a new WHO funded major large multi-centric study by WHO entitled "Study on Polio and Non-Polio enterovirus infections in children with immunodeficiency at multiple medical institutes across India" surveillance of PID patients for poliovirus excretion.
- The Analysis of patients suffering from complications of BCG vaccination requiring intervention has revealed that nearly 50% of them have an underlying primary immunodeficiency. A new multi-centric study is currently being planned to systematically look into this aspect.
- The Institute continues to offer a prenatal diagnosis for various hematological disorders to couples referred from different parts of the country. Prenatal diagnosis was offered to 200 families with thalassemia, 79 inherited bleeding disorders including hemophilia A, B, vWD, and other rare bleeding disorders, 7 families with primary immunodeficiency disorders, 3 families with congenital hemolytic anemia and 3 families with Fanconi anaemia.
- Specialized diagnostic services are provided by different departments including transfusion medicine, hematogenetics, hemostasis and thrombosis, paediatric immunology and leukocyte biology, cytogenetics, and clinical and experimental immunology. More than 20,000 patients from India and abroad have availed these diagnostic facilities.

ICMR-NATIONAL INSTITUTE OF TRADITIONAL MEDICINE, BELAGAVI (ICMR-NITM)

Anti-obesity effect of *Cyperus rotundus* rhizome and *Saraca asoca* stem bark extracts on progesterone-induced obesity in mice

Saraca asoca stem bark and *Cyperus rotundus* rhizome are used in Ayurveda for the management of obesity. Centre investigated their effect on progesterone-induced obesity in mice using hydroalcoholic extract. The results revealed that extracts of *C. rotundus* rhizome and *S. asoka* stem bark and their combination had significant anti-obesity effect in experimental mice.

Evaluation of Immunomodulatory properties of Bergenin

The Bergenin isolated from an ethnomedicine, demonstrated significant reduction of bacillary load and drug-induced immune impairment with long-lasting antigen-specific memory T-cell response when co-treated with anti-tubercular drug isoniazid. Overall it significantly reduced the bacterial burden of a MDR-TB strain, suggesting its role as a potent immuno-modulator as an adjunct therapeutic.

Anti-obesity effect of *Cyperus rotundus* rhizome and *Saraca asoca* stem bark extracts on progesterone-induced obesity in mice

Saraca asoca (SA) stem bark and *Cyperus rotundus* (CR) rhizome is used in Ayurveda for the management of obesity. In the context of prevalent obesity and overweight, study hypothesized that SA stem bark and CR rhizome would be effective in hormone-induced obesity, due to their use in obesity, metabolic and gynecological disorders. Thus, study has investigated their effect on progesterone-induced obesity in mice using hydroalcoholic extract (HE) of SA bark and CR rhizome. The administration of progesterone caused significant increase in body mass index, food and water consumption, adiposities area; and decreased exploratory behaviour, altered serum biochemical parameters (glucose, triglycerides, total cholesterol, high-, low- and very low- density lipoproteins), and adiposity index, compared to normal mice. These parameters were attenuated by treatment with HECR (125 and 250 mg/kg) and HESA (650 and 1300 mg/kg) and their combination (125 and 650 mg/kg) as compared to obese mice. The results revealed that HE of *C. rotundus* rhizome and *S. asoca* stem bark and their combination had significant anti-obesity effect in experimental mice.

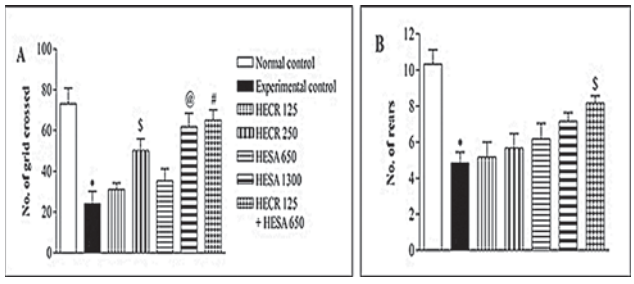


Fig. 11: Effect on Exploratory behavior of mice. A) No. of grids crossed; B) Number of rears.

Data are expressed as mean±SEM (n=6); Doses are expressed as mg/kg. *P<0.001 compared to normal control, $P<0.05, #P<0.01, @ P<0.001compared to experimental control.

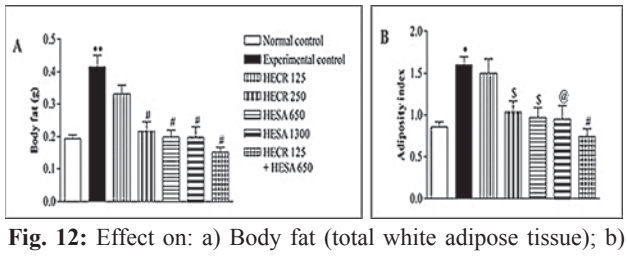


Fig. 12: Effect on: a) Body fat (total white adipose tissue); b) Adiposity index.

Data are expressed as Mean±SEM (n=6); Doses are expressed as mg/kg; *P<0.01, **P<0.001 compared to normal control, $P<0.05, @P<0.01, #P<0.001 compared to experimental control

Preclinical evaluation of safety and efficacy of decoction of RMRC-BM IP_156 for anti-diabetic activity with characterization of active compound(s)

The preclinical results of the test decoction (TD; prepared from shade dried leaves of a plant RMRC-BM IP_156) treated diabetic rats as compared with untreated diabetic rats are as follow:

Significant (p<0.01) decrease in fasting blood glucose and HbA1C in TD-treated group on days 45, and 60; while significant (p<0.001) decrease in cholesterol levels in TD group on day 60. Significant (p<0.001) increase in liver and muscle glycogen in TD-treated group on day 60, with HDL but decrease in LDL in TD group on days 45 and 60. Further,

team observed significant ($p<0.001$) decrease in the number of foot slips in the beam walk test in TD-treated group on day 42; significant ($p<0.001$) increase in latency period in hot plate test in TD group on days 21, 35, and 42 and increase in grip strength in TD group on days 35 and 42. However, TD did not influence the viability of C_2C1_2, 3T3-L1, and Chang liver cells. The IC_{50} was >1000 µg/ml against C_2C1_2, 3T3-L1, and Chang liver cells, confirming the safety of decoction. Cellular GPDH uptake in cultured 3T3L1 adipocytes cells significantly ($p<0.01$) increased to 2.44±0.04 nmol/min/ml following incubation of decoction at 5 µg/ml and the effect was 287% from the basal value. The decoction of the leaves of RMRC-BM IP_156 (80 mg/ml) exhibited 98.67±0.30 % of α-amylase inhibitory activity with IC_{50} of 28.52 ± 0.78 mg/ml. A rapid HPLC method was developed for screening of TD for flavone C-glucosides. Shelf-life studies revealed that TD in the solid-state at room temperature was stable, which is economical for storage.

Preclinical pharmacological evaluation of *Chitraka* roots in experimental colitis

Plumbago zeylanica L root is traditionally used for imflammatory diseases. The roots are subjected to *Śodhana* process before use, but the effect of shodhana on phytochemical content and biological effects is elusive. Hence, the present study investigated the effect of *Śodhana.* Physico-chemical standardization was done by: ash and extractive values, fluorescence characteristics, heavy/toxic metals, aflatoxins, microbial contamination, pesticide residues and a major bioactive phytochemical using plumbagin as a marker of the roots. Further, the effect of *Śodhana* process on toxicity of *P. zeylanica* roots was performed in Zebrafish and rats. The results revealed that *Śodhana* process caused decrease in ash and extractive values ($P<0.001$), total phenolics and flavonoid, and plumbagin content ($P<0.01$) while increase in moisture content ($P<0.05$) of śuddhā roots compared to ashodhit. In fish embryo acute toxicity study, the LC_{50} of śuddhā root extract (637.20 µg/ml) was significantly ($P<0.01$) higher than *ashodhit* root extract (325.36 µg/ml). The adverse effect levels (NOAEL) of *ashodhit* and *śuddha* root were 50 and 400 µg/ml, respectively. In single dose oral toxicity in rats showed no mortality or morbidity, but the cage side observation in both groups revealed black stools in some of the animals treated with *ashodhit* root without affecting other signs. *Śodhana* process induced the significant changes in physicochemical and phytochemical contents and decreased the toxicity of *P. zeylanica* roots. The data are supportive of claimed beneficial effect of *Śodhana* process in reducing toxicity of *P. zeylanica*.

Pharmacological evaluation of cocoa on efficacy and toxicity of Doxorubicin in murine ascites and solid tumor

The natural flavonoids and antioxidants from cocoa beans are known to reverse the cardio-, hepato- and nephro-toxicity. In this study, we hypothesized that treatment with cocoa extracts could help to fight against oxidative stress for patients on DOX treatment due DOX-induced cardiotoxicity. Cocoa-pods have been collected, dried, powdered and subjected standardization by Pharmacognostical evaluation. The standard hydro-alcoholic extract, along with theobromine (60.1±2.9 mg/gm) and epicatechin (50.8±1.03 mg/gm) were estimated by HPLC. The *in-vivo* experiments on cancer-induced mice showed that cocoa rendered better survival ability than doxorubicin.

Studies on TRL in HSV latency

HSV-1 establishes latency in CNS, where astrocytes are the major immune cells. The astrocytes infected with HSV-1F revealed the (i) changed expression of pathogen recognition receptors like Toll-like receptors, DNA and RNA sensors, interferons, and interferon-stimulated genes; and (ii) upregulate TLRs (TLR-2, 6 and 9), MDA5, DAI, (iii) increased expression of type I interferons, and interferon-stimulated genes (IFIT1, IFIT3 and RNase L) that encode antiviral immune response proteins

(Bansode *et al*., 2019). Earlier team had reported that the immunometabolic changes take place during HSV infection.

Evaluation of Immunomodulatory properties of Bergenin

In continuation to earlier work on antiinflammatory potential of Bergenin, isolated from an ethnomedicine, we have demonstrated significant reduction of bacillary load and drug-induced immune impairment with long-lasting antigen-specific memory T-cell response when co-treated with anti-tubercular drug isoniazid. Overall it significantly reduced the bacterial burden of a MDR-TB strain, suggesting its role as a potent immuno-modulator as an adjunct therapeutic .

Nutrition in Leprosy

Leprosy, a disease with neuronal complications and physical disabilities, is classified on host's immune response. Current therapy is lengthy, expensive and bacillary load dependent. Study discussed the nutritional role on susceptibility of *M. leprae* and its multi-drug therapy with a diet plan that can influence immune responses.

Probes to detect metal ions (Zn_2^+) in live cell: risk of Neurodegerative diseases

A propane-methyl-benzaldehyde (H2-SAP) probe with yellow emission (λem 560 nm) was synthesized to bind with Zn_2^+ as H_2O-MeOH mixture and detect diverse bioactive metal ions. The probe can detect intracellular Zn_2^+ in cells and surface water (Dey *et al*., 2019). A sulfaguanidine HL appended Schiff base can bind with Zn_2^+ showed higher antibacterial activity (MIC: 64 µg/ml for ZnL_2H_2O) against *E. coli* and detect trace amount of Zn_2^+ in cultured cells. The probe is non-toxic upto 200 µg/ml and detects the interaction of metal–ligand complex with target protein β-lactamase. While, a hydrazino-carbothioamide-1, is a non-toxic turn-on fluorescent chemosensor with green emission (λem 492) can sense several ions in water and sequentially detect Zn_2^+ and $H_2PO_4^-$ in living cell (Purkait *et al*., 2019). Further, the novel Schiff base L, a fluorescein hydrazine with a phenol functionalized moiety, can selectively sense Zn_2^+ in aqueous-alcoholic solution under normal pH. Photophysical studies showed its chelation enhanced ability with suppression of C-N isomerization and photo-induced electron transfer. We have developed its TLC-based paper strip to detect Zn_2^+ in surface water and cultured cells.

Clinical survey on Goitre prevalence among school children and estimation of iodine levels in salt and urine in rural areas of various Districts of North Karnataka (MRHRU)

The identification of high prevalence of clinical goitre in 6 Districts of North Karnataka has public health importance. The results of the study was presented during stakeholders meeting at Directorate of Health Services, Bengaluru on 17th May 2019 that included Principal Secretary of MoHFW, Director of Health and Family Welfare Services, Govt of Karnataka. Resurveys have been ordered in some districts and projects have been undertaken to increase awareness on consumption of iodized salts.

EXTRAMURAL RESEARCH

Biochemistry

- A study entitled "Synthesis of novel poly-N-substituted glycines (peptoids) congener based on cell selective antimicrobial peptides from gram positive and gram-negative infection" was carried out at Dept. of Biochenology and Bioinfomatics, Jaypee University of Information Technology, Solan, Himachal Pradesh. Suceesfully synthesized short peptides and their N- substituted glycines were screened for antimicrobial activity against gram positve and gram negative including multi drug resistant clinical isolates.As synthesized leads exhibited excellent activity against bacteria these can be taken furhter and develop as next generation antimicrobials.

- A study entitled "Role of cyclic di-AMP in mycobacterial physiology and virulence was taken up atAmity Institute of Integrative Science & Health (AIISH), Amity University Haryana**.** It was shown that Cyclic di-AMP could inhibit the DNA strand exchange activity of mycobacterial RecA and might be further developed as a potential tuberculosis vaccine adjuvant due to its immunomodulatory property.

Immunology

- A project entitled "Study on the role of microparticlesinthepathogenesisofRheumatoid Arthritis and Juvenile ldiopathic Arthritis" was undertaken at JIPMER, Puducherry. Stimulatory effects of Synovial fluid-derived MPs on FLS to release pro-inflammatory chemokines and B cell regulators demonstrate their pleiotropic effects on activating cells participating in the local inflammation, and the MP stimulated-FLS released chemokines can affect leukocyte recruitment and angiogenesis locally in RA synovium, leading to chronic inflammation and consequent joint damage.
- Another study entitled "Cross talk of Dendritic cells with iNKT/TFh and maturation of B cells in vertical hepatitis B virus transmission" was carried at ILBS, Delhi. Increased placental ASGPR expression and co-localization with HBsAg in HBV transmitting mothers showed its role in intrauterine HBV transmission. This study was instrumental in showing the mechanism of HBV intrauterine transmission through ASGPR expression. HBV transmitting mothers and HBV+venewborns showed similar impaired immune profile and defective key immune pathways, essential for functional or efficient immunity.

Medicinal plants

- A study on *Glycyrrhiza glabra* L. Phytochemicals in cancer chemoprevention: insights into molecular mechanism inducing apoptosis in human cancer cells was carried out at Guru Nanak Dev University, Amritsar. The present study brought out the chemopreventive potential and apoptotic nature of *Glycyrrhiza glabra* extract/fractions and its phytoconstituents.
- Another study on transcriptional regulation of adipogenesis and anti-obesity efficacy of *Bauhinia* and *tephrosia*in rats was completed at Sri Venkateswara University Tirupati. It was concluded that isolated pure compounds alpha-stigmasterol and pongamol could be well considered as effective bioactive molecules to mitigate adipogenesis and improves insulin sensitivity through inhibition of amylase , lipase and glucosidase.

Pharmacology

- Established 22 Rational Use of Medicine Centers (RUMCs) in various medical colleges and ICMR Institutes across the India in July 2019 in following institutions: at GSMC KEM Hospital, Mumbai, JIPMER, Gorimedu, Pondicherry, B.J. Medical College, Ahmedabad, PGIMER, Chandigarh, I P M E &R,Kolkata, IGIMS, Patna, CMC, Ludhiana, CSTM,Kolkata, AIIMS-Bhopal, Medical College ,Baroda, VMMC and Safdarjung Hospital,Delhi, AIIMS-Delhi, DMCH, Ludhiana, CMC ,Vellore, St John's Medical College ,Bangalore, NITR, Chennai, RMRI, Patna, NITM,Belagavi, NICED,Kolkata, NIRRH, Mumbai, NIIH, Mumbai, NIN,Hyderabad and NIE Chennai. Under the guidance of a Technical Advisory Group (TAG) set up by ICMR, the network of experts in clinical pharmacology and medicine have put-together an online course on prescription skills for Indian Medical Graduates .The course is meant for the Indian Medical Graduates who are during their internship. This is a self-paced course consisting of 40 modules will cover topics of general principles, prescribing in emergencies, specific therapeutic areas based

on MCI competencies.

- Comparison of the efficacy of Rituximab infusion versus Dexamethasone-cyclophosphamide pulse therapy in management of moderate to severe pemphigus vulgaris was carried out at AIIMS, New Delhi. A total of 51 PV patients were recruited. Of them, 29 received rituixmab (14: LP, 15: RAP) and 22 received DCP along with daily prednisolone and oral cyclophosphamide. The levels of IFNγ, IL17 and IL23 decreased and IL4and IL10 increased post treatment. The levels of IL2 didn't show a clear trend. In conclusions: Both the treatment regimens were found comparable w.r.t number of patients and median time to attain disease control, remission and relapse.

Physiology

- Study on therapeutic effects of antioxidants on age induced alterations in Neural Regulation of Pacemaker Entrainment (Biological Clock) was carried out at University of Hyderabad. The current study was undertaken to further understand the age induced alterations in the Neural Regulation of circadian time keeping system by studying alterations with age in rhythmic profile of Melatonin receptors, MT1a and MT1b in SCN. In addition therapeutic effects of curcumin on age induced changes in rhythmic profile of serotonin and its related compounds, expression of clock genes and Melatonin receptors MT1a and MT1b in SCN were studied.
- The study on elucidating the activator function of E2F5 transcription factor in prostate carcinogenesis was done at University of Calcutta, Kolkata. This study provided definitive evidences that an upregulated expression of E2F5 promotes cell invasion and migration by modulating the level and activity of its downstream targets namely TFPI2, MMP-2 and MMP-9. Another important observation was the ability of artemisinin to lower E2F5 expression and thus reverse the dysfunctional interaction between TFPI2 and MMPs.
- A study on assessment of cognitive and oxidative status in thyroid dysfunction patients and correlation with even Related Evoked Potential & EEG with brain mapping was carried out at Jawaharlal Nehru Institute of Medical Sciences, Porompat, Imphal, Manipur. The findings were suggestive of cognitive slowing which after treatment improves though statistically not significant. QEEG findings along with EEG source analysis are suggestive of involvement of pre-frontal, frontal & temporal areas in hypothyroid patients while parietal, temporal & limbic lobes were involved in hyperthyroid patients.
- The study on investigation to understand cell signalling in noisy environment was conducted at IIT Guwahati with the objectives to investigate, whether background noise limits or potentiates EMT inducing signaling by EGF, to understand the effect of noise on the dynamics of EGF signalling and the effect of network architecture on the relation between EGF signaling for EMT and background noise. It was shown that TGF-β potentiates the dynamics of cell state change in EGF induced EMT.

Pharmacogenomics Task Force

- A study on"Pharmacogenetics of Statin and Clopidogrel in South Indian Coronary Artery is ease Patients" was carried atALM PG Institute of Basic Medical Sciences, University of Madras, Taramani Campus, Chennai. Genetic variants in PK and PD determine the effect of therapeutic response of atorvastatin and clopidogrel. A combined rapid genotyping test for both statin and clopidogrel could serve as a better treatment outcome and precision medicine for CAD patients.
- A study on "Genetic polymorphisms of serotonergic pathways genes and their

association studies with disease severity and response to selective serotonin re-uptake inhibitors in patients with major depressive disorder" was done at CSIR-IGIB, Mall Road, Delhi-110007. Comparison of the top significant genes from GSA and gene expression studies was done and listed the common genes that are significantly associated with MDD susceptibility, and inter-individual variability in therapeutic response at genetic as well as transcriptomic level. These genes are important and can be used as predictive biomarkers for MDD susceptibility and antidepressant response as translational work.

- A study onIdentification of Genes and Pathways involved in Hypo-cholestremic drug responsiveness in human cells by RNAi based functional Pharmacogenomics was taken up at Dept. of Genetics, School of Biological Sciences Madurai Kamaraj University, Madurai. A novel multi-control regulation of 20 genes by miR-33, associated with dyslipidemia has been identified.

SCRT Task Force

- Study on Epigenetic Mechanism in Embryonic Stem Cells Pluripotency and Differentiationwas done at Department of Animal Biology, School of Life Sciences, and University of Hyderabad. The results highlight the importance studying chromatin condensation dynamics as an important epigenetic mechanism manifested by various epigenetic features of chromatin which has wider applications in fundamental understanding of biology of ESC differentiation and its applications thereof in understanding human diseases.
- A study on "Generation of induced pluripotent stem cells for haematological diseases" was carried out at Department of Haematology Adjunct Scientist, Centre for Stem Cell Research, Christian Medical College, Vellore. By this study, iPSC lines were generated from patients with CDA and CDA. This is the first study to generate iPSCs for disease modelling in India.

Translational Neuroscience

- A study entitled "Identification and validation of biomarkers for Parkinsonian syndromes with cognitive impairment" was done in Deptt. of Neurophysiology, NIMHANS, Bangalore. It was shown that Complement Factor H appears as a promising protein marker to distinguish PDCI from PD. These proteins can be used in clinical settings to differentiate between PD with cognitive impairment and PD without cognitive impairment, also from other disorders that mimic Parkinson's disease with cognitive impairment at an early stage.
- A study entitled "Genetics of susceptibility to encephalitis in Japanese encephalitis virus infected children from Uttar Pradesh" was carried out at National Institute of Virology, Gorakhpur**.** The results suggest that the heterozygous genotypes of inflammatory mediators and receptors *TNFA* rs1800629, *IFNG* rs2430561, *CD209* -336 and *MMP9* Q279R polymorphisms were associated with susceptibility to development of encephalitis in JE infected subjects.
- A study on Understanding the Role of Mitochondrial Dysfunction in Inherited Peripheral Neuropathies: A Phenotype-Genotype Correlative Study Using Next Generation Sequencing was done at Dept. of Neurology, NIMHANS, Bangalore**.** The aim was to identify reported and novel variations in patients with inherited peripheral neuropathy with specific reference to those involved in mitochondrial structure and function and to correlate with the clinical phenotype. This was a pilot study wherein patients with demyelinating electrophysiology underwent genetic testing for copy number variations and point mutations in PMP22 as the first step towards establishing a genetic diagnosis. Other CMT genes were not tested in the present

cohort. Use of the next generation sequencing may be an effective technology for uncovering variations in other CMT genes.

- A study entitled "Circulating microRNA as biomarkers to differentiate between Parkinson's disease, multiple system atrophy-Parkinsonism and progressive supranuclear paly- parkinsonism" was done at Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS), Bengaluru. A total of 100 patients diagnosed with Parkinson's disease (n=50), multiple system atrophy-parkinsonism (n=25) and progressive supra nuclear palsy-parkinsonism (n=25) along with 25 age and gender matched healthy controls were recruited for the study. The results suggests that differentially expressed miRNAs in the plasma could acts as a biomarker to identify and differentiate early PD from MSA and PSP cases predominated by Parkinsonism.
- A study on 'From disease phenotype to the molecular mechanism underlying juvenile myoclonic epilepsy'.was done at JNCASR, Bangalore and NIMHANS, Bangalore. The focus was to explore the molecular genetic basis of a relatively common form of a generalized epileptic syndrome: Juvenile Myoclonic Epilepsy (JME). Five novel genes underlying JME, a prevalent class of human epilepsy syndrome, has been identified from the work carried out. These are named: *JME-DES* at 2q33-q36; *EIG8-CASR* at 3q13-q21; *EJM4-TMEM171* at 5q12-q14; *EJM5-CDC20B* at 5p15-q12; and *EJM6-SOX30* at 5q33-q35. These five genes are among a total of 29 JME genes known, to date. Based on studies of about 250 familial and sporadic individuals with epilepsy, this work suggests that an overlapping genetic predisposition may underlie two seemingly distinct clinical entities, generalized and localized epilepsies.

