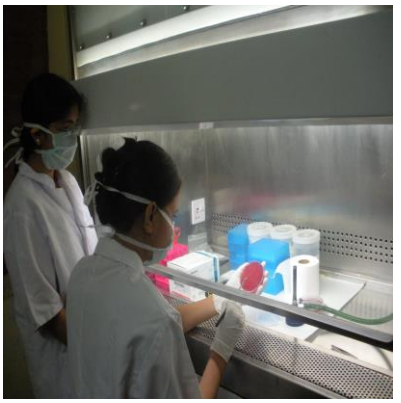
JAI VIGYAN MISSION MODE PROJECT

COMMUNITY CONTROL OF
RHEUMATIC FEVER/ RHEUMATIC HEART DISEASE
IN INDIA

COMPREHENSIVE PROJECT REPORT [2000-2010]



INDIAN COUNCIL OF MEDICAL RESEARCH

ANSARI NAGAR, NEW DELHI

JAI VIGYAN MISSION MODE PROJECT

Community Control of Rheumatic Fever/ Rheumatic Heart Disease in India

Comprehensive Project Report
2000-2010

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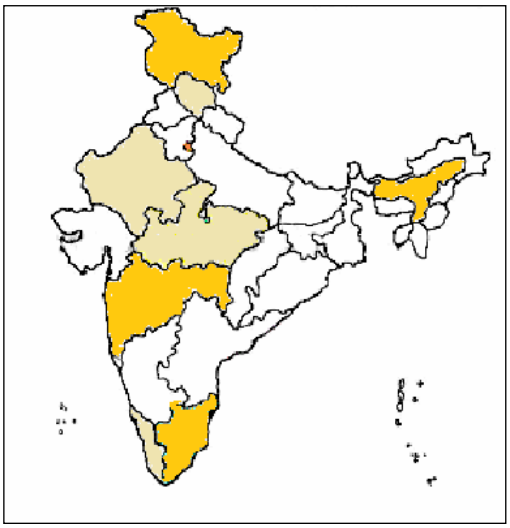

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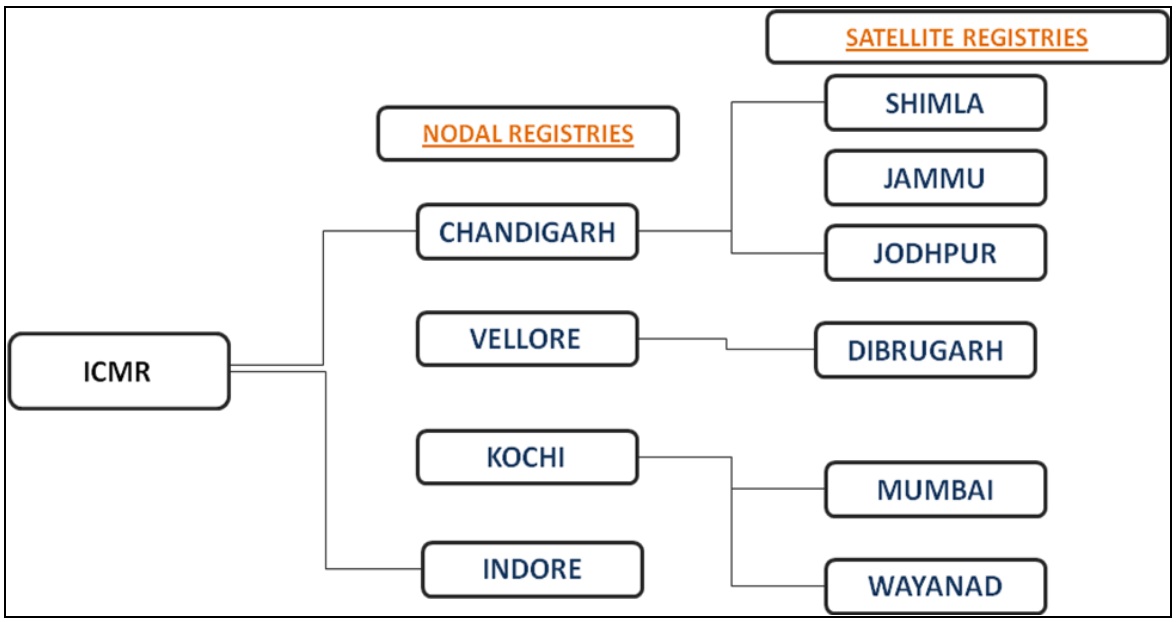

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LIST OF ABBREVIATIONS

AGN	Acute Glomerulonephritis
ABC	Active Bacterial Core
ARF	Acute Rheumatic Fever
ASO	Anti-Streptolysin O
BHS	Beta Hemolytic Streptococcus
BLAST	Basic Length Alignment Search Tool
Bp	base pair
^{0}C	Degree Celsius
CDC	Centre for Disease Control and Prevention
CHC	Community Health Center
CHD	Congenital Heart Disease
cm	centimetre
CMC	Christian Medical College
CTAB	Cetyl Trimethylammonium Bromide
dATP	Deoxyadenosine Triphosphate
dCTP	Deoxycytidine Triphosphate
DDW	Double Distilled Water
ECG	Echocardiogram
dGTP	Deoxyguanidine Triphosphate
DNA	Deoxyribonucleic Acid
dNTPs	Deoxynucleotide Triphosphate
dTTP	Deoxythimidine Triphosphate
EDTA	Ethylene Diamine Tetra Acetic Acid
EtBr	Ethidium Bromide
g	gram
GAS	Group A Streptococcus
GCS	Group C Streptococcus
GGS	Group G Streptococcus
HCl	Hydrochloric Acid
ICMR	Indian Council of Medical Research
IEC	Information, Education and Communication
IPTG	Isopropyl β - D - Galactosidase
kb	kilobase

KCl	Potassium Chloride
kDa	kilodalton
M	molar
µg	microgram
µl	microlitre
m/z	mass/charge ratio
MgCl2	Magnesium Chloride
min	minute
MIS	Management Information System
ml	milliliter
mM	milimolar
MO	Medical Officer
NaCl	Sodium Chloride
NaOH	Sodium Hydroxide
ng	nanogram
NRHM	National Rural Health **Mission**
nM	nanomolar
no.	number
OD	Optical Density
OF	Opacity Factor
PCR	Polymerases Chain Reaction
PBS	Phosphate Buffer Saline
PCR	Polymerase Chain Reaction
PFGE	Pulse Field Gel Electrophoresis
pg	pictogram
PGIMER	Post Graduate Institute of Medical Education and Research
PHC	Primary Health Center
pM	picomolar
ppm	parts per million
RF	Rheumatic Fever
RHD	Rheumatic Heart Disease
RFLP	Restriction Fragment Length Polymorphism
RNA	Ribonucleic Acid
rpm	revolution per minute
rRNA	Ribosomal RNA
SDS	Sodium Dodecyl Sulfate

Sic	Streptococcal Inhibitor of Complement
SOPs	Standard Operating Procedures
STSS	Streptococcal Toxic Shock Syndrome
Taq	*Thermus aquaticus*
TBE	Tris – Borate – EDTA
TCA	Trichloro Acetic Acid
TE	Tris Ethylene Diamine Tetraacetic Acid
THB	Todd Hewitt Broth
TSR	Template Suppression Reagent
TSS	Toxic Shock Syndrome
uv	Ultraviolet
V	Volts
v/v	volume/volume
W	Watt
WHO	World Health Organization
w/v	weight/volume

Preface

The cardinal goal of preventive medicine is to avert occurrence of disease. The goal can be achieved by taking actions at the earliest, limiting the occurrence and/or progression of the disease. When patients and health care providers play their health promotion and specific protection roles, prevention of disease is achieved at a lower cost than the cost of managing the disease once it occurs. However, it is not always easy to undertake health promotion and specific disease prevention activities due to a lack of a clear understanding about the natural history of the disease, preventive strategies and or inadequate resources.

Rheumatic fever (RF) and rheumatic heart disease (RHD) are preventable to a large extent. Most developed countries witnessed a decline in these diseases with a rise in living standards. However, the problem still continues in most of the developing countries as most people still live in poor socioeconomic conditions. Though the association with Group A Streptococcal (GAS) sore throat is well established, the biological mechanism by which RF is 'caused' is not fully understood, hampering the development of a vaccine. Although appropriate treatment of sore throat can prevent the resulting RHD, inadequate health infrastructure is a major constraint in the detection and treatment of GAS sore throat in low socioeconomies.

Early diagnosis of RF and RHD cases and the administration of antibiotics at regular intervals can prevent recurrences of rheumatic fever by preventing streptococcal sore throat. Although healthcare providers have implemented the prevention strategies, the prevention of RF and RHD has not been fully achieved even in developed countries. Outbreaks of RF have occurred among children residing in middle class families in USA. Hence, surveillance of GAS and streptococcal diseases has emerged as a priority issue.

Jai Vigyan Mission Mode Project on Control of Rheumatic Fever/Rheumatic Heart Disease was initiated in India about a decade ago to establish registries of RF/RHD cases in several health institutions of selected districts to develop a model for prevention and control of RF and RHD using the existing health infrastructure. A large number of medical and paramedical personnel were trained for prevention and control of RF/RHD. Health education and teaching/training materials were developed. Survey of GAS *emm* types was undertaken to identify the candidates for a potential vaccine.