Public Health Importance

A study on evaluation of drug utilization patterns among elderly patients at Vardhaman Mahavir Medical College & Safdarjung Hospital , New Delhi. On analysis of 4800 prescriptions, hypertension, diabetes mellitus, gastritis, muscular aches and asthma were recorded as the most common diseases for which drugs were prescribed. Apart from the two chronic diseases- hypertension and diabetes that mandate lifelong therapy, multivitamin / multimineral were prescribed to a large or long durations. An average of 5-6 medicines was prescribed to every patient (range from l-20 medicines) by brand name (84%). Evaluation of potential medications (PIMS) use, that acts as a key indicator of medication prescribing quality was helpful to target key drug categories that have the highest prevalence in the study namely proton pump inhibitors, first generation antihistamines, NSAIDs benzodiazepines and non-benzodiazepine hypnotics, antidepressants, alpha blockers, antipsycotics, PIMS continue to be prescribed to older adults despite evidence of poor outcomes and adverse events.

REGIONAL MEDICAL RESEARCH CENTRES

To deal with health problems of the regional and marginalised population, ICMR has established a total of four Regional Medical Research Centres, which are located at Port Blair (Andaman Nicobar), Bhubaneswar (Odisha), Dibrugarh (Assam) and Gorakhpur (UP). The mandate of these institutes is to focus on the regional health problems and find suitable solutions with the help from the respective state governments. The significant outcome of the research activities carried out by these centres during 2019-20 is mentioned below.

INTRAMURAL RESEARCH

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, BHUBANESWAR (ICMR-RMRCBB)

The institute made important discoveries in both communicable and non-communicable diseases, human resource development programme and translational research. Communicable research programme includes studies on lymphatic filariasis, malarial, diarrhoeal disorder, tuberculosis and diseases of viral origin. Non-communicable diseases include nutrition, sickle cell disease, hypertension, diabetes, maternal and child health. The centre established strong linkage with State Health Department to explore solution to the regional health problems. In last decades, centre has established two field units at Rayagada and Kalahandi in collaboration with Govt. of Odisha, to address on different health issues such as preparedness and prevention of diarrhoeal, malaria, control of IMR, MMR, reduction childhood morbidity and mortality, burden of tuberculosis and augmenting RNTCP through improving nutrition.

The centre involved in human resource activity focused on teaching and imparting training to M.Sc students to complete their six month dissertation sponsored from various reputed Universities in the State and outside the state to complete their 6 month dissertation work. The Centre has been able to launch its first ever Master's program (Master in Public Health) and PhD in public health research. The PhD scholars of the centre are sponsored from UGC and ICMR under fellowship as JRF/SRF. The RMRC Bhubaneswar has been designated as the Resource Centre for Health Technology Assessment and a dedicated unit for Evidence to policy has been set up. The center bring glory in the global research landscape and implement locally available and affordable solutions for endemic and emerging public health challenges in the country.

The centre has established linkages with other ICMR and non-ICMR institution like State Govt. of Odisha, NVBDCP, Delhi, RGI, Gates Foundation, DBT, AIIMS, Delhi, IVI, DST in upgrading the expertise, sharing scientific information and collaborative research programme. Training on vaccinology was undertaken by our scientist at International Vaccine Institute, Seoul, Korea, SGPGI, Lucknow and other reputed institutes.

Collaboration with State Health Department was strengthened in form of consultancy, undertaking

evaluation of health programme, referral diagnostic services, epidemic investigations and disaster management. The collaborative projects were initiated and new agreements and MOUs were signed with different organizations of the state.

REGIONAL VIROLOGY RESEARCH & DIAGNOSTIC LABORATORY

A Regional Advocacy Workshop and meeting was organized for Principal Investigators and Directors of VRDLs from 3 states - Odisha, Chhattisgarh and Andhra for the effective synchronization between Integrated Disease Surveillance Programme (IDSP), National Vector Borne Disease Control Programme (NVBDCP) and VRDL Network under the auspices of the Department of Health Research. The state level representatives from IDSP, NVBDCP of these states, experts from NCDC, New Delhi and WHO Country Office, also participated in this meeting. The major focus was on enabling cooperation between the VRDL network and the different public health programmes. The other issues like Potential for collaboration for virus research, syndromic diagnostic algorithms and VRDL Network data management were also discussed extensively. The meeting was successful in terms of bringing different stakeholders involved in infectious disease surveillance and outbreaks into a single platform. Some of the bottlenecks in sharing of samples and data between the different stakeholders were also discussed. This meeting helped in establishing coordination with different state health authorities for outbreak investigations and sample testing in Regional VRDL.

- Laboratory was WHO accredited for Measles and Rubella on 6th January 2020.

- Laboratory got designated as Nodal/Apex referral centre for the testing and diagnosis of SARS Co-V 2 from 7th March 2020 onwards.

NATIONAL REFERENCE LABORATORY FOR TUBERCULOSIS

RMRC, Bhubaneswar is one of the six National Reference Laboratories (NRLs) of the country which supervises 10 states like Odisha, West Bengal and 8 North East states for quality TB diagnosis under NTEP. It also provides diagnosis and follow up cultures for MDR TB patients on DOTS Plus regimen to 10 districts of Odisha (Bhubaneswar, Puri, Nayagarh, Khordha, Rayagada, Kalahandi, Malkangiri, Kopraput, Nuapada & Nabarangpur).

During the reporting period, NRL Microbiologists carried out the initial assessment visit for establishment of new Tuberculosis Liquid culture laboratories at Aizwal (Mizoram), Silcher (Assam), Nagaland, Shilong (Meghalaya). VSS medical college Burla (Odisha), Mushidabad, & Medinapur (West Bengal).

A total of 7446 TB patient's sample has been processed by different technologies based on the TB diagnostic algorithm of NTEP. Sputum samples from the patients under DOTS plus treatment has been received from 10 districts for liquid culture. Out of the total sample received, 2755 samples were tested by LPA for first line drugs among which 2554 samples were susceptible and 4 samples each were MDR and Rif mono-resistant and 60 samples were INH mono-resistant. A total 244 samples were tested by LPA for second line drugs out of which 131 samples resulted as pan sensitive, 9 were XDR, 79 were only FLQ resistant, 5 were only SLID resistant and none were resistant to low level Kanamycin.

Inoculation for liquid culture was done for 2134 samples, of which about 30% cultures reported as MTB and tested for drug susceptibility. A total of 3271 samples were tested by GeneXpert; out of which 3203 tests yielded valid results, 469 were found as MTB positive. Among the MTB positive 14 samples were found to be Rifampicin resistant, which were referred to districts for DOTS Plus treatment initiation.

A Phase III, Randomized, Double-blind, Three arm Placebo controlled Trial to Evaluate the Efficacy and Safety of two vaccines VPM1002 and Immuvac (Mw) in Preventing Tuberculosis (TB) in Healthy Household Contacts of Newly

Diagnosed Sputum Positive Pulmonary TB Patients

Trial initiated on 4th December 2019 at AIIMS, Bhubaneswar site and on 26th December 2019 at RMRC site. Till date 617 healthy house hold contacts of index TB cases have been enrolled for the vaccine trial.

Human pulmonary paragonimiasis in crab eating communities and smear negative suspected TB cases from some states of India

The project was initiated in two districts, Nayagarh and Mayurbhanj of Odisha based on number of TB cases, geography and crab eating behavior. Crabs were collected from both the districts and examined for the presence of metacercariae. Blood samples of 13 cases with TB like symptoms were found positive by paragonimiasis IgG ELISA.

National Survey for State wise Prevalence of Microbiologically Confirmed Pulmonary Tuberculosis in India

The National TB prevalence survey was conducted in Chhattisgarh and out of 13 selected clusters, survey was conducted in 6 clusters. In Odisha out of 21 clusters, survey was completed in 6 clusters. Due to COVID-19 outbreak the work for remaining clusters is pending.

REGIONAL HUB FOR HEALTH TECHNOLOGY ASSESSMENT

The Health Technology Assessment in India (HTAIn) is entrusted with the responsibility to collate and where needed generate evidence related to the clinical effectiveness, cost-effectiveness, and safety of devices and health programs using HTA approaches. Universal Newborn Hearing Screening (UNHS) is a significant public health initiative as early diagnosis and treatment are critical for cognitive development of children. In India, priority has been provided since 2013, but there is an operational challenge for maximum screening coverage. The HTAIn team of the centre completed the Health Technology Assessment of 'Portable Automated ABR' Neonatal Hearing Screening Device, which was approved by the HTAIn Board, Ministry of Health & Family Welfare, and Govt. of India on February 2020. This instrument is 'portable user-friendly cost-effectiveness technology' to diagnose hearing impairment with improved diagnostic accuracy for universal coverage through first stage screening; which will be soon implemented at a large scale at various public and private health facility for UNHS.

Our HTAIn team are currently working on 'HTA of telemedicine-enabled otoscope for prevention of ear diseases', and 'assessment of cost-effectiveness of "*Durgama Anchalare Malaria Nirakarana* (DAMaN) – malaria control in inaccessible areas" in India'

MODEL RURAL HEALTH RESEARCH UNIT (MRHRU), TIGIRIA

The centre has initiated various studies with an aim to improve the quality of health services in rural areas through MRHRU Tigiria.

- A Community based household survey was conducted in Baliput village of the block, to understand the socio demographic and morbidity pattern.
- Baseline data on status of public health facilities in the block have been obtained from different departments.
- Facility level data collection from SDH Athagarh, CHC Tigiria and CHC Bindhanima has been started to assess the demographic profile, disease status, public health programmes.
- Initiatives has been undertaken in coordination with Medical Officer In-charge of the CHC, Tigiria to improve and standardized the labor room at CHC.
- Situational analysis has been carried out using Focus Group Discussions (FGD) among the teachers and students and the health care staff of the block.

- Geographical information system mapping has been planned for digitalization of the data generation.
- MRHRU has been designated as a field site for providing field exposure to the MPH students and Medtech Interns.
- MRHRU staff has been participating in various seminars and meetings for exploring ground reality of the block.
- A rural cohort tool has been finalized under the coordination of different health personnels and scientists from RMRC Bhubaneswar.

Aspirational District Project with multi-sectoral partnerships at Nabarangpur District, Odisha

The Aspirational District project includes two studies i). Economic Empowerment of Tribal Farming Communities funded by DBT and ii). Farm Based S&T Interventions for Socio-Economic Development in Nabarangpur district funded by RKVY, Govt of Odisha. The project aims on the social and economic development (including health status) of people by using Science & Technology in the farm products. RMRC focuses on the health and nutritional aspect specially on improvement of health status of residential school children by implementing nitri kitchen garden, capacity building grass root health providers local school teacher and SHG group members.

The baseline survey for collection of socio-demographic data, anthropometric measurement was undertaken in two clusters out of four, covering around 925 households. Estimation of haemoglobin and screening for sickle cell anaemia, thalassemia, and malaria parasite was done. Faecal samples were examined for intestinal parasite. In same clusters residential schools were surveyed to assess their health status, hygiene and sanitation practice.

Health awareness campaign was done through poster presentation, exhibition and street play which depicted massages on nutrition and nutritive value of various fruits and vegetables, health and hygiene. Debate competition on Swachha Bharat, Sustha Bharat and video show on common vector borne and non communicable diseases was also conducted in schools.

To showcase the project activity centre took part in district festival "Mondei" at the district headquarter and brochure highlighting aim, objectives, methodology, progress and way forward of the project was distributed. Besides IEC on health and hygiene, general health check-up and anthropometric measurement for general public was provided.

NUTRITION

Assessment of iodine status among pregnant women in Gajapati district of Odisha

The Iodine status of pregnant women was assessed for iodine consumption, thyroid profile, and infant growth following birth, six-months and one-year after birth. The study indicated that the iodine status was declined with duration of pregnancy and increased after delivery and lactation.

Prevalence of fluorosis in the community and development of an appropriate intervention model for prevention and control of fluorosis (ICMR Taskforce in Nayagarh district)

Community assessment for the prevalence of fluorosis in Nayagarh district demonstrated excess fluoride in drinking water source leading to health disorders like dental fluorosis, skeletal and non-skeletal fluorosis. The study warrants for development of an appropriate intervention model for prevention and control of fluorosis.

Prevalence of Vitamin A deficiency disorders among children aged 1-5 years in selected districts of India (Cuttack-Odisha)

Prevalence of Vitamin A deficiency disorders among children aged 6-59 months was studied in Cuttack district of Odisha that revealed vitamin A deficiency is not a major public health problem in terms of Bitot spot; however, it is confined to certain pockets in the community.

Concurrent monitoring and impact Evaluation of Mid-Day Meal programme in Odisha

Concurrent monitoring of MDM programme in 29 districts of Odisha generated baseline indicators for impact evaluation of nutritional and socio-academic improvements in school children. The study revealed 70% attendance of students enrolled maintained gender and social equity, universal coverage of MDM adhering to weekly menu and nutrients-calories and protein. Prevalence of thinness/wasting, overweight/obesity and stunting was 24%, 7% and 32% respectively. Anaemia found to be a public health problem (47%) for children aged 6-14 years in MDM schools in Odisha.

Strengthening of ICDS & MIS Cell of Women and Child Development & Mission Shakti department in Odisha

As per the assigned monitoring and updating of Poshan Abhiyaan dashboard, data collation, compilation, analysis and presentation of ICDS reports is integrated to strengthen capacity building. The study evaluates the supportive supervision monitoring of the Supervisors, CDPOs and nutrition managers supportive supervision monitoring and evaluation of nutrition outcome preparation of convergent nutrition action plan as a mandate. With a goal to achieve cent percent growth monitoring pilot study of Ojan Utshab, data collected for two blocks in Cuttack district is analysed for identifying key bottlenecks on IYCFP, ICDS registers, immunisation coverage, preschool, supplementary nutrition, referral services and VHSND. Collation, review and analysis of routine Rapid Reporting System(RRS) and e-Pragati report is conducted with disaggregation of ICDS projects, sectors besides gender and social category.

Other studies of Public Health importance undertaken by the centre

One Health strategy for elimination of human Anthrax from an endemic district of Odisha: a demonstration project

The MOUs has been signed with different partner institutions, collaborative meetings with district level line departments including Health, Veterinary, Forest & other allied institutes and team formation for development of SOPs, training modules, IEC/ BCC materials has been prepared. Fifty percent of the baseline survey in the district has been completed covering 1652 adults. Intervention Trial has been registered with CTRI (Clinical Trail Registry of India) with No - CTRI/2020/05/025325 [Registered Prospectively on: 22/05/2020].

Assessment of Neonatal Screening Approaches for Sickle Cell Disease and The Effect of Early Intervention in Management of the Disease in Tribal Populations, Research cum Intervention study

Sickle cell disease is highly prevalent among tribes of Nabarangpur, Kandhamal, Kalahandi and Rayagada districts; thus these districts have been selected for the study. For early identification of SCD cases, the neonatal screening was undertaken by HPLC of cord blood sample collected from three major health facilities of Nabarangpur district. We screened 614 tribal neonates and reported SCD prevalence of 0.8%. Neonates with SCD were supposed to be followed up periodically, but it could not be materialised due to the Covid-19 pandemic.

ICMR-Task Force study on Smokeless tobacco and Reproductive and Maternal Health

The preliminary data on tribal slums under Bhubaneswar Municipal Corporation and number of women in reproductive age group with or without having habits of consuming smokeless tobacco in the tribal slums was collected. The questionnaire tools for qualitative survey was developed in collaboration with NICPR and piloted in the community.

Mobile Application for Immunization Data in India (MAIDI)

The baseline work for conducting of study has been undertaken and staff orientation cum training program has been completed. The Mobile

Application and Outline of M-Course is being developed. In-house testing and translation of application in local language (Odia) has been undertaken.

Surveillance of Enteric Fever among rural population: A hospital based Tier-II surveillance in the catchment area of Tigiria block, Cuttack, Odisha

The ground work like staff recruitment and training is completed. The equipment and consumables has been purchased. Sample collection will be initiated once the Covid19 situation becomes better.

Intensified pulmonary Tuberculosis (PTB) case findings among selected high risk clinical groups attending secondary level public health care facilities

The high-risk group patients from MCH clinics, general medical wards, diabetics clinic, geriatric ward and PLHIV attending government health facilities of district and state capital were screened for PTB by clinical symptoms and radiographic findings. Sputum samples of patients were collected and processed for microscopy and TrueNAT. Out of 2861 patients screened 60 were symptomatic and 9 were culture positive. Positive cases were referred to RNTCP for treatment and follow-up.

Profiling of virulent genes in major etiological agents isolated from chronic wounds/ulcers among patients with diabetes in tertiary care hospitals in Bhubaneswar and Cuttack

The pus or necrotic tissue samples were collected from 150 diabetic patients with different grade of ulcers and gangrene attended general surgery ward in state capital hospital. The etiological agents were isolated and the study reported *S. aureus* as the major etiological agent in diabetic foot ulcer. This finding will help in developing diabetic foot management module.

Prevalence and risk factors of Gestational Diabetes mellitus among pregnant women attending a tertiary care hospital in Bhubaneswar

Screening of gestational diabetes mellitus (GDM) by using glucometer among pregnant women attending a tertiary care hospital revealed prevalence of GDM to be 9.89%. This will help in planning for special programme for this vulnerable group.

Anti-mycobacterial evaluation and host toxicity testing of newly synthesized isoniazid-phytochemical conjugate derivatives as prospective anti-TB drug

Ten isoniazid-phytochemical conjugates (IPCs) based on Schiff-base synthesis protocols of medicinal chemistry have been designed. The drug-likeness characters of individual conjugates were validated through Lipinski rules of five (RO5), Prediction of activity spectra for substances (PASS) program, molecular docking energy or binding affinity against wild type and mutant types "enoyl-ACP(CoA) reductase of *Mycobacterium tuberculosis*" as target enzyme, drug-likeness score, toxicity nature and toxicity class, computationally, before synthesis.

To determine the prevalence, risk factors and morbidities of TB and Malaria co-infection among the tribes living in a malaria endemic region of Mayurbhanj district in Odisha

Screening for the presence of signs and symptoms suggestive of PTB and history of ATT was done in 5 villages of Mayurbhanj district. Sputum specimens were collected from individuals having pulmonary symptoms and processed for staining by ZN / FM method and culture by LJ method followed by DST. Three of 16 were found culture positive.

Human Resource Development for Health Research in the area of Health Informatics under the scheme "Support to Indian Institutes for imparting training to the Faculty of Medical Colleges and Research Institutes"

To support human resource development for health research the centre conducted 20 training programme on various aspects of implementation of computational biology and bioinformatics in

health informatics and health care system for state health officials, clinicians from medical colleges, Public Health researchers, scholars and scientists from various research institutes. The training on genomics, proteomics, and *in silico* drug designing was also conducted.

Assessment of the effectiveness of DAMaN in reduction of malaria burden in Odisha

The study was conducted in Sundargardh, Angul, Keonjhar, Kandhamal, Rayagada districts, Odisha with the aim to assess the impact of DAMaN on malaria burden, its impact on pregnancy outcome and nutritional status of under-five children. The detailed household data on socio-economic/ behavioural characteristics of individuals like LLIN use, IRS, MSAT were collected. The anthropometry and Hb estimation and malaria diagnosis was done by rapid diagnostic test, microscopic and PCR. The interim result shows the TPR of 2.7% indicating significant reduction in malaria incidence and the overall LLIN use to be 80%. The impact assessment of the programme is under process of analysis.

Improving the Capacity of Health and community for sickle cell Diseases screening and management: an intervention study in Kalahandi District Odisha

This Task Force study aims to develop effective intervention model for the SCD patients in tribal areas for accessing government health care system and capacity building in terms of knowledge, skill and training of the health care workers at different levels of health system for prevention and management of SCD. The formative research phase data collection has been completed using mixed method in Kandhamal district and is under process of analysis. The screening for SCD has been done by solubility test and subsequently confirmed by HPLC.

The Epidemiology of Scrub typhus in Odisha

The study was undertaken with the aim to estimate the magnitude of scrub typhus antibodies among febrile and clinically ill patients and to study the genotypes and phylogeny of *Orientia tsutsugamushi* circulating in this part of the country. A total of 140 acute febrile illness or history of acute febrile illness patients with acute kidney injury (AKI) were included in the study. The RIFLE criteria found to be 60% of F, 13.3% I, 11.1% R and 4.4% were E. Complications like ARDS was reported in 17.8% and shock in 2.2% of the patients. The study indicated scrub typhus prevalence of 32.14%. Overall mortality rate was 20.0%. Thrombocytopaenia was found to be important predictors of the disease. Karp is the predominant circulating genotype of O. tsutsugamushi in this part of the country. The present study indicates that scrub typhus is grossly under-diagnosed and under-reported cause of AKI from Odisha.

PUBLIC HEALTH IMPORTANCE

Contribution during Covid-19 Pandemic

After the VRDL was designated as Nodal/Apex referral centre for the testing and diagnosis of SARS Co-V 2 on 7th March 2020 the laboratory extended significant support to the state government by providing diagnostic services for COVID-19 cases. It was the only laboratory for testing of Covid-19 virus and we received samples from various health facilities, medical colleges and private hospitals of the state. The first positive case of SARS CoV-2 was recorded on 15th of March, 2020, that helped in the state health department in strengthening epidemic preparedness and mitigation measures.

Capacity building and Human resource development

Sensitization cum preparedness meeting on Novel Corona virus outbreak was organized for the Medical superintendents, Laboratory supervisors and Technicians from various government and private health care facilities of the state. To strengthen state health department's human resource, the training on bio-safety, sample collection, RT PCR and online data entry in ICMR portal was conducted.

Health technology assessment

The health technology assessment of 'Portable Automated ABR' Neonatal Hearing Screening

Device indicated that this instrument is portable, user-friendly cost-effective for diagnosing hearing impairment with improved diagnostic accuracy for universal coverage through first stage screening; which will be soon implemented at a large scale at various public and private health facility for UNHS.

WHO accreditation of VRDL for Measles and Rubella

The laboratory got WHO accreditation for Measles and Rubella in January 2020. It will help in achieving high quality surveillance by early confirmation of the suspected measles, rubella and congenital rubella syndrome. This global laboratory network has key role key in strengthening the efforts taken by WHO for elimination of measles and rubella.

Project contribution for National Award

The multicentric project entitled Farm Based S&T Interventions for Socio-Economic Development in the Aspirational District of Nabarangpur contributed towards "Platinum SKOCH award 2020" for the district administration.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, DIBRUGARH (ICMR-RMRCNE)

COMMUNICABLE DISEASES

Clinical, aetiological and epidemiological aspects of acute encephalitis syndrome (AES) in north-east India

Etiological agents of AES in northeast India identified, and a diagnostic algorithm developed. Based on the findings, recommendations for empirical AES treatment made to the state health authorities.

Rickettsial diseases in the states of Nagaland, Meghalaya and Mizoram

Seasonal distribution pattern and hot-spots of occurrence of the three major rickettsial diseases described. Vectors of these aetiologies were collected and identified.

Effectiveness of single dose of SA 14-14-2 vaccine against Japanese encephalitis (JE)

Drop in effectiveness of single dose SA-14-14-2 vaccine was noticed among adults over seven-years period. Despite the waning effectiveness, the JE incidence rate was found to have reduced.

Genetic characterization of *Orientia spp.* and assessment of Th1/Th2 immune response

All major strains of *Orientia tsutsugamushi* (*viz*., Karp, Kato and Gilliam) were found to co-exist in Assam; Karp being the dominant. IL-10 expression had a role in the differential phenotypic presentation of scrub typhus.

Climate change on seasonality and distribution of insect vector borne diseases

Impact of climate change on seasonality and distribution of insect vector borne viral and rickettsial diseases described in northeast using a remote sensing and GIS-based approach.

Zoonotic pathogens and livestock farms

Isolation and identification of bacterial pathogens along with antibiotic resistance patterns conducted among animal handlers and farm animals from Assam and Meghalaya.

Insecticide resistance in relation to genetic and biochemical factors in JE mosquito vectors

A study on the status of insecticide resistance with special reference to genetic and biochemical characterization in potential mosquito vectors of Japanese encephalitis in Assam.

Bacterial aetiology, antimicrobial sensitivity & risk factors of neonatal sepsis

Bacterial aetiologies of neonatal sepsis are being identified along with antimicrobial sensitivity pattern and associated risk factors in 4 different districts of Assam.

Sentinel surveillance for influenza including avian influenza in India

During the reporting period, more than 500 individuals with severe acute respiratory infections tested for influenza A and B (including the strain information) using molecular methods.

Assessment of acute viral hepatitis and chronic liver diseases in Northeast India

Among patients presenting with various liver diseases across 9 sites of northeast India tested for different hepatitis viruses, including the genotypes and subtypes.

Genetic diversity and cytokine profiling in *Plasmodium vivax* malaria in Assam

The project aims to investigate the genetic variation of *P. vivax* drug resistance genes along with pro- and inti-inflammatory cytokine profiling in simple and complicated malaria cases.

Novel malaria surveillance system (MoSQuIT) along international borders

A mobile based platform was introduced and deployed for malaria surveillance in 3 international border districts of Northeast India.

Additional intervention package for accelerated malaria control

Operational feasibility of additional interventional package (low-cost and customized) for accelerated malaria control in areas with Jhum Cultivators in Tripura is being evaluated.

Mass Drug Administration (MDA) Coverage & Compliance Assessment Survey

The study aimed to assess the MDA coverage and compliance in Dibrugarh. The findings highlighted the need for additional mop-up rounds to enhance MDA coverage and compliance.

Surveillance of Food Borne Pathogens (FBP) from North-East India.

This is a recently sanctioned project that has not been started due to the ongoing COVID-19 pandemic situation.

Cryptosporidium in diarrhoea patients, and drinking water and recreational water sources

Community based study of *Cryptosporidium spp.* among diarrhoea patients and in drinking and recreational water sources, along with their molecular characterization.

Toxoplasma gondii seroprevalence & risk factors in pregnancy

This is a study on *Toxoplasma gondii* seroprevalence and its associated risk factors during pregnancy among tea-tribe population of Assam. Pregnancy outcomes would also be assessed.

Tuberculosis (TB) in tribal areas of Manipur, Nagaland, Tripura and Meghalaya

Generated zone-wise/ state-wise and tribal group-wise data on pulmonary TB, along with insights into the prevalence of multi-drug resistant TB.

National survey for state-wise prevalence of microbiologically confirmed pulmonary TB.

Recently initiated project. So far, three clusters have been surveyed.

Human pulmonary paragonimiasis in crab-eating communities & smear negative TB.

The institute is leading a pan-India study on pulmonary paragonimiasis that is often misdiagnosed as smear-negative pulmonary TB due to similar clinical & radiological picture.

Molecular study of *Mycobacterium tuberculosis* in northeast India

Molecular investigations of *M. tuberculosis* isolates from Tripura, Meghalaya and tea-gardens of Assam using NGS-sequencing to understand the epidemiology & disease dynamics.

NON-COMMUNICABLE DISEASES

Population Based Stroke Registry in Dibrugarh, Assam

A Population Based Stroke Registry and Clinical Stroke Care Pathway using Mobile Stroke Unit was established in Dibrugarh, Assam.

Health and demographic surveillance system in Dibrugarh, Assam (Dibrugarh –HDSS)

A Health & Demographic Surveillance System (HDSS) has been established, comprising of the entire population from sixty contiguous villages and twenty tea gardens from Dibrugarh district.

Intervention through Mobile Phone application to control blood pressure.

A mobile-based application with decision support facility for prevention and control of hypertension was developed.

Germline mutation spectra in multi-ethnic breast cancer patients

The germline mutation spectra of BRCA1 and BRCA2 genes in a large cohort of multi-ethnic breast cancer patients of different ethnicities from northeast described using sequencing. The findings would help in carrying out focused site-specific screening of high-risk subjects.

Epigenetic modifications & liver cancer in high risk incidence region of North-East India

Potential biomarkers for screening, prognostic & therapeutic use in liver cancer investigated.

Screening, awareness and counselling for sickle haemoglobin in tea gardens

Screening, awareness and counselling activities for preventing sickle cell haemoglobinopathies among tea garden labour communities of Dibrugarh and Tinsukia districts of Upper Assam.

Haemostatic derangements in β-thalassemia syndromes

The objective of the project is to carry out biochemical and haematological characterization of the derangements in all 3 arms of the coagulation system in β-thalassemia syndromes.

Oral, breast & cervical cancer screening in tea-gardens of Assam

This demonstration project is being carried out in seven tea-gardens for capacity building of screening activities and early detection of 3 common cancers (breast, oral and cervical).

IMMUNOLOGY

Impact of measles rubella vaccination on population immunity [IMRVI study]

The impact of measles rubella (MR) vaccination campaign on population immunity is being investigated. Field-work and sample collection in 26 clusters from Dibrugarh district completed.

Human immune response to a flavivirus vaccine

Integrative functional analysis of human immune response to JE vaccine SA-14-14-2 in being assayed.

Follicular helper T-cell repertoire in flavivirus infection and vaccination

Immunological aspects of Japanese encephalitis (JE) vaccine SA-14-14-2 studied.

Merozoite surface protein (MSP) and CD4, CD8 derived cytokines in malaria in pregnancy

The role of merozoite surface protein (MSP) triggered CD4, CD8 derived cytokines in the development of malaria during pregnancy is being investigated.

Mobile Application for Immunization Data in India – MAIDI

The pre-situation analysis on full immunization coverage in Dibrugarh district was done. Health workers were trained on the Mobile Application 'MAIDI' for gathering immunization data.

BASIC RESEARCH

Anti-leishmanial properties of medicinal plants from North East India

After interacting with traditional practitioners, thirteen medicinal plants are being screened for isolation and identification of active phytoconstituents with anti-leishmanial properties.

Hybrid Para-Amino-Benzoic Acid-1,3,5-triazine derivatives for antimalarial activity

Hybrid para-amino-benzoic acid 1,3,5-triazine derivatives are being designed with microwave assisted synthesis and evaluated for antimalarial activities.

Point of care diagnostics and drug resistance monitoring technologies for malaria.

A rapid, point-of-care, highly sensitive and specific CRISPR Cas based system for diagnosis and drug resistance monitoring of malaria parasites is being developed.

ELISA kit for JE differential diagnosis within the *flavivirus* serological group

A peptide-based ELISA kit designed to specifically distinguish JE infection among closely related *flavivirus* infections is under development.

OTHER AREAS

Regional Viral Research and Diagnostic Laboratory (Regional-VRDL)

Overall 7,632 samples (nasopharyngeal swab/ throat Swab/ Blood/ CSF/ Stool) were received from different parts of northeast, and a total 19,950 tests were performed on these samples for different viral diagnosis. Six outbreak investigations were conducted in Assam, Meghalaya and Arunachal Pradesh. Diagnostic services for SARS-CoV-2 by real time-PCR, quality control (QC) services for the other designated labs of region, and capacity building for COVID-19 response in the northeastern states are also being carried out.

DBT-Animal house facility for Biotechnology Research in North-eastern Region

This is an infrastructure development project, currently under progress. It would house small lab animals in an advanced animal facility for biomedical research for all northeastern states.

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, PORT BLAIR (ICMR-RMRCPB)

ELIMINATION AND RISK REDUCTION OF INFECTIOUS DISEASES

Double fortified salt (DEC + iodine) as a supplementary measure to the ongoing MDA for eliminating a persistent focus of diurnally subperiodic *Wuchereria bancrofti* towards accomplishing elimination in the entire Nancowry group of islands

The pilot study conducted earlier was successful in eliminating the persistent focus of diurnally sub -periodic filariasis in two islands and the same stagy is being implemented in other two more islands (Kamorta and Chowra) towards the elimination of entire lone focus in the Nancowry group of Islands . Population census through the door to door survey was carried out and generated data on microfilaraemia (*mf*) prevalence and the quantity of double fortified salt required. An interactive advocacy campaign for all the stakeholders was conducted. Thirty-five tons of double fortified salt was prepared with the help of Tamil Nadu salt corporation, procured and transported to the Islands for the distribution .

Control of Tuberculosis among the Nicobarese of Car Nicobar: Consolidating the gains of a strengthened public health system and the recent socio-economic progress

Towards eliminating TB , Sensitization meetings held with stakeholder. Focal group discussions were conducted among the representatives of the tribal council of all the 15 villages and traditional healers

- effective implementation . Population survey, registration and documentation was completed. Active surveillance of chest symptomatic patients - two surveys were conducted in collaboration with DHS. A total 18 new cases of TB detected of which 2 are relapse cases remaining 16 new cases new (include two MDR TB and two mono drug resistance) and active surveillance continued . Regular community awareness programs organized and drug intake of the cases and their follow up is being monitored by the project staff supplementary to the RNTCP staff .

SURVEILLANCE – HOSPITAL-BASED AND COMMUNITY BASED

Conduct of Quality Assurance program for both serological and molecular diagnosis of Leptospirosis, for DHR-Virus Research and Diagnostic Laboratories (VRDLs) across the country

The program was initiated to provide diagnostic support of leptospirosis at VRDS. Proficiency panels for molecular and serological tests (RT PCR, IgM EIA) were developed and provided along with diagnostic kits and reagents to all 30 VDRL laboratories. All 30 laboratories reported the results with 100% concordance for serology and sentinel surveillance using IgM ELISA has been initiated across the country. Out of 30 laboratories , 10 reported the results for RT PCR and awaiting the results from the remaining 20 VRDLs. RT -PCR will be introduced in the surveillance system along with IgM EIA for surveillance of leptospirosis across the country in October – November 2020.

Hospital and community-based surveillance of SARS CoV2 - providing diagnostic support to health care facilities to the whole Islands under DHS and Indian Naval Hospital (24hX7d)

ICMR – RMRC extended the diagnostic support since from 11th March 2020. Strengthened BSL3 and BSL2 plus laboratories to assure the personal safety and safety of the environment. The first common source outbreak of SARS CoV 2 / COVID 19 was detected in March 2020 . The outbreak was investigated in collaboration with DHS and travel history revealed that the source of the outbreak was as results of exposure of a team of people from port Blair participated in a meeting held at New Delhi and arrived back at Port Blair. The outbreak was effectively controlled through contact screening and community surveillance and no mortality has been reported during the upsurge. However thousands of positives for SARS CoV 2 / COVID 19 have been reported subsequently and continued.

State Level Viral Research and Diagnostic Laboratory - Establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities

ICMR -RMRC providing diagnostic support to all health care facilities to whole islands . A total of 2,921 patients suspected viral etiologies were screened. A total of 19 Chikungunya, 309 Dengue, Influenza A - (H1N1)15, (H3N2) 5, Influenza B -Yamagata 1 and Rotavirus 1. The data indicate that multiple serotypes of dengue is circulating. This center also functions as the WHO nodal center for Measles and Rubella- WHO -MR Laboratory network. A total of 36 leptospirosis cases were also identified.

Study on the prevalence of oral premalignant and malignant lesions and the associated viral etiological agents among the tribal population of Car Nicobar Island

A community-based cross-sectional study was carried in five villages and total of 1239 individuals were screened. The most common type of lesion was Smokeless tobacco keratosis (46.1%) and the use of Sukka, tobacco lime user's lesion (24.1%). The most common site involved was buccal mucosa. The cytopathological report revealed 60% have smokeless tobacco keratosis. One suspected oral malignancy case was identified clinically and histopathology is pending. 31 oral scrapings were screened negative for HPV-16 and HPV-18 .

Surveillance of long-term sequelae of Chronic Hepatitis B Infection and Risk reduction among the Nicobarese of Car Nicobar

Nicobarese, had an HBsAg carrier rate of 23%, and the estimated high risk of chronic sequelae of HBV infection would be more than 200 individuals, hence the study was initiated. A total of 212 individuals were screened, 31 were identified as positive for HBsAg and found positivity rate was 14.8% (95% CI: 10.3, 20.3). The positivity among males was 17.1% (95% CI: 7.9, 20.4) and among females was 13.3% (95 CI: 7.9, 20.4). History of Injections, IV Infusion, Blood transfusion and Surgery were found to be common risk factors.

A multi-centric hospital-based study on the epidemiology of keratoconjunctivitis in India

A total of 361 patients diagnosed as kerato-conjunctivitis reported at G. B. Pant Hospital and Agarwal Eye Hospital, Port Blair, were enrolled. Common symptoms included redness of the eye, pain, increased lacrimation, and irritation. Conjunctival swabs /corneal scrapings were collected and screened for adenovirus and 100 samples found positive for Human Adenovirus species D and strain 8 (type 8).

MEDICAL ECOLOGY AND ENVIRONMENTAL BIOLOGY

Developing the model of Anopheles mosquito breeding parameters and their Physico-chemical determinants and application of the model for environmental monitoring of risk to Anopheles breeding in the context of Global Climate Change

The breeding habitats of anopheline mosquitoes were sampled in 15 villages of Car Nicobar island along with associated parameters estimated (Physico-chemical, biological - culicine mosquito immatures, insect predators, phytoplanktons, zooplanktons) towards the development of modal. Four anopheline species were recorded, *viz*, *An. sundaicus, An. barbirostris, An. insulaeflorum* and *An. Subpictus* and *An. Sundaicus* is predominant. The regression model developed showed that pH (-ve), alkalinity (-ve), and hardness(+ve) were found to be influenced anopheline abundance significantly whereas pH on the alkaline side reduced or dropped the anopheline breeding .The plankton, *Gomphonema*, showed a positive influence on anopheline abundance, whereas, *cyanobacteria, Licmophora, Chlamydomonas,* and *Arcella* had a negative influence on the anopheline breeding .

Spatial and temporal variations of potential malaria vector(s) and associated species of *Anopheles* in the Andaman and Nicobar Islands

A longitudinal study to identify the potential breeding habitats of malaria vectors in the Andaman Nicobar archipelago was carried out. A total of 27 villages in three districts of Andaman & Nicobar archipelago were covered. Tehsil wise per dip density of anophelines ranged from 0.05 to 2.58. Anopheline immatures were recorded from 23 different habitat types and eleven anopheline species were identified. *Anopheles sundaicus* and *An. barbirostris* showed diverse habitat distribution. In Nicobar District, *An. sundaicus* alone was collected landing on human bait, while Andaman districts seven species were recorded. Blood meal sources found to be high in *An. sundaicus* fed on cow (42.52%) and goat (61.4%). Human blood index (HBI) for *An. sundaicus* (0.28) was significant.

BASIC AND APPLIED RESEARCH

Whole-genome sequencing to understand the virulence factors of infectious Leptospiral serovars/strains with varied clinical manifestations

This is first study in India conducted on whole genomes of leptospires .A largest number of 78 isolates recovered from patients with different clinical syndromes across the country were sequenced . All are grouped in to Eight species including newly described species viz. L. tipperaryensis , L.

barantonii, L. mtsangambouensis and L. brenneri . The study revealed the identification new plasmids , knowledge on understanding pathogenesis and evaluation of the pathogen. Several proteins were identified and the knowledge generate could be used for the development of vaccine and diagnostics .

Characterization of proteins involved in the adhesion of *Leptospira* to epithelial cells and macrophages and their function

A total of 1290 proteins identified as capable of interacting with human hosts based on their subcellular localization. Further Domain-Domain interactions identification resulted in the identification of 1403 and 18149 interactions from databases. The human proteins belong to 45 macrophage and 158 epithelial locations that interact with leptospiral proteins. Filtering of predicted HPIs between human and *L. interrogans* resulted in 228 interaction involving 47 and 116 unique Leptospiral proteins and human host proteins, respectively.

Public Health Importance

1. Two major projects were initiated to eliminate Diurnally sub - periodic filariasis using Novel strategy - use of double fortified salt (DEC + iodine) as a supplementary to MDA from entire Nancowry group of Islands and Tuberculosis from whole Car Nicobar Island, both are inhabited by indigenous tribes .
2. ICMR – RMRC extended the diagnostic support sinc 11th March 2020 to all health care facilities in whole Islands under DHS and Indian Naval Hospital (24h X 7d). Strengthened BSL3 and BSL2 plus laboratories to assure the personal safety and security of the environment. The first common source outbreak of SARS CoV 2 was investigated in collaboration with DHS in March 2020. Pool testing was first time conducted at RMRC.
3. Developed a model of Anopheles mosquito breeding parameters and their Physico-chemical determinants and application of the model for environmental monitoring of risk to Anopheles breeding in the context of Global Climate Change .
4. ICMR -RMRC providing diagnostic support on suspected diseases with viral a etiology to all health care facilities of whole islands under State Level Viral Research and Diagnostic Laboratory - Establishment of a Network of Laboratories for Managing Epidemics and Natural Calamities . RMRC also part of Measles and Rubella- WHO -MR Laboratory network.
5. Conducted the external Quality Assurance program – molecular (RT-PCR) and serological (IgM EIA) diagnosis of Leptospirosis at DHR- ICMR Virus Research and Diagnostic Laboratories across the country . Proficiency panels were developed and provided along with diagnostic kits and reagents to all 30 VDRL laboratories. 30 laboratories reported the results with 100% concordance for serology and sentinel surveillance using IgM ELISA has been initiated across the country .RT -PCR will be introduced in the surveillance system in October – November 2020.
6. World Congress on leptospirosis was organized at the Regional Medical Research Centre at Port Blair, during November 18-19, 2019, with a theme “Leptospirosis - climate change and the changing epidemiology-opportunities opened up by new insights into genomics & vaccines”. A total of 23 International experts across the world representing from 11 countries and 52 Indian experts attended the Congress . The congress was supported by WHO and ICMR and focused on to update the current scenario and to have an interactive discussion on effective control measures with reference to one health .
7. ICMR-RMRC evaluated a Truenat™ - Micro real time-PCR for rapid diagnosis of leptospirosis at minimal resource settings. The test found suitable to be used at primary health care to provide early and

rapid diagnosis of leptospirosis , to provide highest patient care and at the field during epidemics.

8. First study in India- whole-genome sequencing on large number of 78 leptospiral isolates /strains recovered from patients with varied clinical syndromes across the endemic states of the country completed. The study revealed the identification new plasmids, generated the new knowledge on understanding pathogenesis, evaluation of the pathogen – geographic genomics and several proteins were identified as candidate genes and could be used for the development of vaccines and diagnostics .

ICMR-REGIONAL MEDICAL RESEARCH CENTRE, GORAKHPUR (ICMR-RMRCGKP)

Diagnostic services for suspected Japanese encephalitis (JE) cases from eastern Uttar Pradesh

ICMR-RMRC Gorakhpur, undertake the routine investigation of clinically suspected Acute Encephalitis Syndrome (AES) cases admitted to the BRD Medical College (BRDMC), Gorakhpur and provides diagnostic services that guide the management of cases.

- A total of 1093 clinical specimens (CSF and Serum) were collected from 574 AES cases.
- All the AES cases hospitalized during (1st April 2019 to 31st March 2020) were investigated for detection of anti-*Japanese encephalitis (JE)* virus specific IgM (anti-JE IgM), anti- *Orientia tsutsugamushi* IgM (anti - OTs IgM) and Dengue NS-1 antigen (DEN NS-1 Ag) by ELISA assays as per the ICMR recommendations.
- Anti-OTs IgM positivity was recorded in 349 cases (61.7%) followed by anti-JE IgM in 104 cases (18.4%) and 18 cases (3.1%) for DEN NS-1 antigen.

Setting up of AES Cell at Baba Raghav Das Medical College, Gorakhpur

AES cell is established in the Pediatric ward of the BRD Medical College to co-ordinate the specimen collections, storage, laboratory testing, clinical data collection and analysis.

- Scrub typhus has been associated as the major etiology with AES cases of eastern Uttar Pradesh.
- The genetic sequence analysis confirmed Gilliam genotype is the most prevalent genotype in this area comprising about 90% and the karp genotype is about 10%. of *Orientia tsutsugamushi* (scrub typhus pathogen).

Genetics of susceptibility to encephalitis in Japanese encephalitis virus infected children from Uttar Pradesh

A total number of 403 healthy controls without any history of encephalitis and 237 encephalitis cases positive for JEV by IgM ELISA /PCR were included in this study.

The results revealed a significantly higher frequency of *TNFA* rs1800629 G/A, *IFNG* rs2430561 A/T, *CD209* -336 A/G and *MMP9* Q279R G/A genotypes among JE cases as compared to healthy controls.

The identified SNPs (*TNFA* rs1800629 G/A genotype and *CD209* -336 A/G genotype) in the present study can serve as markers to identify children at risk of developing JE when exposed to JEV.

Etiological investigations of non-AES referred cases from Gorakhpur region

A total of 124 whole blood specimens of Dengue fever suspected cases were obtained from Gorakhnath Hospital, Gorakhpur.

- In these samples PCR based genotyping of Dengue virus revealed the circulation of DEN-1, 2 and 3 serotypes in this region.

Establishment of a Health and Demographic Surveillance System [HDSS], Gorakhpur, Uttar Pradesh

- Basic demographic data collection of 9 villages of the total 28 villages has been completed covering 8402 household and 46360 household members.
- GIS based mapping of HDSS area has been completed.

Development of diagnostic kit for rapid and early detection of *Orientia tsutsugamushi* based on isothermal recombinase polymerase amplification and lateral flow

- The 56kDa gene of Karp and Gilliam strains of *O.tsutsugamushi* were successfully isolated from blood samples of acute encephalitis cases.
- Optimization of isothermal recombinase polymerase amplification has also been initiated using the cloned full length 56kDa gene *O.tsutsugamushi* and with specifically designed primer sets.

Assessment of lymphatic filariasis transmission after post mass drug administration in Gorakhpur district

Gorakhpur district is listed as endemic district of lymphatic filariasis by NVBDCP. Secondary data collection regarding prevalence of lymphatic filariasis patient in Gorakhpur district was under progress with the state health department authorities.

- Finalization of study villages from 19 administrative blocks of this district was completed.
- *Culex quinquefasciatus* mosquito collection was completed from three administrative blocks of Gorakhpur District.

National Survey for state wise prevalence of microbiologically confirmed pulmonary tuberculosis in India

As a part of this multicentric study, the tuberculosis prevalence survey in various districts of eastern Uttar Pradesh was started by the Institute on 05/12/2019.

- This project covers 21 districts and 34 clusters in eastern Uttar Pradesh.
- Four clusters were completed from three districts of this region.

A study of psycho-neurotic disorders and socio - behavioral changes among AES/JE cases recovered in Gorakhpur

- This study was initiated in January 2020; finalization of protocols and collaboration with different agencies is under progress.

Study on Current Status of General Public Health Problems and Level of Health Awareness in Gorakhpur

- The field study has been conducted on 500 participants from 10 HDSS villages.

PUBLIC HEALTH IMPORTANCE

- Setting up the COVID-19 laboratory and initiation of laboratory testing facility of clinical specimens of suspected cases of nCov-19 as per ICMR guidelines.
- Infrastructure for molecular and serological laboratory diagnosis for associated etiologies of acute encephalitis syndrome as per ICMR algorithm.
- Infrastructure and lab were established for the study of Anti Microbial Resistance (AMR) and Malaria diagnosis.
- Health awareness & hand hygiene awareness program for school children
- IEC activities & pamphlets on Health awareness and awareness on JE/AES were distributed in the villages of HDSS site on daily basis.
- Distribution of infographics on JE / AES awareness in 28 HDSS villages (> 3000 families).

- Formulation and distribution of infographics (pamphlets) on SWACHCHHATA & HEALTH HYGENE as part of Swachchha Bharat Abhiyan in HDSS villages (>1200 families).
- Organizing health awareness camps for general public (social, psychological and physical health) in endemic villages of JE/AES in Gorakhpur division.
- An ICMR Training on Biomedical and Health Research Ethics was conducted in collaboration with ICMR-NCDIR Bangalore and BRD Medical College, Gorakhpur. More than 200 participants from various parts of country participated in 2 day workshop.
- A Memorandum of Understanding (MOU) was signed between ICMR-RMRC, Gorakhpur and DDU Gorakhpur University to collaborate and enhance academic exchange for cooperation in research and teaching in furtherance of the advancement and dissemination of learning.
- Stake holder's consultation on AES/JE was organized with state health officials to focus research work on regional health issues.
- Construction work of new building of RMRC also progressed well and 60% of the construction which includes the G+4 building with boundary wall and water storage tank has been completed. Inner walls, laboratory work and floor and ceiling work is in progress.
- Institute also conducted an outreach program and participated in India International Science Festival (IISF)-2019 held in Kolkata in November as well as organized Hindi Diwas (September, 2019), Women's Day (March, 2020) and Foundation Day (September, 2019) during the year, where eminent Scientists and Experts participated and delivered lectures.

Fig. 1: Health Awareness Camps in disease endemic villages .

Fig. 2: Distribution of infographics on SWACHCHHATA & HEALTH HYGENE.

Fig. 3: Training program on Biomedical and Health Research Ethics.