Several researchers from Public health, Cardiology, Microbiology, and Biotechnology fields collaborated with Indian Council of Medical Research (ICMR), New Delhi to conduct this Task Force Project. I take this opportunity to thank members of the Steering Committee, Investigators, Research Officers and Research Assistants who have worked for almost over a decade for the success of this project. Dr. Rajan Tandon, Dr. Bela Shah and Dr. Meenakshi Sharma deserve special appreciation for their untiring efforts in bringing out this report. I hope this project report will be useful to all stakeholders who are involved in the prevention and control programs or in conducting research to develop a vaccine against GAS infections.

Dr. V. M. Katoch
Director General
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February 2015

Acknowledgement

Rheumatic heart disease, a neglected disease, continues to be a burden in India and other developing countries. It is the result of an autoimmune sequalae in response to group A beta hemolytic streptococcus (GAS) infection of the pharynx. Epidemiology of RF and RHD is radically different between developed and developing countries. From 2000 to 2010, the Indian Council of Medical Research (ICMR) has conducted a multicentric 'Jai Vigyan Mission Mode Project' on RF/RHD at Roopnagar (Punjab), Shimla (Himachal Pradesh), Jammu (Jammu and Kashmir), Jodhpur (Rajasthan), Mumbai (Maharashtra), Indore (Madhya Pradesh), Vellore (Tamil Nadu), Kochi (Kerala), Wayanad (Kerala) and Dibrugarh (Assam).

The study was conducted with joint efforts of the Division of Non Communicable Diseases at ICMR Headquarters, Post Graduate Institute of Medical education and Research, Chandigarh, Christian Medical College, Vellore, Amrita Institute of Medical Sciences and Research Centre, Kochi, Govt. Medical College, Jammu, Indira Gandhi Medical College, Shimla, King Edward Memorial Hospital, Mumbai, Desert Medicine Research Center (ICMR), Jodhpur, Mahatma Gandhi Memorial Medical College, Indore and Regional Medical Research Center, North-East (ICMR), Dibrugarh. We are grateful to all the investigators for supervision and leadership and their research teams for data collection and data entry. We sincerely thank the local health authorities of districts and states and school administration for their support who helped in completing this study. We express our sincere thanks to dr Rajesh Kumar for his untiring efforts in bringing out this consolidated report.

I gratefully acknowledge the untiring technical guidance provided by Dr Rajan Tandon and Dr LM Nath during the long journey of the entire study. I am grateful to Dr DS Agarwal , late Dr KB Sharma and all other members of the Steering Committee for reviewing the reports.

My sincere thanks are due to Dr VM Katoch, Secretary Department of Health Research and Director General, ICMR, former Director General, Dr NK Ganguly and Dr Bela Shah, Division of Non Communicable Diseases, ICMR for their sustained support for taking up this task.

I am grateful to my colleagues Dr DK Shukla, Dr Dhaliwal and Dr Ashoo Grover for their support in implementing this project. Last but not the least, I express my heartiest thanks to my administrative staff Mr PK Chawla, Mr Om Prakash and Mr Raju Ponekar at ICMR for their continuous help.

Meenakshi

(Meenakshi Sharma)

Summary

Background

Rheumatic Fever (RF)/Rheumatic Heart Disease (RHD) are a neglected public health problem in India. Anticipation of a declining trend in RF/RHD with improving socioeconomic status, as happened in the developed countries, thwarted health policy development in this area. Despite overwhelming evidence of the cost-effectiveness of registry-based secondary prevention programs, India does not have a national program for prevention and control of RF/RHD. Inadequate understanding of the pathogenesis has hampered research and development for a vaccine against RF/RHD. Hence, Indian Council of Medical Research initiated a Jai Vigyan Mission Mode Project on Control of RF/RHD in year 2000. Epidemiological studies of streptococcal sore throat and impetigo, registry-based surveillance of RHD and school-based surveys for prevalence of RHD were carried out to advance the understanding about the biology of streptococci, the magnitude of RF/RHD and feasibility of implementing RF/RHD control program through the existing health infrastructure.

Methodology

A population based RF/RHD surveillance system was established in about one million populations utilizing the existing health infrastructure in ten districts of nine states of India located in North (Jammu, Shimla & Rupnagar), South (Vellore, Kochi & Wayanad), Center (Indore), East (Dibrugarh), and West (Jodhpur & Mumbai). Mumbai and Indore covered only urban population whereas rest of the centers primarily covered rural population. Initially a listing was done of all primary health centers (PHCs), community health centers (CHCs), district hospitals and private clinics. The number of doctors, health supervisors, auxiliary nurse midwives (ANMs), multipurpose workers (MPWs), laboratory technicians and pharmacists were then listed. Primary schools were identified for carrying out the active survey.

Extensive health education campaigns using multiple media were carried out to increase the awareness about disease symptoms and signs, mode of transmission, prevention and control. Using manuals all medical and paramedical staff of the selected districts was trained for prevention and control of RF/RHD. Patient records/registers, ASO kits, benzathine penicillin injections or oral penicillin tablets, patient monitoring cards and health education materials were made available through the existing health services. RF/RHD registries were established at each of the study site. Regular administration of penicillin prophylaxis among the registered patients was monitored and

referral to a tertiary care was encouraged for availing necessary medical or surgical treatment of patients. As benzathine penicillin injections are banned in few states (Kerala and Tamilnadu), oral penicillin was used in Vellore, Kochi and Wayanad.

Cross-sectional sample surveys were conducted among school children covering 10,000 or 25,000 children at each center in the 5-14 year age group. A sub-set of about 250 children were also followed-up fortnightly in few schools at two centers (Chandigarh and Vellore). Children with a cardiac murmur were identified through history and health checking including auscultation by a physician and were referred to a tertiary care hospital for echocardiography based examination by cardiologist. Throat and skin swabs were obtained from a sample of children and Group A Streptococci (GAS) were identified and *emm* typed using standard laboratory protocols. School surveys were used for estimation of RF/RHD disease burden using a correction factor (number of RF/RHD cases in 15+ year population to be 5.5 times that in 5-14 year-olds). Age and sex distribution, time trend, clinical presentation and compliance to secondary prophylaxis were assessed from registry data.

Results

GAS prevalence ranged from 0.1% (Jammu) to 11.3% (Vellore) in sore throat cases and 0.5% (Chandigarh) to 12.5% (Vellore) among those who did not have sore throat (carriage). GAS prevalence in impetigo cases (studied only at Chandigarh and Vellore) was 2.7% in Chandigarh and 27.3% in Vellore. Skin carriage rates were higher in Vellore (7.9%)**.** The genetically close relatives of GAS, i.e., Group C Streptococcus (GCS) and Group G Streptococcus (GGS) were also found to be common in throat swabs particularly in Vellore and Mumbai centers.

Typing of a total of 567 GAS isolates from all the regions in this study revealed 98 *emm* types with high heterogeneity of circulating strains within and between regions. Most prevalent *emm* types - *emm*112, *emm*11, *emm*82 and *emm*110 of Southern region differed from the most prevalent isolates in northern region (*emm*77, *emm*81, *emm*11, and *emm*71). Overall most prevalent *emm* types in India were *emm*112*, emm*81*, emm*7*, emm*11 *emm*12 and *emm*82.

Some of the predominant *emm* types of western courtiers (*emm*1 and *emm*12) were also found to be prevalent in India (seven *emm*1 isolates were obtained from Vellore, Jodhpur and Shimla). This study for the first time noticed *emm*-4 from Indian community which is a distinct *emm* type. With

the exception of few *emm* types, most of the GAS types identified in India are generally different from the ones taken into consideration while developing multivalent vaccines in USA.

Of the 5590 RF/RHD registered cases, 4936 were RHD and 654 were RF cases. Males and females were 38% and 62 % among RF & RHD cases respectively. In 5-14 year age group, RF was more common (55.3%) than RHD (17%). Secondary prophylaxis coverage with injection Benzathine Penicillin was 92% at Indore, 93% at Dibrugarh and 95% at Chandigarh, whereas secondary prophylaxis coverage with oral penicillin was 75% at Vellore; other centers could not report this data.

Prevalence of RHD in 5-14-year-old students ranged from 0.1 to 1.2/1000 (median 1.1). School survey identified that all the RHD children were not enrolled in the hospital-based registries indicating considerable under-reporting in RF/RHD registries. Hence, the registry data could not be used for estimation of RF/RHD burden. The prevalence of RF/RHD, estimated from school survey using a correction factor ranged from 10 to 161/100,000 population (median 84/100,000 population).

Introduction of Echocardiography and Doppler (E&D) in the evaluation of carditis with acute rheumatic fever has identified the presence of subclinical carditis (SCC), that is, presence of cardiac involvement which cannot be diagnosed clinically. Studies suggest that SCC occur s in up to 30 percent children with acute rheumatic fever. The Utah epidemic in USA between 1985-94 found that clinically identifiable carditis was present in 68 percent with clinically unidentifiable disease in 16 percent giving an overall frequency of carditis in 84 % children. Studies in normal school children have identified 19 to 44 percent asymptomatic, unknown SCC. The data indicate that the estimates obtained in our ten centre study based on clinical evaluation are underestimating the prevalence by a big margin. Studies are underway to estimate the prevalence of SCC to estimate the burden of hidden, clinically undiagnosed rheumatic heart disease in our country.