SUPPORTING FACILITIES

During the period under report, the National Institute of Epidemiology (NIE) at Chennai and the National Institute of Medical Statistics (NIMS) at New Delhi provided statistical assistance to various ICMR institutes. Health systems research (HSR) and social and behavioural research (SBR) were intensified by starting new projects and with the completion of previous projects. Various new agreements and letters of intent were signed with different national and international organizations. Publication and information Division showcased the achievements of ICMR organization in various significant exhibitions throughout the country. The ISRM Division strived to move the organization towards new goals of technology and digitization.

INTRAMURAL RESEARCH

ICMR - NATIONAL INSTITUTE OF EPIDEMIOLOGY, CHENNAI (ICMR-NIE)

India Hypertension Control Initiative

To achieve and support the GOI goal of 25% relative reduction in raised blood pressure the India Hypertension Control Initiative (erstwhile India Hypertension Management Initiative) was launched in November 2017. The program was developed to address the needs and facilitate achieving the target. In the first year, IHCI covered 26 districts across five states- Punjab, Kerala, Madhya Pradesh, Telangana and Maharashtra.

Overall, by end of 2018, 187,017 patients were registered under IHCI, with nearly 63% of the registrations from the State of Kerala alone. The other four states, Punjab, Telangana, Madhya Pradesh, and Maharashtra, contributed 14%, 9%, 8%, 5% to the total registrations, respectively. Nearly, one third of the enrolled patients achieved blood pressure control, and one third had uncontrolled blood pressure despite treatment, with high variation across states. The blood pressure control was higher in PHCs compared to higher-level facilities (43%, 30%, and 27% in PHC, CHC, and district/sub-district hospital, respectively).

The initiative has resulted in effective coordination and commitment among multiple partners; selection of state-specific hypertension treatment protocols; improvement in drug logistics systems and thereby ensuring the availability of protocol drugs; recognition of the value of professional digital blood pressure devices; provision of effective training; ensuring distribution of 30-day supplies of medications to patients; and measurement of blood pressure control each quarter by establishing robust information system allowing, for the first time, systematic and accurate information on hypertension control rates. Community-based surveillance in ten districts are being carried out for comprehensive assessment of impact of IHCI.

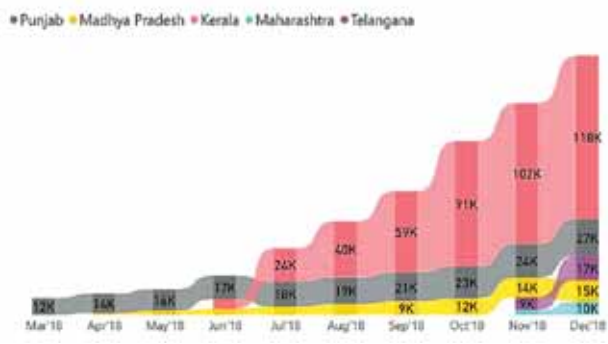


Fig. 1: Registrations of patients with hypertension in the five states by month, India, Jan-Dec 2018.

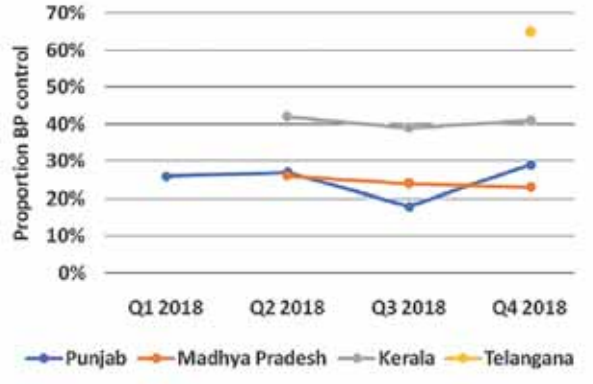


Fig. 2: Blood pressure control among patient cohorts 3-6 months after the registration in four states, India, Jan-Dec, 2018.

Seroprevalence of Chikungunya virus infection, India, 2017: a nationally representative cross sectional serosurvey

Surveillance data from National Vector Borne Disease Control Programme and virology laboratory network suggest continued CHIKV transmission after its 2005 reemergence and highlight the impending risk of outbreaks in different parts of India. Periodic seroprevalence surveys could supplement surveillance information to provide insights on CHIKV circulation, population immunity and understand the risk of future outbreaks. Lack of nationwide data on the seroprevalence of CHIKV led us to estimate age-specific seroprevalence of CHIKV infection in India.

In a nationwide survey among 12,300 individuals aged between 5-45 years residing in 240 clusters (118 rural, 122 urban) from 60 selected districts of 15 Indian states spread across all five geographic regions, the overall prevalence of IgG antibodies against Chikungunya in India was 18.1% (95% confidence interval, 14.2–22.6). The seroprevalence was lowest in northeast (0.3%) and highest in southern (43.1%) region with significant difference between rural (11.5%) and urban (40.2%) areas. The overall seroprevalence of CHIKV among children aged 5–8 years was 9.2%, increasing to 14% among those aged 9–17 years and 21.6% among adults aged between 18–45 years ($p<0.0001$) The difference in seroprevalence between men (18.8%) and women (17.6%) ($P=0.50$) was not statistically significant.

HIV sentinel surveillance among ANC attendees in 7 States

Sentinel surveillance for HIV infection is carried out by NIE since 2006 in 7 States (Tamil Nadu, Andhra Pradesh, Telangana, Karnataka, Kerala, Orissa and Pondicherry) under National AIDS Control Organization It is a periodic ongoing systematic collection, collation, analysis and interpretation of data for (a) tracking of HIV trends (b) understanding the epidemic's characteristics and its level of proliferation through attendees of Antenatal Clinic (ANC at the HIV sentinel surveillance centres as surrogates for general population in the age group of 15-49 years.

In the current (16^{th}) round of surveillance, a total of 1,00,000 blood samples were collected from 250 sites across the 7 states and these data were entered into SIMS, an online data management package. The HIV prevalence and trends are shown in the following table and figure respectively.

Table 1. Prevalence of HIV among ANC clinic attendees: 2018-19.

S.No	State	Total no. of sites	Total No. of Tested	No of HIV Positive	HIV Prevalence (%)
1	Orissa	33	13200	46	0.35
2	Andhra Pradesh	39	15600	47	0.30
3	Telangana	29	11600	27	0.23
4	Karnataka	62	24800	54	0.22
5	Tamil Nadu	71	28400	50	0.18
6	Kerala	14	5600	2	0.04
7	Pondicherry	2	800	0	0
Total		**250**	**100000**	**226**	**0.23**

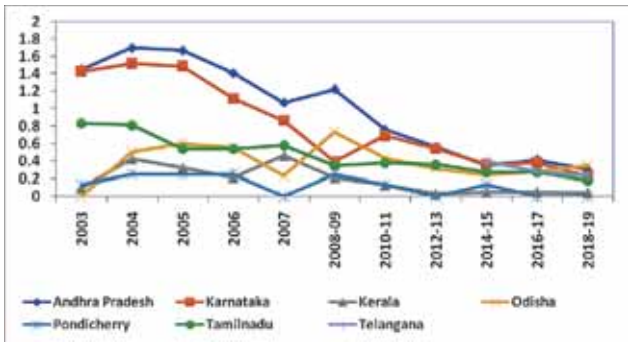


Fig. 3: Prevalence of HIV among ANC clinic attendees: 2003 - 2019.

Congenital Rubella Syndrome Surveillance in India

Rubella infection during pregnancy, especially during the first trimester, can result in miscarriage, fetal death, stillbirth, or a constellation of congenital malformations known as congenital rubella syndrome (CRS). The 11-member states in the WHO Southeast Asia Region committed to eliminate measles and control of rubella/CRS by 2023. Developing and sustaining a case-based surveillance for measles, rubella and CRS is one of the identified strategies towards measles elimination and rubella/CRS control. In view of the introduction of rubella vaccine in India, ICMR has established a facility-based surveillance for CRS in the country. The main aim of this surveillance was to provide baseline estimate of disease burden and also help monitor the impact and progress made by rubella vaccination. The primary objective of the study was to establish a facility-based surveillance for CRS in selected medical colleges/hospitals in different parts of country to monitor the time trends of the disease while monitoring rubella sero-prevalence among the pregnant women over time was the secondary objective.

From every suspected CRS case, information about clinical and epidemiological details were collected in a case-report form. In addition, 1-2 ml blood and one oro-pharyngeal swab was collected and tested for the presence of IgM/IgG antibodies against rubella. For all infants, OP swab was collected from suspected CRS cases and stored at -70^{o}C for detection of rubella virus RNA. Laboratory confirmed CRS patients were followed up periodically for viral excretion. The sera sample and OP swab will be stored 4-8^{0}C until tested.

Twelve surveillance sites enrolled 1416 suspected CRS patients from November 2016 to 15th Oct 2019. Most (45.8%) of the suspected CRS patients were aged between 1-5 months. So far, 219 (15.5%) suspected CRS case-patients were detected on newborn screening, while the remaining were recruited from pediatrics, ophthalmology, cardiology or ENT OPDs of the sentinel sites. The final classification of suspected CRS patients, based on IgM and IgG serology and clinical details is presented in below Figure 5. 47 out of 610 samples (7.7%) tested for O-P swabs so far, were positive by RT PCR.

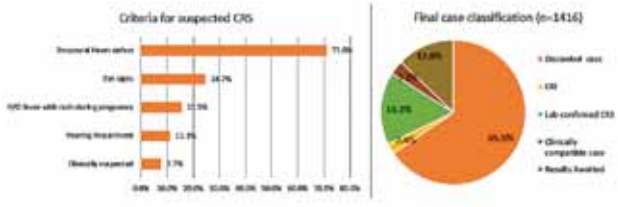


Fig. 4: Snapshot of CRS cases and classification.

Hospital-based sentinel surveillance of S. pneumoniae and other invasive bacterial diseases

The Hospital-based sentinel surveillance of *S. pneumoniae* and other invasive bacterial diseases funded by the MOHFW/UNDP was initiated in December 2016 and phase I was completed in June 2018. This study coincided with the completion of Hib (*Haemophilus influenzae* type B) vaccine coverage throughout the country in early 2017 and the introduction of PCV in mid-2017 under the Universal Immunization Program (UIP). Phase II study started with 6 sites spread across 6 states (including 3 states where PCV is launched). Currently study is ongoing in 14 sites including 4 sites added in Oct 2019. The salient findings and the serotypes of *S.pneumonae* are shown in the following figures.

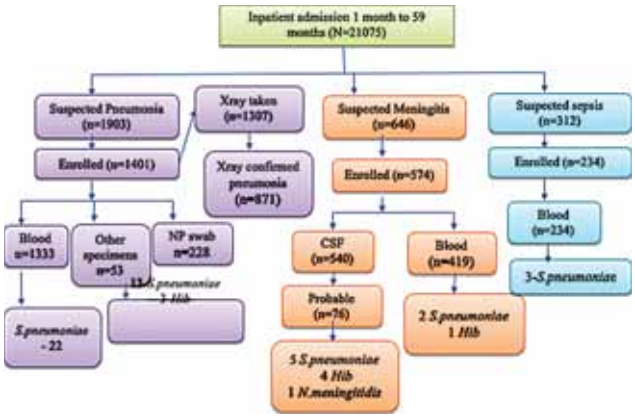


Fig. 5: Pneumonia and IBD surveillance summary.

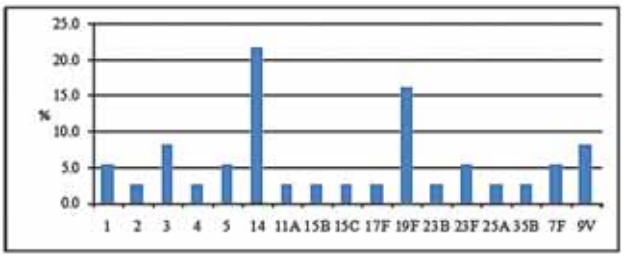


Fig. 6: Streptococcus pneumoniae serotypes distribution between January 2019 and August 2019 (n= 36) across all surveillance sites.

Impact of measles rubella (MR) vaccination campaign on population immunity in India [IMRVI study]

The Government of India (GoI) is committed to eliminate measles and control rubella by 2020. To achieve this goal, population immunity should be at least 90-95% for measles and 80% for rubella. The GoI is currently conducting the largest ever measles and rubella (MR) vaccination campaign to rapidly increase population immunity in children younger than 15 years of age and has begun to provide two doses of MR vaccine through the routine immunization program. Serological surveys are an important tool to directly measure population immunity, identify susceptible populations, and guide immunization strategies to achieve measles elimination and rubella control goals.

Therefore, a study was undertaken to estimate age-specific population immunity to measles and rubella viruses within three age strata (children 9 months to <5 years and 5 to <15 years of age, and women 15 to <50 years of age) in India using serological surveys.

One district in each of the 9 states were selected for the serosurvey based on the geographical location of Model Rural Health Research Units. A two-stage cluster sample survey was conducted in each district. A total of 30 clusters was selected from each district by probability proportional to size linear systematic sampling method. From the selected villages or wards, one Census Enumeration Block (CEB) was selected randomly. Selected CEBs having more than 140 households were further segmented with each segment having atleast 70 households. One segment was randomly selected from the available segments. Within each segment we randomly selected 13 persons from each of the three age groups.

The survey status is summarized in following table.

Table 2: The survey status is summarized in following table.

State	Dates of pre-campaign serosurvey	Dates of post-campaign serosurvey
Punjab	Completed	In progress
Assam	Completed	In progress
Uttar Pradesh	Completed	Completed
Maharashtra	Completed	Completed
Tripura	N/A	Planned
Tamil Nadu	N/A	Planned
Andhra Pradesh/ Telangana	N/A	Planned
Kerala	N/A	Completed

Results of Pre-campaign Sero-Survey

- The population immunity to Rubella was low compared to measles. Population immunity to measles was 71% in UP, 68% in Maharashtra, 63% in Assam and 53% in Punjab. The population immunity to Rubella was 42% in Up, 46% in Maharashtra, 32% in Assam, 39 % in Punjab.

Preliminary findings of Post Campaign Sero surveillance

- The analysis of Maharashtra shows that the Seroprevalence is high for Rubella in the age group between 9 months to 15 years, compared to measles (Rubella 94%, Measles 88%)
- Sero prevalence is similar among women between 15 to less than 50 years for Measles and Rubella (Measles 91%, Rubella 91%)

- Pre/post age-specific seroprevalence curve for Maharashtra is depicted below

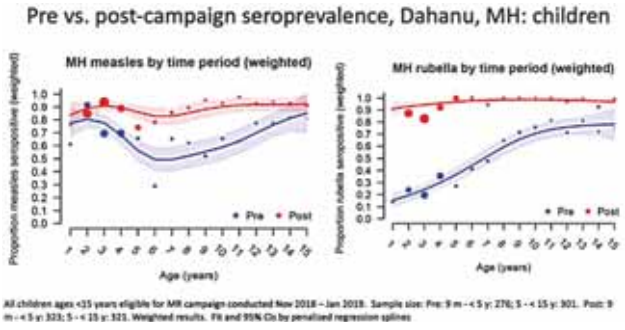


Fig. 7: Pre/post age-specific seroprevalence curve for Maharashtra is depicted.

Integrated Road Traffic Injuries Surveillance (IRIS), Chennai, Tamil Nadu

The centre established road traffic injuries (RTI) surveillance in two hospitals (private and public sector) in Chennai city with the objectives to characterize nature, types, distribution & pattern of RTIs, describe clinical management and outcomes of treatment of hospitalized RTIs and describe factors associated with fatal RTIs. Centre did surveys to describe RTIs at the community level in a sub-urban locality.

Trained nurse investigators used tablet-based data collection tool (designed on the basis of WHO surveillance tool for RTIs) to collect data [Personal identifier, Socio-demographic, Accident identification (Site, weather, climate and light conditions), Road, Vehicle, Person related data, Pre-hospital admission, Ambulance, Clinical Treatment and Outcome details] through a combination of interview of patients or their respondents and abstraction of information from hospital records. The information at the community level was collected from key informants every two-weeks in Ayapakkam cohort.

Centre collected information on 2077 cases from public sector hospital and 140 cases from private sector hospital. The community-based data was available for 255 cases.

The centre developed tools for situational analysis, surveillance in public health facility, surveillance in private health facility and surveillance in community.

Prevalence and intensity of soil transmitted helminths among at-risk cohorts in states of Madhya Pradesh, Rajasthan, Bihar and Tirpura, 2019

Soil-transmitted helminths (STHs) are most common infections worldwide and commonly affect poor and most deprived communities. It is estimated that 220.6 million children in India need deworming to avert the negative consequences of STH infections. The team conducted a cross-sectional study among primary school children studying in 56 primary schools to estimate the prevalence and intensity of STH among at-risk groups (age from 1 to 19 years) to guide the school-based deworming program in states of Madhya Pradesh, Rajasthan, Bihar and Tirpura. Information about socio-demographic details, defecation and hand-hygiene practices and stool samples were collected from at-risk groups. Stool samples were examined using Kato-Katz method.

During June-August 2019, a total of 3169 (Madhya Pradesh) and 3027 (Rajasthan) school children and in Tirpuraa total of 2074 Pre-School aged children, School aged children and adolescents provided stool samples and completed the questionnaire. The overall prevalence of any STH was 3.25% (95% CI: 2.04-5.15) in Madhya Pradesh and 0.66% (95% CI: 0.26-1.67) in Rajasthan and in Tirpura was 1.88% (95% CI: 0.65-5.30) adjusted for clustering. Hookworm was the most prevalent STH in states of Madhya Pradesh and Rajasthan, with a prevalence of 2.59% (95% CI: 1.59-4.17) and 0.40% (95% CI: 0.17-0.92) respectively. And in Tirpura, Ascaris was the most prevalent STH with a prevalence of 1.30% (95% CI: 0.53-3.18). Majority of the STH infection were of low intensity in all the three States.

Indian Network of Population-Based Surveillance Platform for Influenza and Other Respiratory Viruses among Elderly (INSPIRE)

Older adults (aged 60 years or above) account for 8% of total population in India (2011). This proportion is projected to reach 19% by the year

2050. Influenza associated ARI is an important cause for high mortality and morbidity among elderly. However, there is paucity of literature related to this problem. The available reports are from facility based or limited to small population, which might underestimate the true buren. Hence, it is important to estimate the burden of infections with influenza and other respiratory viruses in this vulnerable age group through a population-based cohort study is necessary. ICMR-NIE is conducting a multi-centric study led by AIIMS, New Delhi with the following objectives.

i. To estimate the incidence of influenza- and RSV- associated acute respiratory infections (both upper and lower), outpatient clinic visits and hospitalizations among a community cohort of older adults (>60 years)

ii. To describe the risk factors for influenza- and RSV-associated ALRI, hospitalization, ICU admission and mortality among older adults

iii. To estimate the annual cost of influenza associated acute respiratory infections among older adults in India from the societal perspective

iv. To estimate the effect of influenza and RSV infection on frailty and cognition among a community dwelling cohort of older adults

The households in the study area were mapped by the field staff by house to house visit. The households with the elderly persons aged 60 years and above were identified. We obtained written informed consent from the potential participants before enrollment.

The staff nurses undertake weekly ARI surveillance using standardized tools and collect nasal/throat swabs from the persons suffering from ARI. We collect data using Tablet computers with pre-structured questionnaire designed and programmed in Open Data Kit 1 (ODK 1). In phase II, in addition to incidence of ARI and we collect data on economic burden due to ARI, burden of the illness due to hospitalizations, effect of ARI frailty index and risk factor, are also being collected. The swab samples are being tested as per the CDC protocol in NIE Laboratory. For external QC we send 5% samples to AIIMS, New Delhi.

The centre recruited 1562 elderly population. We started ARI surveillance in August 2018. Till July 2019, 219 participants were lost to follow up due to various reasons. We enrolled 184 participants in August 2019 and currently 1527 participants are under surveillance. The incidence of ARI was 121.9 (115.5-128.7) per 100 person years and influenza associated ARI incidence was 5.3 (3.9-6.7) per 100 person years.

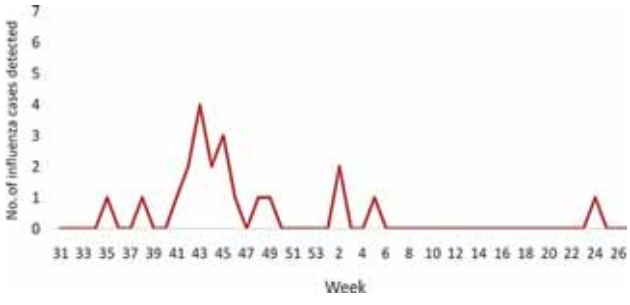


Fig. 8: Seasonality of influenza transmission.

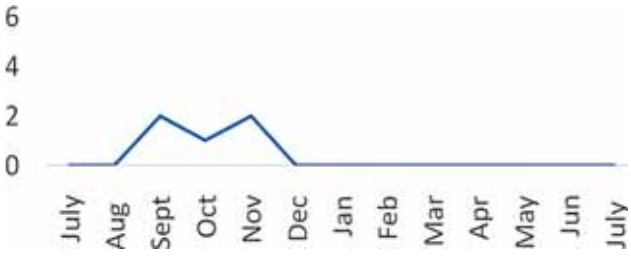


Fig. 9: Seasonality of RSV transmission.

Rotavirus Vaccine Impact Assessment Study

Rotavirus is the most common cause of severe, dehydrating acute gastroenteritis (AGE) among children under-five years of age in India, causing an estimate 11.37 million illnesses, 3.27 million outpatient visits and 872,000 inpatient admissions each year and resulting in Rs 10.37 billion each year in direct costs. An indigenous Rotavirus Vaccine ROTAVAC, based on a neonatal rotavirus strain (116E), recently completed a successful Phase III clinical trial in which 3 vaccine doses given at 6, 10, 14 weeks of age were 56% effective against severe rotavirus AGE. ROTAVAC has been licensed in India and in 2014, the Government of India recommended inclusion of rotavirus vaccine into the Universal Immunization Programme (UIP) of India. Rollout of ROTAVAC, in a phased manner, from 2016.

The project was designed with the following objectives.

A. Acute gastroenteritis surveillance

1. To identify cases of rotavirus among children less than five years of age hospitalized for AGE and to determine the circulating rotavirus genotypes pre- and post-introduction of ROTAVAC using sentinel hospital surveillance sites
2. To measure changes in attendance rates of all-cause AGE and severity of presentations at the sentinel surveillance sites pre- and post-introduction of ROTAVAC
3. To determine the effectiveness of a completed series of ROTAVAC against laboratory confirmed severe, rotavirus AGE under conditions of routine use in India, using existing sentinel hospital surveillance sites and case-control methods. Additional secondary objectives of the case-control study include:

   – Determination of vaccine effectiveness against specific rotavirus genotypes

   – Determination of vaccine effectiveness of a partial series of ROTAVAC

   – Determination of potential waning of ROTAVAC effectiveness during the study period

4. To implement surveillance for intussusception in a network of pediatric hospitals in India

B. Intussusception surveillance

Primary

1. To describe the epidemiology (e.g., age distribution and seasonal patterns) of intussusception hospitalizations among children <2 years of age.

Secondary

2. To determine the proportion of intussusception-associated hospitalizations that requires surgical treatment.
3. To determine the proportion of intussusception-associated hospitalizations that result in death.
4. To describe potential infectious etiologies of intussusception by assessing for infectious pathogens in stool samples from intussusception cases and matched controls without intussusception.

The study was a multi-centric vaccine impact surveillance project involving sentinel sites which had in-patient facilities submitting clinical data and samples for rotavirus testing and characterization. All children less than 5 years of age admitted with acute diarrhea were enrolled after obtaining informed and written consent from parent/ guardian. Clinical information and a stool specimen were tested for presence of rotavirus by ELISA and characterized by PCR. For intussusception surveillance, intussusception cases and controls (non-intussusception, non-infectious hospitalized patients) with age, gender and location matched were enrolled. Surveillance staff completed a control case report form, including limited information on demographics, diagnosis, and discharge date as well as collected stool specimen.