Conclusions

GAS pharyngitis is more common in the North whereas in the South GAS impetigo is more common. GAS *emm* types prevalent in India vary a lot from one region of the country to another region.

RF/RHD continues to be a public health problem in India. Registry-based secondary prevention program within the existing health services of India is a feasible strategy for RF/RHD prevention and control.

Recommendations

(a) Wide heterogeneity in Group A Streptococcal *emm* types observed in India should be considered while considering a vaccine development strategy.

(b) Surveillance of GAS, GCS, GGS diseases and *emm* types should be continued to monitor the time trends in various geographic areas of India.

(c) School Health Program under National Rural Health Mission, intending to cover 12,88,750 Government and private aided schools, should include registry-based secondary prevention prophylaxis for RF/RHD control utilizing the existing health services of India.

Future Research

Studies on following components need to be undertaken:

(i) Health System Research – e.g. to understand how health system should intervene to deal with non-compliance for secondary prophylaxis/benzathine penicillin

(ii) Economic benefits of undertaking RF/RHD control program

(iii) Newer diagnostic methods for GAS

(iv) Long term prospective studies for understanding the natural course of subclinical RHD lesions

(v) Vaccine development against Group A Streptococcus.

1. Introduction

Acute Rheumatic Fever (RF) and Rheumatic Heart Disease (RHD) are epidemiologically associated with *Streptococcus pyogenes* pharyngitis. *Streptococci* are a large group of gram-positive, nonmotile, non–spore-forming cocci about 0.5-1.2 µm in size. They often grow in pairs or chains, hence the name (from Greek) streptos - meaning easily bent or twisted, like a chain.

S*treptococcus* pyogenes displays streptococcal group A antigen on its cell wall. They typically produce zones of beta-hemolysis (the complete disruption of erythrocytes and the release of hemoglobin) when cultured on blood agar plates (1). Therefore, these bacteria are also called Group A β hemolytic Streptococci (abbreviated as GAS).

1.1. History

S. pyogenes was first described in the 5th century by Hippocrates. Billroth in 1874 demonstrated presence of these organisms in patients with wound infections. Fehleisen isolated the chain-forming organisms in pure culture from erysipelas lesions in 1883. Rosebach named the organism *S. pyogenes* in 1884. They belong to the phylum firmicutes and the lactic acid bacteria group. In these bacteria, cellular division occurs along a single axis, and thus they grow in long chains or pairs. Studies by Schottmueller in 1903 and JH Brown in 1919 led to the knowledge of different patterns of hemolysis described as alpha, beta, and gamma hemolysis. **S**treptococci were further classified by Lancefield (1933) into serotype groups based on M-protein precipitin reactions (2). The traditional sero-typing has been replaced by *emm* typing. This gene-typing system is based on sequence analysis of the *emm* gene, which encodes the cell surface M protein. More than 200 *emm* types have been identified by the Centers for Disease Control and Prevention (3).

In the early 1900s, Dochez, George, and Dick identified hemolytic streptococcal infection as the cause of scarlet fever. The epidemiological studies of the middle of last century helped in establishing a link between GAS infection and acute rheumatic fever (RF) and acute glomerulonephritis (AGN).

Classification of streptococcal infections drastically changed in the early 1930's when Dr. Rebecca Lancefield, an American bacteriologist, pioneered a new serotyping system based on the group specific antigenic composition of cell wall polysaccharides. She divided Streptococci into eighteen groups from A through H and K through V. In addition, several serotypes were reported on the basis

of their M proteins, the streptococcal surface proteins that represent one of the best-known virulence determinants of this pathogen. Rebecca Lancefield established the critical role of M protein in disease causation. Today, M protein typing is used as an epidemiological marker to identify Group A Streptococcal (GAS) isolates. As a result of novel sequencing technologies that can be applied to serotyping of the *emm* gene (coding for M protein), more than 200 *emm*-types have been reported, including the category of non-typable isolates (3).

1.2. Streptococcal Diseases

Streptococcus pyogenes causes a wide variety of diseases in humans. It is one of the most common causes of acute bacterial pharyngitis that leads to RF/RHD. Impetigo, a common skin infection, is also caused by *S. pyogenes* and is associated with acute glomerulonephritis (AGN). In rare cases, *S. pyogenes* causes invasive diseases such as cellulites, bacteremia, necrotizing fasciitis, and toxic shock syndrome (TSS) (4).

1.2.1. Sore Throat

A wide variety of viruses and bacteria cause sore throat, which is transmitted through droplets under overcrowded conditions, and is more common in winter and early spring. It is not always possible to differentiate clinically between GAS and other viral sore throats. The presence of GAS in upper respiratory tract may reflect either acute infection, when patient experiences an antibody response or a carrier state, where person harbors the organism but does not show an antibody response. It is difficult to differentiate between both conditions clinically though it is possible to differentiate these conditions by streptococcal antibody studies.

The risk of an attack of acute rheumatic fever (ARF) following GAS pharyngitis has been reported to be 0.3% under endemic conditions, and as much as ten times higher (3%) during epidemic conditions (5). During the winter and spring seasons in temperate climates, up to 20% of the school-aged children may be GAS carriers. A throat culture for GAS in a sore throat case is supportive of the diagnosis. Adequate antibiotic treatment of the streptococcal sore throat is effective in reducing occurrence of ARF cases.

1.2.2. Scarlet Fever

Scarlet fever is another manifestation that can follow streptococcal sore throat. It is usually contagious. Symptoms of streptococcal sore throat with red rash appear on the sides of the chest and abdomen. Rash appears as tiny, red pinpoints and has a rough texture like sandpaper. There may also be dark red lines in the folds of skin and patient may get a bright strawberry-red tongue and flushed (rosy) face, with pale color of the mouth. The skin on the tips of the fingers and toes often peels. In severe cases, there may be high fever, nausea and vomiting. Like streptococcal sore throat, it can also be treated with antibiotics. Scarlet fever is a rare occurrence now-a-days, though it was readily seen during epidemics in the last century.

1.2.3. Skin Infections

Skin infections occur most frequently during the summer, when exposure to insect-bite is more common. Impetigo is highly contagious bacterial skin infection which is common among pre-school and school children. It affects top layers of the skin. Impetigo is usually caused by staphylococcus but it can also be caused by GAS. Impetigo presents as small blisters or scabs, turning to yellow or honey-colored crusts, mostly seen around the nose and on the face. The infection is spread by direct contact with lesions or with nasal carriers. Other skin lesions caused by GAS are cellulites and erysipelas. Cellulite is an inflammation of deep underlying tissues whereas erysipelas is an inflammatory disease of the upper layers of the skin.

1.2.4. Invasive Diseases

Streptococcus pyogenes has been described as an emerging cause of severe infections, which are sometimes life-threatening. The infections are termed as "invasive diseases" whenever bacteria get into parts of the body where these are usually not found such as the blood, muscle, or the lungs. Two of the most severe, but least common, forms of invasive GAS disease are necrotizing fasciitis and streptococcal toxic shock syndrome (6).

Necrotizing fasciitis is a rapidly progressive disease which destroys muscles, fat, and skin tissue. The patients with streptococcal toxic shock syndrome (STSS) were described as young without predisposing factors and had flu-like complaints as the primary symptoms. Approximately about 25% of patients with necrotizing fasciitis and 35% of patients with streptococcal toxic shock syndrome (STSS) die (CDC). Reports of fatal infection with invasive GAS have been increasingly recognized in the United States since 1987. People with long-term illnesses like cancer, diabetes, and kidney

disease, and those who use medications such as steroids are at higher risk for invasive diseases. Recently, severe and fulminant cases of GAS meningitis have also been reported.

Evidence suggests that strains of streptococci with increased pathogenic potential are appearing. An increasing number of patients are being identified who have various, unusually severe, soft tissue infections associated with marked systemic toxicity, bacteraemia and shock. Systemic surveillance of invasive diseases has not yet been organized in developing countries, including India.

1.2.5. Acute Glomerulonephritis

Acute post-streptococcal glomerulonephritis (AGN) occurs primarily in children and young adults, with males being affected twice as often as females. Individuals over 40 years can also be subjected to the disease (7). The epidemiology of AGN is related to its presence in southern and temperate climates, where pyoderma associated glomerulonephritis was demonstrated to peak in the summer. In northern climates, acute glomerulonephritis is associated with throat infection (7).

The characteristics of post streptococcal AGN include edema, hypertension, hematuria, urinary sediment abnormalities and decreased serum complement levels, with little fever (8). There is a latent period of 1 to 4 weeks (average 10 days) between the streptococcal infection and development of acute glomerulonephritis. Antistreptococcal antibody titers for anti-DNase B or antihyaluronidase are elevated (7, 9). In glomerulonephritis following pyoderma or skin infection, the latency period may be 3 to 6 weeks and the ASO titers are generally low. Recurrent attacks of glomerulonephritis do not cause more severe disease, and in general there is no permanent damage to the kidney in children following the disease attack. However, according to Bisno (1995) 1% or fewer children develop severe or irreversible renal failure, but in the adult population this may be a different scenario, with more AGN patients developing chronic glomerulonephritis or hypertension (8).