During August 2017 - September 2019, 947 eligible cases of children under 5 years of age with AGE were enrolled. Stool samples from 796 cases were available for testing and 27.1% were positive for rotavirus. Highest positivity (35.6%) was observed among children between 12 to 23 months followed by 24-35 months (34.9%) and 06-11 months (32.5%). Rotavirus positivity was higher during cooler months and decreased positivity was seen during 2019 in comparison to the same period between 2017 and 2018. Analysis of distribution of various rotavirus genotypes showed the preponderance of G3P[8] strains (72.3%) followed by G1P[8] strains (9.3%). None of the positive cases had the vaccine strain type i.e. G9P[11]. One hundred and twelve intussusception cases and 57 controls were enrolled during the reporting period. Stool specimen from only one intussusception case was positive for rotavirus (G3P[8]).

Outbreak of Acute encephalopathy syndrome, Muzaffarpur, Bihar, 2019

Outbreaks of acute neurologic illness affecting young children and associated with high case-fatality rates had been reported in the Muzaffarpur district of Bihar state in India since 1995. A large outbreak of acute encephalopathy occurred in Muzaffarpur in 2019. We investigated the outbreak to identify risk factors associated with the illness

Centre conducted an unmatched case control study. A child aged 2-14 years, hospitalized either at Sri Krishna Medical College Hospital (SKMCH) or KrishnadeviDeviprasadKejriwal Maternity Hospital (KDKMH),Muzzafarpur with new-onset seizures or altered sensorium during 15-25 June was considered as case. From each case village, we selected up to four controls – two household and two community controls. Using a standardized questionnaire, trained investigators interviewed cases and controls or their care takers (preferably mothers) to collect information about Socio-demographic-economic characteristics, illness profile, health seeking, risk factors, preventive and promotive factors. Case-patients were interviewed in hospital, while controls were interviewed in their households.

Centre included 61 case-patients and 239 (101 household, 138 community) controls in the study. The mean age of cases was lower than controls (5 versus 6.1 years, p=0.010); 59.7 % cases and 48.6 % controls were aged <=5 years. On univariate analysis, case patients were more likely to be young female children aged less than 5 years. A higher proportion of cases were malnourished and consumed litchi in last one week before onset of illness. When compared with controls, children with AES were more likely to have missed their night meal and slept in empty stomach (Table 1). On multivariable analysis, young female children [adjusted OR (AOR): 2.3, 95%CI 1.2–4.5] aged less than five years [adjusted OR (AOR): 2.6, 95% CI: 1.1–5.8] and night meal (AOR: 4.9, 95% CI: 2.3 –10.6) had higher odds of developing AES.

Table 3: Outbreak of Acute encephalopathy syndrome, Muzaffarpur, Bihar, 2019.

Risk factors	Household controls OR (95% CI)	Community Controls OR (95% CI)	All controls OR (95% CI)
Age <=5 y	2.6 (1.4 - 5.0)	1.4 (0.7 -2.5)	1.8 (1.0 -3.1)
Female sex	1.8 (0.9 - 3.5)	2.0 (1.1 -3.7)	1.9 (1.1 -3.4)
Ate litchi in 24 h	0.9 (0.5 -1.8)	1.1 (0.6-2.1)	1.1 (0.8 -1.4)
Ate litchi in previous 7 days	1.3 (0.6 -2.8)	3.3 (1.6 -6.7)	2.3 (1.2 -4.5)
Skipped evening meal	4.1 (2.0 -8.3)	4.3 (2.2 -8.3)	4.1 (2.2 -7.5)
BMI for Age	2.2 (0.9 -5.1)	2.7 (1.2 -6.0)	2.5 (1.1 -5.4)

In Muzaffarpur and adjoining districts, young female children with malnourishment, consuming litchi during the season and sleeping in empty stomach were associated with higher risk of developing AES among children. Of these risk factors skipping night meal or sleeping in empty stomach was the commonest exposure.

NATIONAL INSTITUTE OF MEDICAL STATISTICS, NEW DELHI (ICMR-NIMS)

Clinical Trial Registry-India

CTRI is an online portal for registering Clinical Trials conducted in India and surrounding countries without their own trial registry. CTRI is coping with the voluminous amount of trials being submitted in the era of COVID-19 pandemic by working 24 X 7. It has implemented the WHO recommendation of IPD share on its portal. The CTRI scientists have also been providing technical support to many other ICMR projects.

Estimation of HIV burden in India and its states, data management and analysis of HIV Sentinel Surveillance (HSS) 2019-20:

ICMR-NIMS is the apex body for HIV estimations in India and has been generating HIV estimates on key indicators, with NACO (National AIDS Control Organization), Government of India since 2003. The two major activities during 2019-20 were:

(i) Recognizing the need for generating granular information on the HIV epidemic piloting of district level PLHIV estimation methodwas conducted in Gujarat, Maharashtra, Mizoram, Tamil Nadu, and UP.Three of them were "Spectrum" software based and the other two were based on excel/ spreadsheet. Based on

UNAIDS criteria checklist, the 'sub-epidemic creation in State model' received the highest score and rank, it was selected as the method for district level HIV burden estimations under NACP. This method was validated and approved by the Technical Resource Group on HIV Surveillance and Estimations.

(ii) Technical report of HIV Estimation 2019 was prepared and submitted to NACO for release and dissemination. The HIV Estimations 2019 process is given below:

Fig. 10: The HIV Estimations 2019 process.

National Data Quality Forum

National Data Quality Forum (NDQF) was launched on 24-7-2019 by Prof V K Paul, member of NITI Aayog, in the presence of Secretary DHR and DG ICMR. The objective of the project is to improve the quality of India's health surveys and administrative data, implemented by various stakeholders in the country. During the launch of NDQF Awards of Data Q-thon, an initiative to crowd source insights on the quality of data (survey and program data) that are used to design public health programs and policies was given. The event was attended by stakeholders as well data generators and consumers.

Determination of cut off and correlates of delay in seeking treatment of febrile illness

The study was carried out using the data of previous study on health seeking behaviour.The findings of the study present the optimum cut off of two days delay for seeking treatment of febrile illness especially in malaria endemic areas.

Spatio-Temporal Variations in Malnutrition among Children of Tribal and Non- Tribal Population of India

Level & Trends from various rounds of NFHS (1992-2016). The broad aim of this study is to develop an online geo-referenced online database on malnutrition among children comparing Tribal and Non-tribal populations for each state and district of India is prepared for reference to policy makers, programmers and planners. The specific objectives of the study would be i) To develop an online geo-referenced database with state level and district level indicators of under-nutrition and its correlates separately for tribal and non-tribal populations ii) To compare the spatio-temporal variations, spatial variations using NFHS 4 data and temporal variations using NFHS-2, 3 and 4 state level indicators. iii)To provide district-wise analytical information for facilitating in developing a district plan of action for meeting the SDG on malnutrition (Goal 2.2).

"Strengthen Research in Ayurveda by utilizing the CTRI Platform and Impart Capacity Building Program in Research Methodology" under the program Leveraging traditional Medicine of ICMR. This project aims at developing customized data set items for registering Ayurveda studies.

Evaluation of Impact of Antiretroviral Therapy under National AIDS Control Programme in India [The ART Impact Evaluation- India Study (ARTIE-India)-Northern Region

The objectives of the study are to (i) assess the impact of ART programme on mortality, morbidity, including opportunistic infections profile, hospitalization rates and incidence of TB and quality of life in PLHIV in NACO supported ART Centres in India at National and Regional level; and (ii) assess the implementation of the ART programme with reference to the clinical and programmatic goals of ART program under NACP.The secondary data extraction and both quantitative and qualitative primary data collection, data cleaning, data analysis, and internal review meeting by core team were completed. Draft summary report was prepared and submitted for review to NACO. The final draft report is under process.

Development and pilot testing of intervention strategies for smokeless tobacco and areca nut cessation among tribal women in Manipur

The overall objective is to develop culturally appropriate cessation strategies for smokeless tobacco and areca nut use among tribal women users in Manipur. Primary data collection for the study has been initiated and is in progress. Secondary data analysis of Global Tobacco Adult Survey-1&2 was conducted to understand patterns and predictors of smokeless tobacco use among women in the age group of 18-49 years. Multivariate logistic regression revealed that age, education, wealth quintile, region, were significant predictors of current daily SLT use among women. Analysis of National Family Health Survey-4 is in progress to understand associations of SLT use with health outcomes.

Investigating foetal and maternal factors for perinatal mortality in India- A systematic review and Meta-Analysis

The aim of this systematic review is to identify maternal and fetal factors predicting perinatalmortality in India which will enable us to generate strong evidence and streamline future thrust areas for research. The first level screening of articles has been completed and full text review is under progress.

Socioeconomic Inequality in Households Financial Burden Associated with Non-Communicable Diseases in India

The objective wasto understand the Socioeconomic inequality in out-of-pocket health Expenditure, Catastrophic Health Expenditure, hardship financing and poverty due to health care expenditure associated with non-communicable diseases in India.One in every six household had faced catastrophic health expenditure. More than half of the households faced hardship health financing among those who were taking treatment in private hospitals.

Gain in life expectancy by age after elimination of death due to specific cause in selected states of India using MCCD data

The study aims to estimate the gain in life expectancy by age after partial and complete elimination of ten leading causes of deaths viz., certain infectious and parasitic diseases (A00-A99); neoplasms (C00-D48); diseases of blood & blood forming organs & certain disorders involving the immune mechanism (D50-D89); endocrine, nutritional and metabolic diseases (E00-E89); diseases of the nervous system (G00-G98); diseases of the circulatory system (I00-I99); diseases of the respiratory system (J00-J98); diseases of the digestive system (K00-K92); diseases of the genitourinary system (N00-N99); and injury, poisoning and certain other consequences of external causes (S00-T98) in selected states of India by constructing multiple decrement life tables and cause-eliminated life tables.The study will analyse the data of Medical Certification of Causes of Death (MCCD) for the year 2017 available under the domain of the Registrar General of India (RGI).

Quality of Care in Maternal and Newborn Health in Rural India

A Multilevel Modelling:This study aims to examine the quality of antenatal care (ANC), safe delivery, and post-natal care among the Indian women and to ascertain the association between quality of ANC, safe delivery, and post-natal care with early neonatal mortality in India. Findings revealed that about 18% of eligible women were devoid of any ANC while more than half (about 59%) received ANC services that did not match the quality mandated by the WHO and Government of India. It was observed that postnatal care delivered by unskilled healthcare personnel were more efficient in saving precious neonatal lives within 24 hours of birth is necessary, especially among the high focus states of the country. Regarding the continuum of care encompassing all the components of maternal and newborn care (Antenatal, Delivery and Postnatal care), major dropouts were noticed in the postnatal care utilized by the newborns while the almost 90% of all women accessing antenatal care utilized quality delivery care services.

Public Health Importance

- Clinical trials registry India, a flagship programme of ICMR is hosted at the ICMR-NIMS and running successfully for the last 13

years and catering to the clinical research. In India and neighbouring countries where there is no trial registry of their own. At present more than 27000 trials are registered and maintained in CTRI. Recently a separate data set items have been developed and finalised for registering Ayurveda studies.

- National Data Quality Forum has been established at ICMR-NIMS to create an ecosystem to ensure data quality. A National Consultation was conducted with stakeholders.
- HIV 2019 estimates have been generated and submitted to NACO. The district level HIV estimates methodology was piloted in five states of India and the report has been submitted to NACO.
- The study on Improvement in the Utilization of RCH services through Male Participation among the Saharia Tribes in Gwalior District, Madhya Pradesh was completed in July 2018, and based on the recommendation of the Project Review Committee two workshops to disseminate the findings of the study were conducted in Bhopal and Gwalior, MP with state health authorities.
- Study on Malaria elimination and estimation of disease burden in Punjab has been completed and estimation of malaria burden has been provided. Though the state has taken several measures to eliminate malaria, the study reveals the presence of malaria especially in some of the areas of Punjab. The detailed report has been submitted to Indian Council of Medical Research, New Delhi.
- The draft report of Anti-retroviral therapy (ART) programme Impact Evaluation (ART-IE) study has been submitted to NACO.
- Developed a Behaviour Change Communication Model for improving the male participation in maternal and child health care services for the Saharia Tribes in Madhya Pradesh that is ready for implementation.
- ICMR-NIMS has generated national and state level disease burden estimates for 2017 in its report submitted to the MoHFW.
- The detailed final report of the National NCD monitoring survey of India - in collaboration with ICMR-NCDIRhas been presented and submitted to the MoHFW.
- The final report of the study on Comparing strategies for Cause of Death Study has been submitted to the funding agency.
- The Institute conducted a workshop on Multilevel modelling and provided statistical support to various PhD, MD/MS and MSc students as part of its academic activitiesSection II
- Running Clinical Trials Registry India successfully for the last 13 year.
- Engaged in estimation of HIV burden estimates for India and states/UTs for the last 17 years, since 2003.
- Physician certified verbal autopsy found more accurate than Computer certified methods in the Cause of death study
- WHO 2016 verbal autopsy tool was field tested in both urban and rural areas.
- Disease burden estimates generated for India and its states for 2017 using WHO method.
- Studies in Santhal and Saharia tribes threw light on health utilization and improving male involvement in health seeking behaviour

Fig. 11: National Data Quality Forum (NDQF) was launched on 24-7-2019 by Prof V K Paul, member of NITI Aayog, in the presence of Secretary DHR and DG ICMR.

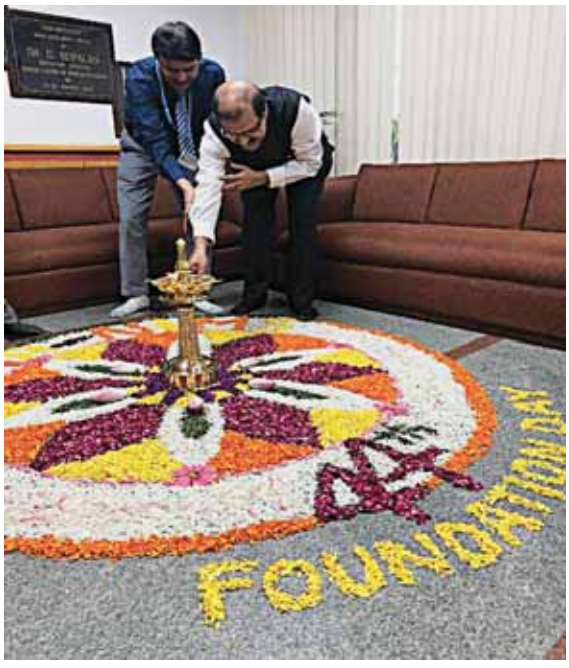


Fig. 12: Celebration of Foundation Day.

EXTRAMURAL RESEARCH

SOCIO-BEHAVIOURAL & HEALTH SYSTEMS RESEARCH (SBHSR) DIVISION

During this year, the Socio-Behavioural & Health Systems Research (SBHSR) Division has initiated studies on health care access to scheduled tribe population. Also, projects towards understanding and strengthening of health systems in the country, as well as on understanding the social and behavioural determinants of health have been funded. Some of these projects have been concluded during this year. Of them, two national task force projects on road traffic injuries are important. During the current year, the Division has initiated three national task force projects on health care issues among scheduled tribe population. Following is the description of the projects funded during the current year.

Studies on healthcare access to the tribal population

The national task force projects that have been initiated in the current year addressed three important health issues among the tribal population. The first project is to develop effective intervention model for the sickle cell disease patients in tribal areas for accessing government health care system and capacity building in terms of knowledge, skill and training of the health care workers at different levels of the health system for prevention and management of sickle cell disease. Several community-related and health-system related issues are studies during the formative phase and based on these issues, intervention is being developed and implemented. This study is implemented in 6 tribal districts. The second study is to develop implementation strategies for strengthening selected non-communicable diseases (hypertension, diabetes and chronic obstructive pulmonary disease (COPD)) related continuum of care under National Programme for Prevention & Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke (NPCDCS) among scheduled tribe population. This implementation research is going on in six tribal districts. The third implementation research study addresses improving the health care access and quality in the context of achieving Universal Health Coverage (UHC) among scheduled tribes in 9 tribal districts in the country.

In addition to the above three national task force projects, the Division has funded fourteen adhoc projects, which addressed different health and health care issues of the tribes. An action research project from Andhra Pradesh is developing models for effective preventive and curative care by mobilizing the ethnomedical practitioners in Savara tribal community for partnering with public health functionaries. It advocated a collaborative approach to healthcare for the tribal people, which is culture-sensitive and emotionally relatable to them because of the presence of their local healers in the care-matrix. Another study examined the health-seeking behaviours and issues related to healthcare service access and its utilization by tribal elderly in Kerala. It identified deterring factors to the rate of healthcare access and service utilization by tribal elderly which would enable policymakers to strategize optimal healthcare system responsiveness. Another ethnographic study aimed to describe the preventive and treatment-seeking behaviour and practices concerning malaria in tribal population of Chhattisgarh.

Prevalence of urinary tract infections (UTI) among tribal women of Tamil Nadu was studied. Preventive measures, awareness towards UTI and practice of screening bacterial infection with the use of foldscope among tribal women were implemented. This study helped to understand the menstrual hygiene and knowledge about UTI among tribal women. Another study reported the awareness, health-seeking behaviour and influencing factors, and social stigma related to two mycobacterium diseases (tuberculosis and leprosy) among the tribal population in relatively inaccessible areas of Pathanamthitta and Idukki districts of Kerala. From some tribal areas of Tamil Nadu, the prevalence of primary dysmenorrhea and effect of a combined exercise training program on associated menstrual symptoms among school-going girls is reported.

A model programme (Model for Oral Cancer Eradication) for prevention, screening and treatment of oral pre-cancer and cancer is implemented among Narikurava tribal population of Puducherry. This study reported the prevalence of pre-cancerous and cancerous lesions and tested a model for screening and prevention. Another study from Odisha is being implemented an accessible model for oral potentially malignant disorder screening in the tribal settings. A study among North-East tribes of Assam and Mizoram documented various cardio-metabolic related risk factors including hypertension, elevated fasting blood glucose, obesity and metabolic syndrome with the help of artificial intelligence techniques, mainly machine learning tools such as classification, clustering and prediction models, etc. It will further conduct health awareness campaigns on diabetes and cardio-metabolic disease among the tribal population of the north-east region.

A dairy-based intervention is being developed among the tribal population of Uttarakhand by ICAR's National Dairy Research Institute. The study is aimed to improve the health-seeking behaviour of the people by improving the health and livelihood of the tribal population through a dairy-based intervention. Another study from Delhi explores the healthcare access and profile of health and nutrition status of the migrant tribal population of Delhi and the challenges in the health care access. A study from Maharashtra used intersectionality theory to understand variations and similarities in responses across and within tribal communities. It is to explore the political, social, economic and cultural determinants of health inequalities experienced by the tribal communities. Also, it identified the barriers and facilitators to acceptability and uptake of health services. Another study from Maharashtra focused on improving access to cancer screening with the existing government health system and identified the challenges for the same. This study is being implemented the screening of common cancers and NCDs among women in a tribal block involving the state health system and the community.

Health systems research on road traffic injuries (RTIs)

The Division has supported two national task force projects on road traffic injuries and they have been concluded during the current year. The first study has established an electronic-based comprehensive and integrated RTI surveillance system in five places in India, viz., Chennai, Chittoor, Tehri-Garhwal, Delhi and Jaipur. The study demonstrated the feasibility of establishing the system within the public health system, and epidemiological data has been collected through this system. The second project has developed a structured evidence-based intervention model for safety, efficacy and quality of post-crash pre-hospital and in-hospital trauma care services to improve the outcome in RTI victims. This study was conducted in five cities, viz., Bengaluru, Delhi, Karamsad, Lucknow and Thrissur. An Android-based trauma registry is used to collect pre and post-intervention trauma-related data. The impact of the intervention in terms of outcome in RTI patients is being analysed. Besides, the Division has supported some adhoc projects, specifically on health systems responsiveness on the growing burden of the RTIs.

Other health systems research and socio-behavioural research studies

A cultural epidemiological study has been initiated in Satara and Palghar districts of Maharashtra for generating evidence for strengthening

implementation of National Collaborative Framework for Care and Control of Tuberculosis-Diabetes Comorbidity. It reviewed the programme performance indicators for ascertaining progress made by Revised National Tuberculosis Control Programme (RNTCP) and National Programme for Prevention and Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke (NPCDCS) concerning joint TB-Diabetes collaborative activities as envisaged by the National Framework. The study would provide important insights into the ground-zero status of TB, diabetes comorbidity care, control and management issues from patients' as well as providers' point of view. Influence of demographic, clinical, genetic and pattern of management in maintaining long term abstinence among patients of alcohol use disorders who received treatment from de-addiction centres in Thrissur district, Kerala was studied. This study evaluated the pattern of management in different de-addiction centres and find out the influence of treatment pattern on the outcome. It further studying the status of markers indicative of acute or chronic alcohol consumption (state markers) as well as markers of genetic disposition for alcohol dependence (trait markers) among the alcohol users.

Perspectives of people, physicians and pharmacists on sociocultural and environmental drivers of antibiotic resistance was studied in Karnataka. This study is being developed an innovative provider-based, individual-verified approach to estimate the burden of antimicrobial resistance in rural India. The study further understands pharmacists' perspective in dispensing antibiotics and physician perspectives on antibiotic use and misuse. Structure, staffing and factors affecting infection control nurses were studied in Karnataka. It explored the existing structure and staffing pattern of the infection control department and to identify factors affecting infection control practices. Menstrual hygiene practices of adolescent girls with intellectual disability are studied in a study from Chandigarh. Randomized controlled crossover study on mindfulness training to improve resilience in Indian college students is progressing in IIT-Kharagpur. It developed and tested a mindfulness training intervention for attention and emotional regulation.

A qualitative study on the determinants of acceptance and hesitancy towards Japanese encephalitis vaccines in Alappuzha district is underway. This study provides the response, perceptions and views of the community including their trust towards vaccine about the reasons behind the vaccine acceptance and or the hesitancy. The study also explores how peer-to-peer communication influence vaccine hesitancy. A study on life habits, daytime sleepiness and chronotypes on sleep disturbance and daily and seasonal sleep patterns among school students is going on in Aizawl, Mizoram. This explores the factors associated with sleep duration and sleep quality. Also, it understands that whether a life habit factors such as viewing an electronic display at night, irregularity of dinner time, frequent caffeine intake at night, sunlight exposure in the bedroom in the morning, and the brightness of the room in the night affects sleep and sleep-related factors. A prospective cohort study to understand the humanistic and economic burden of rheumatoid arthritis is studied in Puducherry. It assesses the costs from the societal perspective using a bottom-up approach.

Obstructive sleep apnea among commercial vehicle drivers and it correlates with road traffic accident are studied in Delhi. This study determines the prevalence and risk factor for obstructive sleep apnea in commercial vehicle drivers. This study is to develop strategies to increase awareness of the problem and develop an action plan for the management of obstructive sleep apnea. An educational intervention study to bring awareness of head injury while driving among the patients with epilepsy is underway in Delhi. This study assessed the awareness in patients with epilepsy and their caregivers about driving prohibitions as per the motor vehicle act, 1938. Patients with epilepsy are to be educated through a multipronged educational intervention and to evaluate the impact

of the intervention. Cognitive and psycho-social intervention for persons with dementia in Rural India is underway in Chennai. This study identified resources for dementia care including social support systems in the rural community. The feasibility of delivering a comprehensive intervention model including cognitive stimulation therapy is being studied.

Impact of migration on the psycho-social and economic well-being of elderly pandit migrants is being studied from selected north Indian cities. Health-risk behaviours among adolescents, particularly the role of difficulties in emotion regulation, parenting style and personality characteristics are studied from IIT-Ropar. A case-control study design is being used in which initially assessment of adolescents for their indulgence into health risk behaviours would be done and then the characteristic attributes of those high and low on specific behaviours would also be identified. Another study from Delhi assessed and identified factors affecting the availability, accessibility, acceptability and quality (AAAQ) of burns care in secondary and tertiary health care facilities. The co-designing approach to develop a pathway of care with improved availability, accessibility, acceptability and quality of burns care and rehabilitation is innovative and would foster learnings for using similar approached in other conditions requiring prolonged rehabilitation. Another study assessed the economic burden of childhood injuries in different socio-cultural settings in Tamil Nadu and developed a cost-effective intervention model for the prevention of childhood injuries.