The pathogenic events that lead to the development of post streptococcal AGN are related to an immunologic phenomenon involving immune complexes, nephritogenic streptococcal proteins or both. Several mechanisms have been proposed, including immune complex deposition, reaction of antibodies cross-reactive with streptococcal and glomerular antigens, alteration of glomerular tissues by streptococcal products such as a proteinase or streptokinase, and direct complement activation by streptococcal components deposited in the glomeruli (7).

1.2.6. Rheumatic Fever and Rheumatic Heart Disease

ARF, considered as a classical disease of poverty, commonly appears in children between the ages of 5 and 15 years in developing countries. It occurs 1–3 weeks after an untreated GAS pharyngitis and is an inflammatory disease, with marked tendency to recur. The cross-reactivity to antibodies is a type II hypersensitivity reaction. The M-protein of GAS generates antibodies that cross-react with auto antigens on interstitial connective tissue, particularly that of the endocardium and synovium which can lead to significant and serious clinical illness involving the heart including inflammation of all three heart tissues (pancarditis). Some cases of RHD may not have history of a recognized RF.

ARF is often clinically diagnosed based on Jones Criteria which were first published by Dr. T. Duckett Jones in 1944, as a set of guidelines for the diagnosis of ARF. These criteria have been periodically revised by the American Heart Association in collaboration with other groups. According to revised Jones criteria, the diagnosis of RF can be made when two of the major criteria or one major criterion plus two minor criteria, are present along with evidence of streptococcal infection (10). Major criteria include carditis involving the heart, migratory polyarthritis of large joints, subcutaneous nodules, erythema marginatum of skin and less likely as Sydenham chorea (which occurs months after an initial attack causing jerky involuntary and purposeless movements, muscle weakness, slurred speech, and personality changes). The most common clinical finding is a migratory arthritis involving multiple joints. Other indicators of GAS infection such as a DNAase or ASO serology test confirm the GAS infection. Minor criteria include fever, elevated ESR, increased P-R interval and arthralgia etc.

The rate of development of RF in individuals with untreated streptococcal sore throat is estimated to be 0.3% in endemic and 3% under epidemic condition. For individuals with a history of RF the risk rises to 50%. The risk of disease progression is determined by number of times RF occurs in an individual. Isolation of GAS from upper respiratory tract may reflect either infection or a ‘carrier’ state in both symptomatic and asymptomatic individuals. Most initial episodes of ARF can be prevented by treatment of GAS sore throat with appropriate antibiotics. Recurrences of RF can be prevented by regular administration of antibiotics after the initial attack to prevent occurrence of GAS sore throat. It is important to distinguish ARF from rheumatic heart disease (RHD). RF is an acute inflammatory reaction with pathognomonic Aschoff bodies histology and RHD is non-inflammatory sequelae of ARF.

RHD is the most common acquired pediatric heart disease worldwide which can be mostly prevented. The earliest report of RHD in India dates back to 1910. The younger age of onset of RHD seen in India is a feature of both public health and clinical importance. The consequences of RHD include: continuing damage to the heart, increasing disability, repeated hospitalization and premature death usually by 35 years or even earlier. The severity of RHD and the prognosis depend on the extent of the carditis. Endocarditis can develop with aseptic vegetations along the valve closure lines, particularly the mitral valve. Chronic RHD mostly affects the mitral valve which can become thickened with calcification of the leaflets.

Juvenile mitral stenosis, described in India, is a severe rapidly progressive disease affecting children. It is closely associated with organic tricuspid valve disease, severe pulmonary artery hypertension and congestive heart failure (11). On occasions, it may occur in older age groups, in the epidemics occurring in closed populations like military recruits, crowded living conditions and those in contact with school children.

RHD is the commonest heart disease associated with pregnancy. It is found in about 1% of pregnant women which leads to significant maternal and fetal morbidity and mortality (12-13). RHD is considered as one of the major indirect causes of maternal mortality in developing nations (14). Physiological changes occurring in the cardiovascular system during pregnancy has a negative impact on the health of pregnant women suffering from RHD.

1.3. Prevention and Control

Prevention and control of diseases caused by *S. pyogenes* can be achieved by education of parents, teachers and health care providers regarding the source, transmission, clinical course, treatment, and complications of *S. pyogenes* infections. Parents can also be educated regarding importance of primordial, primary, secondary and tertiary prevention. Salient features of these preventive strategies are provided below in tabular form.