Evaluation of the effect of three selected Indian ragas, namely, Hindel, Puriya and Todi on electrophysiological parameters and salivary stress markers was evaluated through a randomized control trial in Bengaluru, Karnataka. The effects on electroencephalography and the relaxation effect of these ragas in blood pressure, salivary stress markers and stress are studied. The study demonstrates that music can be prescribed as an effective adjuvant in the treatment of hypertension along with other lifestyle modifications. A study is conducted in Delhi to assess the spiritual problems and concerns faced by Indian palliative care patients and to develop the guidelines for treatment. This study integrated the specificity of Indian society, culture, and spirituality. Another study analysed the constructed notions of employability of women TB patient workers across various work spheres and examined its implications for their employability. Financial support was one of the major unmet needs of working patients. The study also endorsed that occupational safety and health concerns are often less prioritized in informal work arrangements. Financial support was needed the most in the symptomatic period, during diagnosis and at the beginning of treatment due to employment loss and earning loss due to TB.

A cross-sectional descriptive study was conducted to assess the health literacy and its attributes among the adult population of Madhya Pradesh. The study concluded that a health information system should develop the contents based on health literacy levels of end-users. A study was conducted for the development and validation of a prototype of a web/mobile app-based positive psychological intervention for adolescents. With an increasing number of mental health cases in India, such e-intervention would be beneficial and cost-effective. Efficacy and effectiveness of Information, Education and Communication (IEC) activities for health awareness and promotion among women was assessed in Rajasthan. Respondents acknowledged the sufficient supply of the materials, though mostly in the form of posters and pamphlets, which were reported to be futile. This study suggested the failure of reach of IEC media like radio, posters and hoardings that are heavily employed in promotional activities for health. Another study evaluated the IEC strategies employed and health education materials produced by different national programmes from the provider's and user's perspective. Though IEC strategies and interventions have contributed to change in knowledge, behaviour and attitude of patients as well as the general population to

some extent, it has been reported that there is still a wide gap and lack of awareness about their causes, available diagnosis and treatment options. A cross-sectional study assessed the impact of health education and awareness of the use of health care systems with the involvement of stakeholders in reducing neonatal mortality rate in the migrant population living in Hyderabad. Majority of the mothers were aware of the Janani Suraksha Yojana programme and the majority of them utilized it. A community-based intervention from Delhi demonstrated the effectiveness of social and behaviour change communication (SBCC) strategy in the prevention and control of dengue in slums and slum-like pockets. Another study from Gujarat designed and tested a behaviour change strategy to improve uptake of services for severely malnourished children through the Integrated Child Development Services (ICDS) scheme.

A study from Chandigarh developed and implemented an innovative multi-level psychosocial intervention for sexually-active men sex with men (MSM) to promote periodic HIV testing (as per the national guidelines). It has the potential to be scaled up in other parts of India and may contribute to a reduction in HIV transmission among MSM. Another study captured the morbidity load of a population, based on the type of illnesses prevalent at a given point of time, the treatment-seeking behaviour for those illnesses by levels of care and the cost involved in the treatment and the pattern of referral followed. It is to estimate the health care facility required to cater to the curative health care needs of the population across various levels. A study assessed the utilization and issues related to the effective delivery of Government's health care services, schemes and programmes for marginalized groups in Maharashtra. This study found out key problems and issues related to health schemes that are meant for marginalized groups. A study from Tamil Nadu designed and evaluated the prototype health information system for rural women.

Impact analyses of the structural factors influencing effective service delivery and utilization of maternal and child health services were conducted in Kashmir. A comparative analysis of inequality in primary health care system was conducted in Kerala and Assam. It identified the reasons for inequality and inequity in health care seeking. The impact of the involvement of self-help groups in improving reproductive health-seeking behaviour and service utilization by tribal women was assessed in the Nasik district of Maharashtra. This model is successful and can be scaled-up in other tribal areas. Quasi-experimental research with pre and post without a control group was conducted to promote psychosocial competencies among rural Government school children in Karnataka. The outcome of the project would help in integrating psychosocial competency related activities in schools. A study assessed the internal consistency and content validity of comprehensive healthy eating and living index by adapting healthy eating index and combining with lifestyle indices for adolescents in the Indian context. Economic analysis of health-seeking behaviour of Hansen's disease (leprosy) was carried out in Tamil Nadu.

A School Based Health Correlates through Gandhian Perspective of health

To commemorate 150th birth anniversary of Mahatma Gandhi Indian Council of Medical Research (ICMR) had launched Mission SHAKTTI (School based Health Awareness, Knowledge Test and Training Initiative) in 2019. A total of 36 schools of different zones, i.e. North, South, East and West Delhi participated in this programme. The selection of schools was done keeping well representation of different location zones and affiliation of authorise body (Govt., Public and Co-Ed.). Children studying in class 8th onwards were part of the said programme. The programme was followed by a pre-assessment of basic about health perspective in regards to Gandhian philosophy on health. A talk (visual presentation) was shown to school children through explanatory mode and subsequently, a quiz session on Gandhian health philosophy was also conducted to create awareness among school children. A short questionnaire was administered to the students in their school. An attempt was made to check students' knowledge about Gandhiji advocacy on health.

Public Health Importance

During this year, the Socio-Behavioural & Health Systems Research (SBHSR) Division has initiated studies on health care access to scheduled tribe population. Also, projects towards understanding and strengthening of health systems in the country, as well as on understanding the social and behavioural determinants of health have been funded. These projects focussed on understanding the issues related to the access to the health care services, various health promotion and diseases control programmes. Some projects are intervention studies aimed to develop and test interventions for control and manage various health problems. Two national task force projects on road traffic injuries have concluded. Following is the description of the projects funded during the current year.

Studies on healthcare access to the tribal population

During the current year, the Division has initiated three national task force projects on health care issues among scheduled tribe population. These projects addressed three important health issues among the tribal population. The first project is to develop effective intervention model for the sickle cell disease patients in tribal areas for accessing government health care system and capacity building in terms of knowledge, skill and training of the health care workers at different levels of the health system for prevention and management of sickle cell disease. The second study is to develop implementation strategies for strengthening selected non-communicable diseases (hypertension, diabetes and chronic obstructive pulmonary disease (COPD)) related continuum of care under National Programme for Prevention & Control of Cancer, Diabetes, Cardiovascular Diseases & Stroke (NPCDCS). The third implementation research study addresses improving the health care access and quality in the context of achieving Universal Health Coverage (UHC) among scheduled tribes in 9 tribal districts in the country. In addition to these three national task force projects, the Division has funded fourteen adhoc projects, which addressed different health and health care issues of the tribes.

Health systems research on road traffic injuries (RTIs)

The Division has concluded two national task force projects on RTIs in the current year. The first study has established an electronic-based comprehensive and integrated RTI surveillance system and demonstrated the feasibility of establishing the system within the public health system. The second project has developed a structured evidence-based intervention model for safety, efficacy and quality of post-crash pre-hospital and in-hospital trauma care services to improve the outcome in RTI victims. Besides, the Division has supported some adhoc projects, specifically on health systems responsiveness on the growing burden of the RTIs.

INNOVATION & TRANSLATION RESEARCH (ITR) & INTELLECTUAL PROPERTY RIGHTS (IPR), DIVISION

During the period under review highlight of activities is as follows:

***Patents filed*:** A total of 10 patents applications were filed during Fiscal Year 2019-2020 with the Indian Patent Office. Out of these, eight are from intramural institutes and two from extramural. One design application is filed. 4 PCT applications (One extramural and rest intramural) were filed during this period with 2 National phase applications in China and Brazil.

***Patents Granted*:** During this period, 11 patents (8 Indian and 3 international patents) has been granted and 2 design applications has been registered. A total of 24 patents (14 Indian patents, 6 foreign patent applications and 4 foreign patents) were maintained and 2 designs were maintained.

Technology commercialization: Besides expanding patent portfolio, enormous efforts were being put towards commercialization of ICMR technologies initiating from website advertisement to showcasing at various exhibitions to finalize the

collaborators till transferring the technologies. As a result 5 different technologies are under pipeline of technology transfer and 1 technology was transferred.

For strengthening the commercialization activities of ICMR's technologies, the council has an in-house mechanism and technology commercialization agency Biotech Consortium India limited (BCIL). Six technologies have been assigned and BCIL is in process of exploring the commercialization of technology.

ICMR has also entered into an agreement with Federation of Indian Chambers of Commerce and Industry (FICCI) for both national and international commercialization of health technologies under HTAC program. HTAC program has three components viz. Commercialization component, training component and exposition component. Two components viz. training and exposition has been successfully achieved. Quick look report of 10 technologies and deep dive exercises prepared by IC2 was completed. Commercialization of two technologies is under process.

A total revenue of Rs. 1.50 lakh generated through technology transfer activities.

Showcased ICMR's technologies in Tech 4 Seva- a joint initiative of Unnat Bharat Abhiyan and Vijnana Bharati held 12th Aug. 2019 at IIT Delhi.

Training to intern of TIFAC-DST under KIRAN scheme of DST has been provided for the year 2019-2020.

HUMAN RESOURCE PLANNING AND DEVELOPMENT (HRD), DIVISION

A. FELLOWSHIPS

1. **JRF (Junior Research Fellowship)** -ICMR JRF fellowship exam 2019 was conducted on July 21, 2019 in collaboration with Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh at the 12 Centers *viz.,* Bengaluru, Bhopal, Bhubaneswar, Chandigarh, Chennai, Delhi, Guwahati, Hyderabad, Kolkata, Mumbai, Srinagar (J&K) and Varanasi. In 2019, a total of 145 JRF (135 Life Sciences and 10 Social Sciences) were selected and out of which 41 JRFs have joined in different Institutes till date and joining process is still ongoing until 31.12.2020.
2. **ICMR Centenary PDF (Post-Doctoral Fellowship)-** A total of 79 PDF's proposals were received during 2019-20, 40 were shortlisted as per the eligibility criteria for personal discussion, out of which 16 PDFs were selected and were approved for funding. Fifteen of them have joined for the year 2019-20 (joining awaited for one approved PDF).
3. **MD-MS/Ph.D. Fellowship-** Programme is being carried out at three Centers *viz*; King George's Medical University (KGMU), Lucknow, National Institute of Mental Health and Neuro Sciences (NIMHANS), Bengaluru and Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai. During 2019 out of 15 allotted slots a total of 08 candidates were selected (KGMU- 03 NIMHANS- Nil and SRIHER- 05).
4. ICMR Chairs for Sr. retired medical/ biomedical teachers/scientists

    i. **Dr. C.G. Pandit National Chairs-** These prestigious Chairs of ICMR have a provision of remuneration of Rs 1.00 lakh per month and contingency grant of Rs. 7.50 lakh/year per Chair. The duration of Dr. C.G. Pandit National Chair is for five years (three years extendable by another two years after assessment of the progress and plans). Retired medically qualified persons are eligible for one Chair and retired non-medical/ bio-medical/ professors/ bio-medical teachers are eligible for the other Chair. The persons should preferably be the Fellows of all the National Science Academies. At a given point of time, only two such Chairs will exist. At present both the Biomedical and Clinical Chairs are ongoing.

ii. **Dr. A. S. Paintal Distinguished Scientist Chairs of ICMR-** Distinguished Scientist Chairs are open to retired scientists/ medical teachers who may belong to Medical/Bio-medical/Life Sciences with the excellent track record in the field of medical application. All the perks/ remuneration of Distinguish Scientist Chairs of ICMR will be at par with the existing Chairs of ICMR *i.e.* Rs. 1.00 lakh per month as a remuneration and Rs. 7.50 lakhs per year as a contingency grant. The duration of Chair will be for five years (three years extendable by another two years after assessment of the progress and plans). Usually two Chairs will be established at one point of time; their number will not cross five at any given point of time. Presently, all four Chairs are occupied.

5. **STS (Short Term Studentship)-** During the year 2019-20, a total of 10177 MBBS/BDS students registered from all over the country, out of which 6159 students finally submitted their proposals, which were reviewed by Scientists/Experts in the concerned subject areas from Faculty of Dental Colleges and 26 ICMR institutes. Out of which 1238 students had qualified for carrying out the STS-2019 research project. Finally, a total of 1171 students had successfully submitted the STS 2019 report, after successful review, 1085 students were approved for stipend of Rs. 20,000/- to each student and certificates from ICMR for STS 2019.

6. **Nurturing Clinical Scientists (NCS) Scheme-** A total of 12 Clinical Scientists were selected for 2019 and out of which only three have joined the fellowship till date. Remaining joining is still awaited until December 2020.

7. **ICMR-Emeritus Scientist (IES)-** In total 56 applications were received for IES. The Expert Committee selected 17 applications for the award of IES.

8. **ICMR- Adjunct Faculty Scheme-** The Scheme was implemented from April 2019 onwards after approval from GC of ICMR. One Adjunct Faculty has joined ICMR-NIMS.

B. FINANCIAL SUPPORT

1. **MD/MS/DM/MCh/MDS thesis support-** This scheme is primarily aimed at promoting good quality research in medical colleges through students pursuing post-graduation courses as well as to improve visibility and accessibility of their research work to larger research audience, as it is mandatory to publish one paper in an indexed journal. Out of **525** thesis proposal received **100** proposals were awarded financial assistance for the year 2019-20.

2. **International Travel Grant to non-ICMR scientists-** A total of 266 applications were approved for International travel grant support from April 2019 to February 2020, as in March 2020 the meetings were further postponed due to COVID-19 health emergency.

3. DHR-ICMR Funded Workshops on Clinical Training/Translational Research-

For the year 2019, a total of 165 workshop applications on Clinical Training/Translational Research were approved for funding support until January 2020, as the Scheme has been freezed until further notice due to COVID-19 health emergency.

C. MISCELLANEOUS PROGRAMS

ICMR Awards & Prizes- A total of 46 Scientists and Young researchers were given the ICMR Awards in 31 different categories for the year 2017 and 2018. A total of 249 applications have been received for the year 2019-20 in 20 different award categories, which are under evaluation and screening.

Public Importance

Short-Term Studentship (STS)

1. The stipend of STS from the year 2020 has been increased to Rs. 50,000/- for two

months by the GC of ICMR, and also the value of the ICMR CNMC-STS Excellence Award has been increased to Rs. 50,000/- to be divided equally to five selected candidates (Rs. 10,000/- to each) from the year 2019 onwards.

2. **ICMR Awards/Prizes-** As approved by the Governing Council of ICMR, the prize/award money of all categories of ICMR Awards has been increased and the prefix 'ICMR' has been added to all Awards name. The ICMR-B. R. Ambedkar Award prize money has been increased to Rs. five lakhs from the existing Rs. one lakh and ICMR-Basanti Devi Amir Chand Prize from Rs. 50,000/- to Rs. two lakhs. The awards carrying prize money of Rs. 1.0 lakh have been kept the same where as for all the rest categories of ICMR awards carrying award/prize money of Rs. 20,000/- and Rs. 10,000/- have been increased to Rs. 50,000/- as the minimum amount to be awarded by ICMR for ICMR Awards 2019 and onwards.

3. **MD/MS/DM/MCh/MDS thesis support-** The Scheme was made completely Online from the December 2019 batch.

INTERNATIONAL HEALTH (IHD), DIVISION

The International Health Division (IHD) in ICMR co-coordinates international collaboration in biomedical research between India and other countries as well as with national & international agencies such as Ministry of Science & Technology, Indian and foreign missions and WHO etc. There are few specific Agreements/MoUs signed by the Ministry of Health and Family Welfare with other countries and rest are those signed directly by ICMR/DHR with international organizations/ institutions such as INSERM in France, German Federal Ministry of Education and Research (BMBF) and Helmholtz Association (HGF) in Germany; National Institutes of Health (NIH) in USA; International AIDS Vaccine Initiative (IAVI), USA; Swedish Research Council for Health Working Life and Welfare (FORTE) in Sweden; National Health and Medical Research Council (NHMRC) in Australia; London School of Hygiene and Tropical Medicine (LSHTM) and Medical Research Council (MRC) in UK; Drugs for Neglected Diseases Initiative (DNDi) in Switzerland; Global Alliance for Chronic Disease (GACD); Research Council of Norway (RCN) in Norway; Russian Foundation for Basic Research (RFBR) in Russia; National Institute of Infectious Disease (NIID) in Japan; The International Vaccine Initiative (IVI) in South Korea; African Union (AU) in Africa; Department of Medical Research (DMR), Myanmar.

Purpose of International Cooperation

The purpose of these Memorandum of Understanding (MoU) and Joint Statements has been for exchange of scientific information; exchange of scientists/ technicians; joint execution of scientific projects and organization of joint scientific, seminars, workshops and symposia in identified areas of cooperation.

Highlights and Major Achievements

Joint Working Group (JWG) and Joint Steering Committee (JSC) Meetings

The regular meetings of Joint Working Group (JWG) or Joint Steering Committee (JSC) with various countries/international institutes/ organizations are organized to review, develop and finalize joint collaborative programmes, decide future plans of action and identify priorities for bilateral cooperation.

In addition, the International Health Division has also represented ICMR in various bilateral/ multilateral Joint Committee Meetings coordinated by MEA, DST and MOH & FW, Govt. of India for cooperation with various countries. Following JWG/JSC meetings under various MoUs and Joint Statements have been held and were attended:

1. 6th meeting of **India-Sweden** Joint Committee (JCT) on Science & Technology at Stockholm, Sweden wherein the progress made under ICMR-FORTE Collaboration was reported

upon and new areas of cooperation in Health Sciences were suggested during 2nd and 3rd May 2019

2. Strategic Board meeting of Global Alliance for Chronic Diseases (**GACD**) at National Institutes of Health (NIH), USA on 19th June 2019
3. **Indo-US** Joint Steering Committee (JSC) meeting on Diabetes at National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) NIH, USA held on 20th June 2019 followed by visit to various Institutes of NIH (Fig.1)
4. 10th meeting of **India-Taiwan** Joint Committee on Cooperation in Science and Technology between India & Taiwan at New Delhi held on 25th July 2019
5. 4th meeting of **India-Sri Lanka** Joint Committee Meeting (JCM) on S&T organized by Department of Science & Technology (DST) at New Delhi held on 14th August 2019
6. Joint Working Group (JWG) meeting under **Indo-US** Collaboration in Environmental & Occupational Health (EOH) at ICMR Hqrs., New Delhi held on 30th August 2019
7. 2nd meeting of **India-Denmark** Joint Committee on Cooperation in Science & Technology at New Delhi held on 22nd November 2019

Exchange Visits

The IHD supports and coordinates the international travel of Indian scientists engaged in approved bilateral collaborative research projects under various MoUs and Joint Statements with other countries. A total of 40 exchange visits of scientists/ officials to and from India were arranged under various international collaborative programmes/ projects.

Health Ministry's Screening Committee (HMSC)

The research projects involving foreign assistance and or collaboration in biomedical/health research are submitted online by the Indian investigators to ICMR for approval of Govt. of India through Health Ministry's Screening Committee (HMSC). The International Health Division of ICMR acts as the Secretariat for HMSC. The projects are peer reviewed by the concerned Scientific Divisions at ICMR and then placed before the HMSC for consideration and decision. During the year 2019-20, four meetings of Health Ministry's Screening Committee were held wherein 234 projects were considered and out of which170 projects were approved for international collaboration/assistance with agencies from USA, Germany, France, Canada, Australia, Sweden, UK, WHO and several other foundations and foreign universities. Out of which, seven projects were considered & approved as co-funded by ICMR under ICMR-NIH, USA Call in HIV and five projects were under ICMR-BMBF, Germany Call in Anti-Microbial Resistance.

Since the beginning of 2020, HMSC meetings are held at a regular interval of alternate months in a calendar year.

International Visitors/Dignitaries

The Division also organized/attended discussion during visits by various visitors to ICMR from foreign countries/agencies such as Her Majesty Queen Silvia of Sweden(Fig.4), Yale University, USA; BMGF; DMR Myanmar: Taipei Economic and Cultural Center (TECC)in India Taiwan: Johns Hopkins Bloomberg School of Public Health, USA; Brunel University London; Office of Science and Innovation from Embassy of Sweden; Benha University, Egypt.

ICMR-DHR International Fellowship Programme

The ICMR International Fellowship Programme for Indian biomedical scientists aims to augment capacity strengthening of institutions involved in basic, applied, epidemiological and clinical sciences through exposure of Indian researchers to the latest international advancements in knowledge, to understand the disease and find strategies for their prevention and cure.

Announcement of applications for ICMR-DHR International Fellowships for 2019-20 was put up on ICMR/DHR websites and also published in National Newspapers.

During the year 2019-2020, the ICMR-DHR International Fellowships were awarded to 25 Senior and 31 Young Indian Scientists

The reports of senior and young ICMR International Fellows, who had undertaken the Fellowship during the year 2018-19 were placed on ICMR website.

India Africa Health Sciences Platform

First Call for Applications for ICMR/AU-STRC Health Practitioners/Researchers Capacity Building Scheme (Training Courses in India 2019) was announced on ICMR and AUSTRC websites with last date of submission of Applications as 30th June, 2019. Call was for seven training courses at 3 ICMR Institutes-NICPR, Noida; NIN, Hyderabad; NIE, Chennai. Ninety-five African Health Practitioners/ Researchers from 26 African countries were trained under this call (Fig.2)

Second call under ICMR/AU-STRC Capacity Building Scheme Training Courses in India 2020 was launched with the last date of submission of applications on 29thFebruary 2020. Call was for 8 training courses at 4 ICMR Institutes-NICPR, Noida; NIRT, Chennai; NIRRH, Mumbai and NIV Pune. Review of Applications is under process.

Call Guidelines and Request for Applications for joint health research projects under the MoU are being finalized in consultation with AU-STRC.

New initiatives

1. Newton Bhabha Fund programme: Indian Council of Medical Research partnered with British Council UK for the Researcher Links Workshops under the Newton Bhabha Fund programme for a period of 3 years. Researcher links workshops are designed to provide financial support to bring together a UK/Indian bilateral cohort of early career researchers to take part in workshops to meet the overarching objectives.

   The first joint call was advertised on website of ICMR and British Council on 17th July 2019 in the area of HIV/ TB and the closing date for submission of applications was 9th August 2019. After joint review one application was selected for funding under this call.

2. ICMR/NIH/BMGF Clinical Research fellowship: The Indian Council of Medical Research (ICMR), the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health (NIH) and the Bill &Melinda Gates Foundation (BMGF), signed a Declaration of Intent on 17th November 2019 on clinical research fellowship programme (Fig.3). It is a programme for early and mid-career scientists within India and the USA to help in expanding the cohort of physician scientists focused on research that will advance discovery to improve clinical practice and benefit public health in both countries. The implementation plan and guidance document are under preparation in consultation with NIH & BMGF.

Fig. 13: Meeting with Dr. Anthony S. Fauci, Director, NIAID (NIH), USA in his office on 20th June 2019.

Fig. 14: Meeting of 3rd batch NICPR Course-3 under ICMR-AU STRC Health Practitioners/ Researchers Capacity Building Scheme with Director-General ICMR at Indian Council of Medical Research (ICMR) Hqrs., New Delhi on 24th October 2019.

Fig. 15: Signing of Declaration of Intent between ICMR-NIAID-BMGF in the presence of Mr. Bill Gates, Co-Chair, BMGF at ICMR Hqrs., New Delhi on 17th November 2019.

Fig. 16: Meeting on India-Sweden Roundtable discussion on Health & Dignified Aging during the visit by Her Majesty Queen Silvia from Sweden at AIIMS, New Delhi on 3rd December 2019.

RESEARCH MANAGEMENT, POLICY, PLANNING & COORDINATION (RMPPC)

RMPPC is engaged in work related to preparation of various policy, planning documents, write-ups on achievements, impact analysis, *etc.* through coordination with various ICMR Institutes and stakeholdlers' consultations. It has coordinated major activities assigned by MoHFW, NITI aayog, Office of PSA like Trend analysis of resource investment in Health and Health Research, Rating and Ranking of Centrally Funded R&D Organisations and the preparation of providing technical inputs and assisting in releasing various important policy documents and reports of ICMR like ICMR Media Policy, ICMR Disaster Management Plan *etc.* It has also planned and coordinated various activities to commemorate 150th anniversary of Mahatma Gandhi. It has also been instrumental in various activities like setting up of a new Regional Medical Research Centre at Gorakhpur (UP); setting up of a communication unit; new field station at Keylong in Himachal Pradesh *etc.* It is also involved in Research synthesis through Evidence to Policy that 'helps people make well informed decisions about policies, programs and projects by putting the best available evidence from research at the heart of policy development and implementation' as well as prepare Policy briefs on successful interventions. It also coordinates activities of the Communications Unit as well as helps in providing scientific inputs and assists in finalizing the Outcome Budget/Annual Plan/Annual Action Plan, etc. It also supervises and coordinates Parliament Questions/Parliamentary Assurances and other Parliamentary Matters including Parliamentary Standing Committee meetings and action taken reports.

Gandhi and Health @ 150

To commemorate 150th birth anniversary of Mahatma Gandhi, a range of activities were organized by ICMR on theme " Gandhi & Health @ 150"

Collector's Edition of Indian Journal of Medical Research was published entitled, Gandhi & health @ 150. It was released by His Holiness The Dalai Lama on 20th March 2019. The Hindi version of the same has been released recently by Hon'ble Health and Family Welfare Minister, Dr. Harsh Vardhan on 16th October,2019. This edition features articles on the health file of Mahatma Gandhi, his medical legacy, his virtues and their importance in the current health scenario followed by writings from the pens of ardent Gandhian followers and a special section that documents the role played by ICMR and its 26 institutes over the last 100 years following Gandhian thoughts.

Fig. 17: Release of "Gandhi aur swasthya @150" by Hon'ble Health and Family Welfare Minister, Dr. Harsh Vardhan.

Mission SHAKTTI (School-based Health Awareness, Knowledge Test and Training Initiative)

A School-Based Dissemination Programme initiated by ICMR in collaboration with Directorate of Education and National Gandhi Museum in 36 schools of Delhi to take forward the Gandhiji message of Health and Hygiene adopting physical fitness, meditation, balance diet and cleanliness for Happy and Healthy India. Around 2800 students participated in the event. This program was also replicated in Jabalpur (by ICMR-NIRTH) and Kolkata (during IISF 2019) where around 400 students participated. It is planned to be extended in other parts of the country in future.

Fig. 18: Mission SHAKTTI: School Based Health Awareness Campaign, an initiative by ICMR in 36 schools of Delhi.

Lecture for medical fraternity

A talk by Prof. Mark Lindley, well-known Gandhian scholar, on "A Comprehensive Sketch of What Mahatma Gandhi Said and Did re: Health, Nutrition, Hygiene and Health Care" on 17th February, 2020 was organized by ICMR in collaboration with All India Institute of Medical Sciences (AIIMS), New Delhi. Prof. Lindley is associated with Gandhi Research Foundation, Jalgaon and is also the Professor of Eminence at Babasaheb Ambedkar Marathwada University, Aurangabad. The lecture potrayed the life and philosophy of Mahatma Gandhi in context of health and healthy living practices that would benefit the future generations particularly in coping with communicable and non-communicable diseases following Mahatma's footsteps.

Health Research Conclave

As part of India International Science Festival-2019, Health Research Conclave was organized during 7-8th November 2019 at Kolkata. It provided a platform where eminent health scientists and researchers interacted with each other as well as with media, policy makers and general public. The theme of the conclave was 'Translating Research in to Action for Improving Health of the Population' where eminent health experts spoke on Tribal Health, Nutrition, Medical Innovations and Emerging Infections. Around 250 delegates participated in the event. Fifty delegates (Ph.D. and post-doctoral scholars) from various institutions across the nation presented their work through oral and poster presentations. The oral and poster presentations were evaluated by jury for three best oral and poster award presentations.

Evidence to Policy

With an aim to translating research in to impact, workshop on writing effective Policy Briefs were conducted at Regional Medical Research Centre, Gorakhpur to train ICMR and collaborating scientists. Around 47 scholars were trained. As an output of this and earlier workshops, eight

policy briefs were finalized and published on Fluorosis, Anthrax and TB.

Standard Treatment Workflows (STWs)

The first volume was released by Bill Ga tes, Co-chairman and co-founder of the Bill & Melinda Gates Foundation; Dr V K Paul, Member, NITI Aayog; Dr. Indu Bhushan, CEO, CEO, AB-PMJAY and the National Health Authority (NHA on 17th November 2019. It includes 50 diseases across 9 specialties. They will serve as uniform treatment guideline for doctors in primary and secondary healthcare settings. About 300 experts across India's government and private hospitals have been roped in to prepare STWs for 100 common illnesses, ranging from kidney diseases, infections in children to cardiac diseases.

Fig. 19: Release of First volume of Standard Treatment Workflows of India developed with the goal of empowering primary, secondary and tertiary care towards achieving Universal Health Coverage.

Biomedical Communications

To streamline and accelerate the communication related activities of ICMR and its Institutes as well as to enhance the brand building a Communication Unit with the support from GHS was set up at ICMR Hqrs which is linked with ICMR Institutes. A network of Nodal Communications Officers (NCOs) has been formed. The first physical meeting of all NCOs was held on 6th Feb 2020. The meeting identified the communications-related gaps and challenges at the institute level, developed the strategies to address those gaps and trained the NCOs for effective messaging, press releases and media strategies. A comprehensive guide to best practices in social media was also released during the event.

- In order to strengthen ICMR's communication capacity, 2 social media training workshops were organized at Pune and Agra. A total of 28 scientists including the Directors, nodal communication officers (NCOs) and senior scientists from each ICMR institute participated in the workshops.
- Communications unit also conducted the weekly media analysis to see the trends and visibility of ICMR. The analysis captures the tonality, count and key themes of the media articles along with a list of ICMR leaders who have been quoted. It also captures a snapshot of the availability of social media handles of ICMR and its Institutes.
- First ever ICMR's media policy was developed and released.
- Around 11 Press interactions of DG ICMR were coordinated to disseminate the achievements and future strategy for national health achievements of ICMR. Also, regular opinion articles, interviews of directors of different institutes were facilitated through CU.
- Short films were developed for 5 ICMR institutes (NIN, NIV, NIRT, NICED and NIRRH) to showcase their achievements and films were also developed for launch of various major activities like MERA India, Mission DELHI etc.
- A social media campaign with #WeareICMR was conducted and it reached around 2 million social media handles on Twitter and the hashtag was mentioned in more than 1500 tweets on the platforms. The social media posts were also shared by the Ministry of Health and Family Welfare (attached), National Health Portal and other key stakeholders across the health space. The campaign also saw the highest engagement across Facebook (increase of over 2000 followers), Twitter (increase of 1500 followers) and Instagram (increase of over 300 followers) of ICMR Handle which resulted in the highest increase in the following of the respective account.

- CU also facilitated in designing the ICMR documents like ICMR Award booklet, BSL-3 guidelines etc.

COVID-19 Communications: In the wake of unprecedented COVID-19 situations, a crisis communication plan and team was formed. Two Press briefings with DG, ICMR were coordinated and relevant press releases were made. A whatsApp group was formed with media journalists for seamless and clear communication.

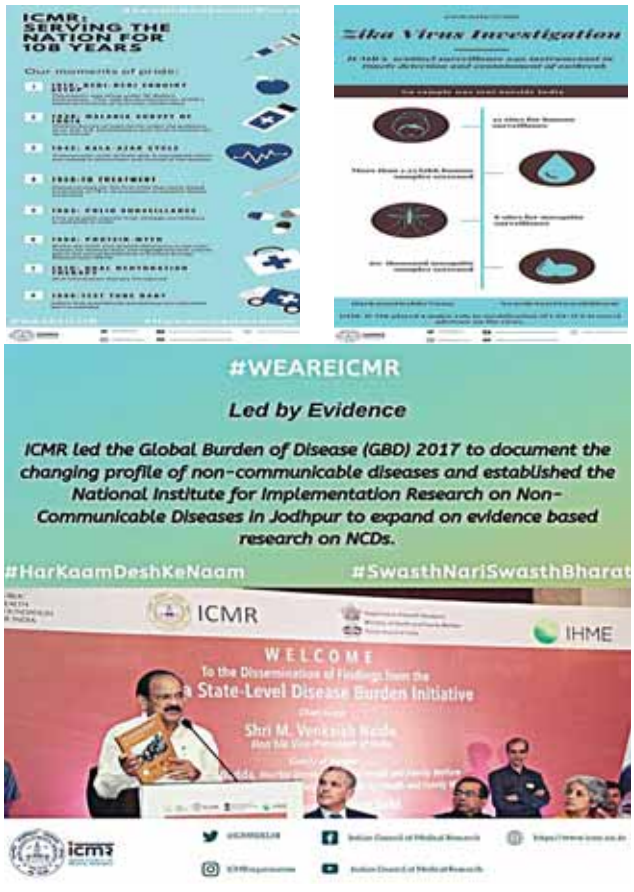


Fig. 20: Glimpses of Social Media Infographics prepared for research dissemination.

ICMR Disaster Management Plan 2019

RMPPC developed and released ICMR Disaster Management Plan 2019. The rationale of the disaster management plan is to equip the department and its associated offices/labs to assess risk and manage disaster effectively. In this document, DHR-ICMR has provided detailed Disaster Management Plan (DMP) for national component as well as contingency plan for the Department and its attached bodies.

Fig. 21: Disaster Management Plan 2019 and ICMR Media Policy.

INDIAN JOURNAL OF MEDICAL RESEARCH (IJMR), DIVISION

The Indian Journal of Medical Research (IJMR) is a monthly biomedical journal of national and international repute and is the flagship journal of the Indian Council of Medical Research (ICMR). During the financial year 2019-2020, it has completed 106 successful years of uninterrupted publication, with 12 issues brought out in two volumes each year. The IJMR is available full text, free on the internet with a searchable menu. The IJMR has wide circulation within and outside India and is included in all global indexing and abstracting services. The journal is available full text free on the web at www.ijmr.org.in. IJMR archive is also made available at www.ijmr.org.in with the full text of articles available free in PDF format since the inception (July 1913). The IJMR App has been made available for the Android version of the tablet as well as iPad since January 2017.

The IJMR publishes Editorials, Commentaries and Review/Mini review articles on topics of contemporary biomedical interest contributed by eminent global experts. Other than these, Research Correspondences, View Points, Perspectives, Systematic reviews & Meta-analyses, Clinical Images, Students' IJMR, Letters to the Editors and Book reviews are also published in addition to Policy Documents and Special/Status Reports occasionally.

The impact factor for the year 2019 was 1.503 (Clarivate Analytics, 2020).

A total of 11 issues (including a special issue) were published in the 2019-2020 financial year with the total number of submissions amounting close to 3000. Of these, about 36 per cent articles were received from countries other than India. One thousand one hundred eighty one reviewers were involved in the peer-review process, of whom 27 per cent were from USA, 36 per cent from Europe, 19 per cent from Asia (excluding India) and 18 per cent were from the rest of the world. Figure 22 depicts the total number of articles published in the IJMR during 2019-2020 under various categories; 46 percent were original research articles, followed by 15 per cent review articles. View Points, perspectives, Special reports, Policy guidelines, *etc.* Constituted 11 per cent of the articles published.

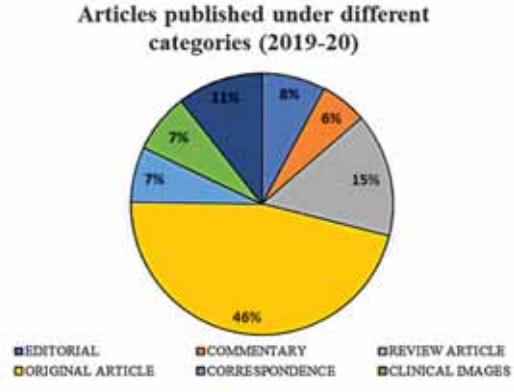


Fig 22: Articles published in the IJMR under various categories during 2019-2020.

Close to 200 articles were published in the said financial year, with 20 per cent articles from foreign countries such as the USA, UK, Thailand, P.R.China, Turkey, Iran, France, Croatia, Spain, Sri Lanka, Brazil, Australia, Serbia, South Africa, Bangladesh, Mexico and Malaysia. Figure 23 depicts the percentage of articles submitted, published and reviewers' contribution from India and foreign countries.

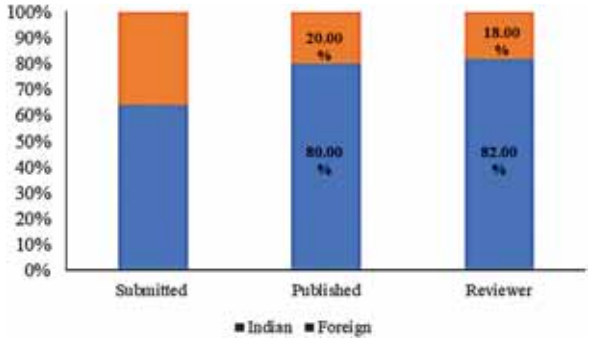


Fig. 23: Indian vs. foreign articles submitted, published & reviewers' contributed in the IJMR during 2019-2020.

In 2020, given the COVID-19 emergency scenario, efforts were doubled at IJMR to publish articles most relevant to COVID in fast track to ensure dissemination of most opportune information to readers and policymakers. In this regard, such articles were made available Ahead of Print on www.ijmr.org.in on a timely basis. The February & March 2020 (Volume 151, Issues 2 & 3) issue was published as a special issue entitled "India & COVID-19" (Fig. 24). Drs Rajesh Bhatia & Priya Abraham were the guest editors for this issue. In this special issue, one Editorial, one View point, seven Perspectives, three Review articles, one Policy Guidelines, one Protocol, six Original articles and four Research Correspondences were published.

Fig. 24: Special Issue on COVID-19 published in February & March 2020.

Besides articles, selected books on contemporary topics were also reviewed by senior experts in the respective biomedical research areas. A total of 26 book reviews were published during the reported financial year.

Efforts are now being focussed on more Special Issues on COVID-19. Also a supplement on Clinical Images, from the Clinical Images Competition conducted in 2019 is presently under compilation. Other than these, a Special section on HTA is in pipeline as well, besides regular monthly issues for the subsequent financial year as under report.

MEDICINAL PLANTS (MPD), DIVISION

Development of a Standardized Formulation for Preventing or Delaying the Development of Type-2

Diabetes in Subjects with Pre-diabetes.

During the year, the pre-clinical pharmacological, safety and some of the GLP regulatory toxicity studies on the developed Phytopharmaceutical product have been completed. Further, Completion of all GLP regulatory toxicity studies, submission and approval of Phytopharmaceutical IND and conducting a Phase –I human study will be done. Subsequent to successful completion of phase I study, a multicenteric phase II clinical trial will be initiated on the developed product.

Development of a Formulation for Treatment of Sleep Disorders.

The pre-clinical pharmacological studies, safety studies and GLP regulatory toxicity studies on the developed product have been completed.The GMP batch manufacturing and clinical efficacy and safety evaluation on the developed product is being planned through conducting a well designed, multicenteric, randomized, double-blind, controlled clinical trial at 4 Premier/ National institutes. The clinical phase of the project is currently under progress.

Joint Phytopharmaceutical Drug Development Programme of ICMR, CSIR and DBT

Under this new initiative on joint development of the Phytopharmaceutical drugs, out of the 9 leads initially identified, 2 projects have been prioritized, the status and development made on these are as described below:

a. Cannabis based Phytopharmaceutical Drug (THC: CBD ratio, 1:1) in Management of Cancer Pain

b. Boswellia based Phytopharmaceutical Drug for Treatment of Osteoarthritis

The projects are for a total duration of 5 years and to be completed in 4 different phases. The first three phases of product development i.e. CMC, preclinical efficacy, safety and pharmacology studies were planned to be completed mutually by CSIR and DBT in about 2 years time. During the year the work on the first phase of developing CMC is under progress. ICMR will undertake and support IND dossier submission to DCGI, preparation of clinical trials protocols, obtaining regulatory clearance for clinical trials and conducting trials with compilation of results etc after completion of the above studies.

Review Monographs on Indian Medicinal Plants

The programme aims at consolidation of Indian research contributions (published information) at the various National laboratories/institutions across the country in the area of medicinal plants and present the compiled information in series on Reviews on Indian Medicinal Plants which serve as comprehensive, informative & reliable source of information providing information on new leads, thus helping in systematic and planned evaluation of Medicinal plants, including drug design, basic and applied research.During the year 21st and 22nd volumes in this series have been published. The preparation of Volume 23 is in progress.

- The Monographs on 95 plant genera and 417 species covered under the 21st volume (Piq-Pre) have been published.
- The Monographs on 41 plant genera and 161 species covered under the 22nd volume (Pri-Qui) have been published.

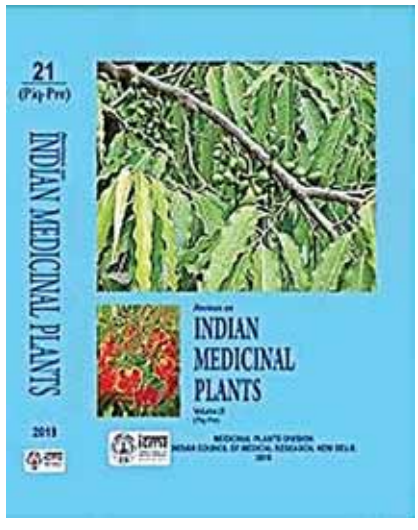


Fig. 25: Reviews on Indian Medicinal Plants Vol. 21.

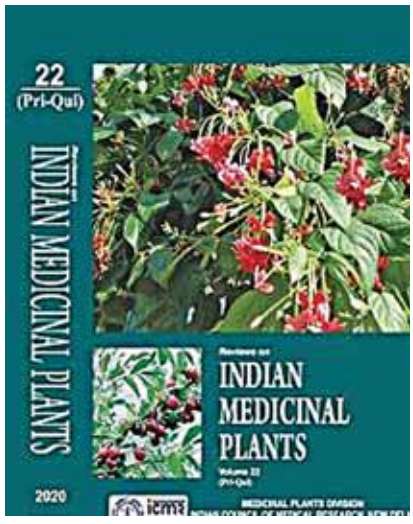


Fig. 26: Reviews on India Medicinal Plants Vol. 22.

Quality Standards of Indian Medicinal Plants

During the year, Quality standards on 31 Medicinal Plants Monographs were developed, and published as Vol. 17 as part of series on "Quality Standards on Indian Medicinal Plants".

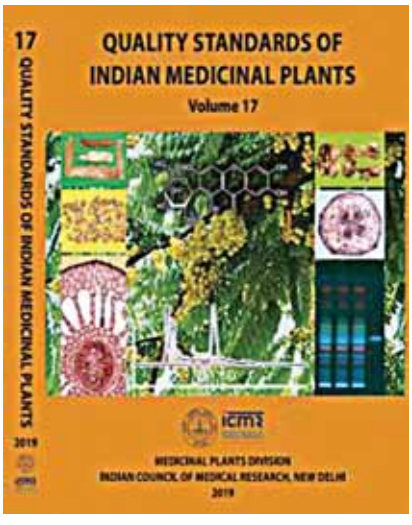


Fig. 27: Quality Standards on Indian Medicinal Plants Vol. 17.

Safety Review Monographs on Indian Medicinal plants

The second volume of this publication is under progress and 70 monographs have been completed. The monographs comprise of comprehensive published information mainly on historical use, pharmacopoeial status, preclinical general toxicity/ safety, mutagenicity/genotoxicity, reproductive safety, adverse effects observed in clinical trials, safety in pregnancy, safety in children, case reports and herb-drug interactions (if reported any).

Development of a Website exclusively dealing with Medicinal Plants

A website has been developed exclusively on the Divisions activities and hyperlinked with the ICMRs main website is regularly being updated.

Publication & Information (P&I), Division

HINDI UNIT

ICMR PATRIKA

ICMR continued to publish the monthly Hindi "ICMR Patrika" during the year. The articles on major health topics were *Aahar ki gunvatta mehatavapuran* (April, 2019); *Rashtriya Poshan Sansthan: Poshan ke maadhyam se rashtra ko sasakt banane ke 100 varsh (Bhag-I)* (May, 2019); *Rashtriya Poshan Sansthan: Poshan ke maadhyam se rashtra ko sasakt banane ke 100 varsh (Bhag-II)* (June, 2019); *Argonomics: Swasthya avam utpadakta sudran samanyee* (July, 2019); *Bharat mai Pariwar Niyojan ke isthithi* (August, 2019); *Atiraktadaab: Bharat mai ek gambhir swastha chunotti* (Sept.-Oct., 2019); *Rashtriya Poshan Sansthan: Khadhya jeev vish se khadhya suraksha tak ke yatra* (Nov-2019).

Varshik Prativedan 2018-19

Brought out the Hindi version of ICMR Annual Report 2018-19 as *Varshik Prativedan* 2018-19.

Dissemination of Biomedical Information

A large number of education and extension activities during the year were carried out throughout the country to disseminate the achievements of ICMR at various platforms .The major outreach activities were as follows:

- **Govt. Achievements and Schemes Expo :** Pragati Maidan, New Delhi, 1-3rd August, 2019.
- **Destination Uttarakhand - 2019**: In collaboration with Uttarakhand State Council for Science and Technology, Dehradun, 18-20th July, 2019.
- **Ujjwal Himachal Pradesh -2019:** Chamba, 28-30th July, 2019.

- **2[3rd] National Health Education:** Kolkata, 28-31[st] August, 2019.
- **Rise in Haryana - 2019:** Hansi, Haryana, 29-31[st] August, 2019.
- **24[th] Sundarban Kristi Mela-O-Loko Sanskriti Utsab**: South 24 Parganas ,West Bengal, 20-29[th] December, 2019.
- **"Technology Outreach as an Enabler for inclusive & Sustainable Development – Tech. for Seva":** under joint initiative of Unnat Bharat Abhiyan and Vijnana Bharati at IIT, Delhi, 10-12[th] August, 2019.
- **8[th] Bhopal Vigyan Mela (BVM-2019):** CSIR-Advanced Materials and Processes Research Institute at Bhopal, 13-16[th] September, 2019.
- **7[th] Indian National Exhibition cum Fair-2019:** Bengal Human Resources Development Foundation, Kolkata, 25-29[th] September, 2019.
- **Vision Rajasthan-2019:** Udaipur, Rajasthan, 17-19 September, 2019.
- **Mega Science, Technology & Industry Expo, IISF 2019:** Kolkata, 5-8[th] November, 2019. Three institutes viz., ICMR- National Institute of Malaria Research, New Delhi, ICMR-National Institute of Nutrition, Hyderabad and ICMR- National Institute of Virology, Pune showcased their achievements. ICMR also participated in the **Health Research Conclave** on 7-8[th] November, 2019 at Biswa Bangla Convention Centre, Kolkata with an aim to provide a platform where eminent health scientists and researchers can interact with each other as well as with media, policy makers and general public. The theme of the conclave was 'Translating Research into Action for Improving Health of the Population' where eminent health experts spoke on Tribal Health, Nutrition, Medical Innovations and Emerging Infections. The day II of the Conclave had two parallel sessions: a) Young Scientists Talks along with oral and poster presentations by Ph.D. and post doc research scholars; b) Special Session on Gandhi & health @150 entitled "Mission Shaktti"

Fig. 28: IISF 2019 Dignitaries on the Dias.

Fig. 29: DG ICMR Dr Balram Bhargava lighting the lamp.

Fig. 30: ICMR team at the Stall.

Fig. 31: Participants at the Health Research Conclave.

- **15[th] Jatiya Sanhati Utsav-O-Bharat Mela - 2019:** Sonarpur, District South 24 Parganas, Kolkata ,West Bengal. ICMR's Kolkata

located 2 Institutes viz. NICED & ROHC (East) participated in this Exhibition, 14-18th December, 2019.

- **Sanrachna - 2019:** Kathua (J&K), 5-7th December, 2019.
- **107th Indian Science Congress:** University of Agriculture Sciences, Bengaluru, Karnataka, 3-7th January, 2020. The Science Congress was inaugurated by the Hon'ble Prime Minister of India Shri Narendra Modi on 3rd Jan., 2020. The Pride of India Expo was inaugurated by Dr Harsh Vardhan, Hon'ble Union Minister of Science & Technology and Earth Sciences who visited ICMR pavilion and interacted with the ICMR Scientists. The Council also showcased its activities and achievements by displaying posters, live demonstrations, publications, films and distributing pamphlets etc. Four institutes of the ICMR viz NIMR field stations [Bengaluru, Guwahati and Raipur]; NIV, Pune; NIN, Hyderabad; NIOH-ROHC, Bengaluru participated. A large number of visitors including students, research scholars, VIPS, Faculty, academicians visited the ICMR stall with great enthusiasm.

Fig. 32: Hon'ble Prime Minister of India Sh Narendra Modi inaugurated the 107th Indian Science Congress.

Fig. 33: Dr Harsh Vardhan, Union Minister of Science & Technology at ICMR Stall.

Fig. 34: Honble Vice President Sh Venkaiah Naidu giving prize to ICMR Scientists for the most Informative Stall.

- **3rd India International Innovation Fair-2019:** Hyderabad, Telangana, 1-3rd December, 2019.
- **Chuka Scientific Literacy cum Health & Wellness Festival:** Mandla, Madhya Pradesh, 5-7th December, 2019.
- **Bengaluru Tech Submit:** Bengaluru, 18-20th December, 2019.
- **Destination Daman & Diu – 2019:** K V Ground, DIU, 14-16th December, 2019.
- **Destination Gujarat - 2019:** Surendra Nagar, Gujarat**,** 18-20th December, 2019.
- **Rise in Uttar Pradesh – 2020:** Ghaziabad Uttar Pradesh, 14-16th February, 2020

INFORMATICS, SYSTEMS AND RESEARCH MANAGEMENT (ISRM), DIVISION

The division of ISRM has a mandate to nucleate and support informatics in medical research through focused programs and services. During the year 2019-20, the Division of ISRM worked in the areas of Data Management of COVID-19 and other research projects, Analytics, Dissemination, Networking, Development of Web portals and research management. The division provided wide range of services to the medical fraternity as well to the administration and finance. The Division also worked on strengthening collaborations with National and International organizations. Major programs and the achievements are given below

DATA MANAGEMENT AND DISSEMINATION

Data Management Laboratory In line with the objectives under the Pillar II of the ICMR Strategic Vision Document 2030, the division maintains nearly **220** web portals hosted in ICMR Server or NIC Cloud related to different research projects, administration and finance of ICMR HQ and its institutes. The division developed nearly **60** data collection and analysis portals and website for ICMR and its institute during FY 2019-2020. A few important programs for which the Division developed data collection and analysis portals include:

ICMR COVID-19 Data Portal which can be accessed at https://cvstatus.icmr.gov.in . Since December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has globally affected 195 countries. First case of SARS-CoV-2 has been reported on end of January 2020 In India. The COVID-19 testing and data management were challenging. The division developed dedicated portal to manage COVID-19 testing and analysis.

COVID-19 Testing Laboratories Location portal which can be accessed at https://covid.icmr.org.in. It is portal to navigate and find out nearest COVID-19 Testing Laboratories location across the country.

India Cancer Research Consortium (ICMR-ICRC) which can be accessed at https://icrc.icmr.org.in . ICMR-ICRC has been established under ICMR-DHR to strengthen our fight against cancer. It will bring together stakeholders with interests in basic sciences, clinical and translational research and public health policy related to cancer. The portal enables online submission form for concept proposal submission in ICRC.

Clinical Decision System to Identify Histogenesis in cases of Carcinoma with Unknown Primary is a web based tool which is enabled to access the histopathology knowledgebase (Histopathology KB) a collection of histopathology images from different organs with diagnostic remarks from registered pathologist. This dataset can be used for both teaching and research purpose.

The division supports ICMR institutes for enriching and technically upgradation of institute official websites. The official website of ICMR-Regional Medical Research Centre, Gorakhpur; ICMR-National Institute of Malaria Research, New Delhi; ICMR-National Institute of Pathology, New Delhi; ICMR – Vector Control Research

Centre, Puducherry have been developed during this financial year.

DARPAN a Dashboard for Analytical Review of Projects Across Nation portal has been configured and launched for DHR-ICMR (https://dhr.dashboard.nic.in). It provides administration, at a glance, the status of different departmental activities with an architecture for presenting dashboard in respect to the monitoring of schemes at different levels.

ICMR-AIIMS COMPUTATIONAL GENOMICS CENTRE

Genomics tools and techniques are revolutionizing medical research through better diagnostics and prognostic markers and personalized risk models for non-communicable disease such as cancer. ICMR established a Computational Genomics Centre in collaboration with AIIMS. The Centre is fully operational and is assisting medical professionals from AIIMS and other medical research institutions in analyzing genomics data. The primary objective of ICMR AIIMS Computational Genomics Centre (IACGC):

a) To create awareness of application of genomics tools and techniques in medical research

b) To provide assistance/consultation to medical professionals in designing experimental protocol, choice of technology, tools etc.

c) To conceptualize and initiate collaborative projects with medical researchers involving genomics tools and techniques

A total of 76 requests have been received in the year 2019. Complete profile of service requests received and processed by IACGC is shown in Figure below:

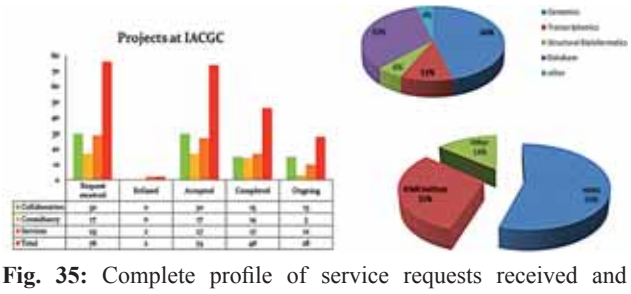


Fig. 35: Complete profile of service requests received and processed by IACGC.

List of Institutes and departments to which the services/collaborations have been/are being extended is shared below:

- AIIMS, New Delhi – 14 Departments / centres: Anatomy, Biochemistry, Biotechnology, Biophysics, Dr. BRA Institute-Rotary Cancer Hospital , Dr. R. P. Centre for Ophthalmic Sciences, Forensic Medicine, Gastroenterology, Neurology, Microbiology, Pathology, Paediatric, Urology
- ICMR Institutes – More than 10 ICMR institutes
- Others – 10 University/Institutes: Safdarjung hospital, New Delhi; JNU, New Delhi; IP University, New Delhi; Jamia Millia Islamia University, New Delhi; Jamia Hamdard, New Delhi; Amity University, NOIDA; BHU, Varanasi; AIIMS, Bhubaneswar
- International Project: Selcuk University, Turkey; Department of Informatics, University of Oslo, Norway; CDC, USA (through AIIMS Microbiology Department)

Information about the activities of the Centre is available at http://genomics.icmr.org.in

CONNECTIVITY AND COMMUNICATION SERVICES

The centre is managing internet and LAN connectivity at ICMR Headquarters and institutes of ICMR. The Division is providing software based Video Conferencing Services to ICMR and its institutes. The Division also managed email accounts of ICMR employees on 'icmr.gov.in' domain.

ELECTRONIC RESEARCH MANAGEMENT SYSTEM

Extramural research is promoted by ICMR through Open-ended research on the basis of applications for grants-in-aid received from researchers/scientists in regular employment in the Universities, Medical Colleges, Postgraduate Institutions, recognized

Research and Development Laboratories and NGOs from all over in India. In order to improve efficiency of processing of its Extramural Research Program and to save efforts of the Investigators, ICMR has shifted from manual receipt and processing of extramural projects to web-based interactive system since January 2012. ePMS is a cloud service for Project proposal submission, evaluation and monitoring system. The main vision of ePMS system is to provide Transparent & Centrally Controlled electronic Proposal Evaluation and Grant Disbursement to support R&D Institutions.

Fig. 36: Stakeholders of ePMS system.

Fig. 37: ePMS system as of today.

During the period (10th Dec 2019 till 17th Jan 2020), total **2904** detailed proposals were received online, out of which, total **773** full proposals wereTechnically Approved after evaluation by Technical Divisions.

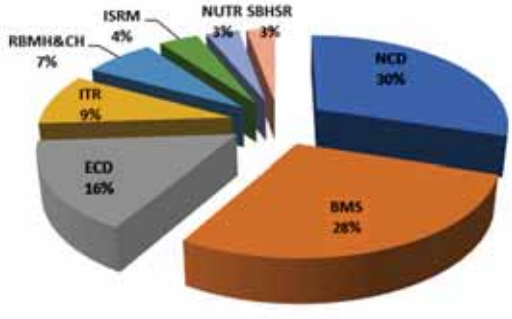


Fig. 38: Percentage Share of received adhoc detailed proposals, Division wise- 2019-20.

Table 4: Top 20 Major Discipline wise received adhoc detailed proposals- 2019-20.

Major Discipline	No. of proposals	% of proposals
Oncology	208	7.16
Pharmacology	148	5.10
Translational Research	115	3.96
Bioinformatics	114	3.93
Neuroscience	105	3.62
Cellular & Molecular Biology	102	3.51
Biochemistry	100	3.44
Nutrition	85	2.93
Tuberculosis & Chest Diseases	82	2.82
Drug Development Initiatives	75	2.58
Reproductive Health	73	2.51
Cardiovascular Diseases	67	2.31
Antimicrobial Resistance	66	2.27
Mental Health	66	2.27
Child Health	65	2.24
Diabetes	65	2.24
Viral Diseases	61	2.10
Innovation	59	2.03
Immunology	54	1.86
Genomics	49	1.69

Table 5: Top 20 Institutions wise received adhoc detailed proposals- 2019-20.

Institute	No. of proposals	% of proposals
All India Institute of Medical Sciences (AIIMS), New Delhi, Delhi	231	7.95
PGIMER, Chandigarh, Punjab	136	4.68
All India Institute of Medical Sciences, Bhopal, Madhya Pradesh	50	1.72
King George Medical University, Lucknow, Uttar Pradesh	44	1.52
Panjab University, Chandigarh, Chandigarh	44	1.52
All India Institute of Medical Sciences, Bhubaneswar, Orissa	37	1.27
All India Institute of Medical Sciences, Rishikesh, Dehradun, Uttarakhand	34	1.17
Kasturba Medical College, Manipal, Manipal, Karnataka	33	1.14
Kongu Engineering College, Erode, Tamil Nadu	30	1.03
Jamia Hamdard, New Delhi, Delhi	29	1.00
Manipal Academy of Higher Education, Udupi District, Karnataka	26	0.90
Manipal College of Pharmaceutical Sciences, Manipal, Karnataka	24	0.83
National Institute of Virology (ICMR), Pune, Maharashtra	22	0.76

Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu And Kashmir	22	0.76
Banaras Hindu University, Varanasi, Uttar Pradesh	20	0.69
National Institute of Mental Health and Neuroscience (NIMHANS), Bangaluru, Karnataka	20	0.69
Birla Institute of Technology, Ranchi, Jharkhand	19	0.65
Manipal College of Nursing, Mangalore, Karnataka	19	0.65
National JALMA Institute of Leprosy and other Micobacterial Diseases, Agra, Uttar Pradesh	19	0.65
Aarupadai Veedu Medical College & Hospital, Puducherry, Puducherry	18	0.62

During the year, Extramural Fellowship (RA/SRF) Proposal Submission opened for one month (1st -31st Jan 2020). During the period, total **2189** fellowship proposals were received online and after evaluation by Technical Divisions, total **815** fellowship proposals wereTechnically Approved.

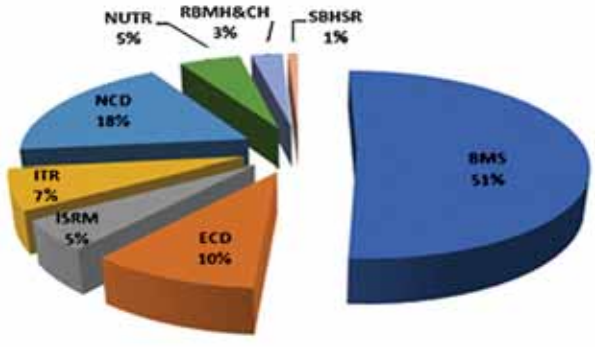


Fig.39: Percentage Share of received fellowship proposals, Division wise- 2019-20.

Table 6: Top 20 Major Discipline wise received fellowship proposals- 2019-20.

Major Discipline	No. of proposals	% of proposals
Cellular & Molecular Biology	207	9.51
Oncology	143	6.57
Pharmacology	139	6.39
Nanomedicine	116	5.33
Biochemistry	115	5.28
Bioinformatics	113	5.19
Drug Development Initiatives	112	5.15
Nutrition	106	4.87
Medicinal Plants	93	4.27
Nanotechnology	83	3.81
Translational Research	80	3.68
Genomics	46	2.11
Tuberculosis & Chest Diseases	45	2.07
Diabetes	38	1.75
Immunology	37	1.70
Neuroscience	37	1.70
Microbial Infections	35	1.61
Antimicrobial Resistance	34	1.56
Reproductive Health	34	1.56
Toxicology	32	1.47

Table 7: Top 20 Institutions wise received fellowship proposals- 2019-20.

Institute	No. of proposals	% of proposals
Jamia Hamdard, New Delhi, Delhi	138	6.34
All India Institute of Medical Sciences (AIIMS), New Delhi, Delhi	90	4.14
Jamia Milia Islamia, New Delhi, Delhi	74	3.40
Post Graduate Institute of Medical Education & Research, Chandigarh	47	2.16
University of Kashmir, Srinagar, Jammu And Kashmir	44	2.02
Aligarh Muslim University, Aligarh, Uttar Pradesh	42	1.93
Banaras Hindu University, Varanasi, Uttar Pradesh	42	1.93
Manipal College of Pharmaceutical Sciences, Manipal, Karnataka	38	1.75
Jawaharlal Nehru University, New Delhi, Delhi	34	1.56
JSS College of Pharmacy, Nilgiris, Tamil Nadu	34	1.56
Sher e Kashmir University of Agricultural Sciences & Technology Kashmir, Srinagar, Jammu And Kashmir	31	1.42
King George Medical University, Lucknow, Uttar Pradesh	29	1.33
University of Hyderabad, Hyderabad, Telangana	25	1.15
Bharathiar University, Coimbatore, Tamil Nadu	24	1.10
Vellore Institute of Technology, Vellore, Tamil Nadu	22	1.01
Baba Saheb Bhimrao Ambedkar University, Lucknow, Uttar Pradesh	21	0.97
Central Drug Research Institute, Lucknow, Uttar Pradesh	20	0.92
Central Food Technological Research Institute, Mysore, Karnataka	20	0.92
BITS, Pilani - Hyderabad Campus, Hyderabad, Telangana	19	0.87
JSS Academy of Higher Education & Research, Mysore, Karnataka	19	0.87

A call for proposal was advertised through National newspapers and DHR website under Grant-In-Aid

scheme of DHR between July 1, 2019 to August 14, 2019 inviting full length proposals. In response to the call, **1055** full proposals were received. After screening of the proposals by a Screening Committee at DHR; **158** proposals were found suitable under the DHR areas. Further, it has been decided by the Competent Authority that the remaining **897** proposals will be considered by ICMR under Extramural Adhoc Scheme. Out of **897** proposals, total **237** proposals were Technically Approved after evaluation by Technical Divisions of ICMR.

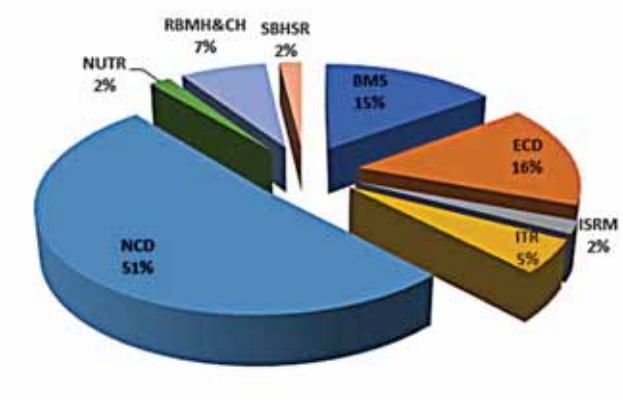


Fig. 40: Percentage Share of received DHR-GIA proposals, Division wise- 2019-20.

Table 8: Top 20 Major Discipline wise received DHR-GIA proposals- 2019-20.

Major Discipline	No. of proposals	% of proposals
Oncology	158	17.77
Mental Health	47	5.29
Neurological Science	43	4.84
Cardiovascular Diseases	38	4.27
Diabetes	36	4.05
Environmental Hygience and Occupational Health	34	3.82
Tuberculosis	34	3.82
Child Health	29	3.26
Maternal Health	28	3.15
Epidemiology	27	3.04
Nanomedicine	25	2.81
Biomedical Devices	23	2.59
Pharmacology	22	2.47
Ophthalmology	21	2.36
Urology	21	2.36
Immunology	18	2.02
Medicinal Plants	18	2.02
Bioinformatics	17	1.91
Health System Research	16	1.80
Nutrition	16	1.80

Table 9: Top 20 Institutions wise received DHR-GIA proposals- 2019-20.

Institute	No. of proposals	% of proposals
All India Institute of Medical Sciences, New Delhi	93	10.46
Postgraduate Institute of Medical Education and Research, Chandigarh	65	7.31
All India Institute of Medical Science, Bhopal	21	2.36
All India Institute of Medical Sciences, Rishikesh	16	1.80
Jamia Hamdard (Hamdard University), New Delhi	16	1.80
Jawaharlal Institute of Postgraduate Medical Education and Research, Pudducherry	15	1.69
Amrita Institute of Medical Sciences and Research Centre Amrita University, Kochi	12	1.35
Acharya & BM Reddy College of Pharmacy, Bengaluru	11	1.24
University of Madras, Chennai	10	1.12
CSIR-Indian Institute of Toxicology Research, Lucknow	9	1.01
Jamia Millia Islamia, Delhi	9	1.01
ICMR-National Institute of Research in Reproductive Health, Mumbai	8	0.90
Kasturba Medical College, Manipal	8	0.90
King George's Medical University, Lucknow	8	0.90
National Institute of Mental Health and Neuro-Sciences, Bengaluru	8	0.90
Bharathiar University, Coimbatore	7	0.79
Manipal School of Life Sciences, Manipal	7	0.79
Amity University, Gurugram	6	0.67
Banaras Hindu University, Varanasi	6	0.67
Annamalai University, Chidambaram	5	0.56

Two 'Call for proposals' programmes were also launched during the year which resulted in receipt of **334** proposals online and after verifying/checking the duplication/incompleteness/Not in proper

format/missing documents, all these proposals were forwarded to concerned division, online, for further processing. These included a). Call for proposal on Research areas in Leishmaniasis (14-08-2020 - 30-09-2020 by ECD Division) (63 proposals), b). Call for proposal under North East Seed Grant scheme (07-08-2020 - 30-09-2020 by RBMH&CH Division) (271 proposals).

MANAGEMENT OF ICMR SOCIAL MEDIA SITES

The division is working tirelessly to enhance the outreach of five Social Media Handles of ICMR-- Twitter, Facebook, YouTube, Instagram and LinkedIn. The followers, likes, engagements of all Social Media Handles are increasing each day. The #WeAreICMR campaign was launched and major research activities of ICMR HQ and its institutes, Profile of Director General, Additional Director General, Head of ICMR HQ Division and Director of Institutes were posted in social media. Division also participated in #HarKaamDeshKeNaam campaign announced by MoHFW and shared major achievements of ICMR and its institutes. Social media became an important tool to disseminate COVID-19 information. The important information on COVID-19 testing strategy, COVID-19 Testing, Testing Laboratories and new development are being shared in social media.

MANAGEMENT OF DIRECT BENEFIT TRANSFER (DBT) SCHEMES

There are currently 6 Direct Benefit Transfer schemes from ICMR. Online team collected transaction data pertaining to direct benefit transfer schemes from online research management portal, technical divisions and Account section; then updated this information on the DBT portal every month. ISRM division integrated all the schemes with DBT App so that MIS integration became possible and further integration with UMANG platform is in progress.

MANAGEMENT OF ICMR ANNUAL REPORT

Compilation, editing, publishing, timely laying in parliament and distribution of Annual Report of ICMR was successfully achieved by the Division. Annual Report pertains to all activities- research as well as several Government of India initiatives as well as achievements of ICMR Headquarters as well as its 26 institutes & approximately 100 field units.

ICMR INSTITUTES/CENTRES

ICMR INSTITUTIONAL NETWORK

1. ICMR National JALMA Institute for Leprosy & Other Mycobacterial Diseases
   Dr. M. Miyazaki Marg, PO Box 101,
   Tajganj, **Agra -** 282001
   Uttar Pradesh

2. ICMR National Institute of Occupational Health
   Meghani Nagar, **Ahmedabad** - 380 016
   Gujarat

3. ICMR National Institute of Traditional Medicine
   Belagavi, National Highway No.4,
   Belagavi - 590010,
   Karnataka

4. ICMR National Centre for Diseases Informatics and Research
   Nirmal Bhawan - ICMR Complex (II Floor), Poojanahalli Road,
   Off NH-7, Adjacent to Trumpet Flyover of BIAL Kannamangala Post,
   Bengaluru - 562 110,
   Karnataka

5. ICMR National Institute for Research in Environmental Health
   Kamla Nehru Hospital Building, Gandhi Medical College Campus,
   Bhopal - 462 001,
   Madhya Pradesh

6. ICMR Regional Medical Research Centre
   Chandrasekharpur, **Bhubaneswar** - 751023,
   Odisha

7. ICMR National Institute for Research in Tuberculosis
   No.1 Sathiyamoorthy Road Chetput, **Chennai** - 600031,
   Tamil Nadu

8. ICMR National Institute of Pathology
Safdarjang Hospital Campus P.O. Box No. 4909, **New Delhi** - 110029
Delhi

9. ICMR National Institute of Epidemiology
Second Main Road, Tamil Nadu Housing Board, Ayapakkam,
Near Ambattur, **Chennai** - 600 077
Tamilnadu

10. ICMR National Institute of Medical Statistics
Post Box No. 4911, Ansari Nagar, **New Delhi** -110029
Delhi

11. ICMR National Institute of Malaria Research
Sector-8, Dwarka, **New Delhi** - 110077,
Delhi

12. ICMR Regional Medical Research Centre, NE Region
Post Box No. 105, **Dibrugarh** - 786001,
Assam

13. ICMR Regional Medical Research Centre Gorakhpur
Baba Raghav Das (BRD) Medical College Campus,
Gorakhpur - 273013,
Uttar Pradesh

14. ICMR National Animal Resource Facility for Biomedical Research (NARFBR)
National Centre for Laboratory Animal Sciences, NIN Campus,
Jamai Osmania P.O. **Hyderabad** - 500 007
Andhra Pradesh

15. ICMR National Institute of Nutrition
Jamai - Osmania (P.O.), Tarnaka,
Hyderabad - 500 007,
Andhra Pradesh

16. ICMR National Institute for Research in Tribal Health
Nagpur Road, Garha, **Jabalpur** - 482 003,
Madhya Pradesh

17. National Institute for Implementation Research on Non-Communicable Diseases
New Pali Road, **Jodhpur** - 342 005,
Rajasthan

18. National Institute of Cholera and Enteric Diseases
P-33, C.I.T. Road, Scheme XM Beleghata, **Kolkata** - 700 010,
West Bengal

19. ICMR National Institute of Immunohaematology
13th Floor, New Multi-storied Building, KEM Hospital Campus,
Mumbai - 400012,
Maharashtra

20. ICMR National Institute for Research in Reproductive Health
Jehangir Merwanji Street, Parel,
Mumbai - 400 012,
Maharashtra

21. ICMR National Institute of Cancer Prevention and Research (NICPR)
I-7, Sector - 39, **Noida** - 201301
Uttar Pradesh

22. ICMR Rajendra Memorial Research Institute of Medical Sciences
Agam Kuan, **Patna** - 800007,
Bihar

23. ICMR Regional Medical Research Centre
Post Bag No. 13, **Port Blair** - 744 101,
Andaman and Nicobar Islands

24. ICMR Vector Control Research Centre
Indira Nagar, **Puducherry** - 605006
Puducherry

25. ICMR National AIDS Research Institute
G-73, MICD Complex, Bhosari, **Pune -** 411026
Maharashtra

26. ICMR National Institute of Virology
20 A Dr Ambedkar Road, **Pune** - 411 001
Maharashtra

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