1.3.1. Primordial Prevention

A consolidated effort is necessary to improve the socio-economic condition of the poorer strata in society, particularly to ensure proper housing to reduce overcrowding and malnutrition. Health education program should generate awareness regarding maintenance of both personal and environmental hygiene and about all the factors that predispose to GAS infection.

Prevention Strategies for ARF / RHD

Causal Pathway	Type of Prevention	Prevention Measures
Group A Streptococcal (GAS) sore throat	Primordial Prevention	Reduction in overcrowding, poverty and malnutrition Improve access to healthcare
Rheumatic Fever	Primary Prevention	Treatment of GAS sore throat with antibiotics/ development of GAS vaccine to reduce transmission, carriage and development of ARF
Rheumatic Heart Disease	Secondary Prevention	Regular prophylactic antibiotics for people who had ARF and are at risk of recurrence (for prevention of development of RHD) or in established RHD cases (prevention of progression of disease)
Heart Failure	Tertiary Prevention	Surgical and medical interventions to reduce mortality and morbidity

1.3.2. Primary Prevention

Primary prevention involving treatment of upper respiratory tract infection due to GAS is directed towards eradication of the bacteria from the throat, thus preventing initial attack of ARF. Studies have demonstrated that appropriate antibiotics given in the course of streptococcal infections prevent the subsequent development of RF. Some RF cases may not have a history of preceding sore throat.

The most appropriate antibiotic treatment for prevention of RF and RHD is Benzathine Penicillin G injection. The infection can usually be eradicated by a single intramuscular injection of Benzathine Penicillin G or by ten days treatment with oral penicillin. Failure to eradicate GAS from throat occurs more frequently with oral penicillin than with Benzathine Penicillin G injection. Penicillin remains the drug of choice as it is safe, effective and inexpensive. For patients allergic to penicillin, erythromycin is an acceptable alternative.

Efforts to ensure primary prevention of RF should be focused on education of general community regarding proper treatment for sore throat. Health personnel also need to be trained regarding early diagnosis and effective treatment of streptococcal pharyngitis. However, due inadequate laboratory resources, diagnosis of GAS is usually not feasible in developing countries. It is difficult to distinguish GAS sore throat from viral sore throats on clinical basis. Till date, no effective vaccine is currently available against streptococcal diseases though a number of candidate vaccines are in development phase. A safe and effective vaccine may become available within one or two decades.

1.3.3. Secondary Prevention

Secondary prevention is the regular administration of an antibiotic, usually penicillin, to a patient who has had RF or RHD in order to prevent colonization or infection of the upper respiratory tract with GAS to avoid subsequent development of the recurrent attacks of RF. For more than 20 years, World Health Organization has recommended secondary prevention as a cost-effective and practical strategy that can be effectively delivered within a coordinated program using a registry of patients even in the poorest countries. Secondary prevention strategy has shown to reduce recurrences, morbidity and mortality. Even with optimal patient adherence, the risk of recurrence is higher in individuals receiving oral prophylaxis than in those receiving intramuscular benzathine penicillin G.

1.3.4. Tertiary Prevention

Tertiary prevention is directed towards prevention of disability and premature death by surgical or medical management of heart failure and valve surgery, i.e., balloon mitral valvuloplasty or surgical mitral commissurotomy or valve replacement etc. The high cost of prosthetic valves, inadequate and limited facilities for operative procedures are barriers in provision of valve surgery to RHD patients in developing countries.

1.4. Jai Vigyan Mission Mode Project: Prevention and Control of RF/RHD

Prevention and control programs based on primary and secondary prevention strategies have been successfully implemented in most of the developed countries and in few developing countries. However, government health systems have not yet included RF/RHD in their priorities in most of the developing countries including India. Large scale demonstration projects that show that RF/RHD prevention and control program can be implemented successfully within the existing health services are needed for advocating policy and program development in this area. Surveillance of GAS and the diseases caused by it is also a priority to track temporal changes for prompt public health action. A safe and effective vaccine development for prevention of GAS diseases should also be a priority as

GAS is acquiring resistance against many commonly used antibiotics; though fortunately it still remains sensitive to penicillin but emergence of penicillin resistant strains can't be ruled out. Hence, in order to address some of these issues, Indian Council of Medical Research initiated a Jai Vigyan Mission Mode Project on RF/RHD Control in several districts of India.

2. Review of Literature

As discussed earlier in Chapter 1*, S. pyogenes* is responsible for wide spectrum of human infections ranging from upper respiratory tract infections (pharyngitis), skin infections (impetigo and pyoderma) to invasive diseases (cellulites, bacteraemia, necrotizing fasciitis and streptococcal toxic shock syndrome) and non-suppurative sequels such as ARF and AGN. ARF is the most common sequel which further leads to RHD, a condition where the heart muscles and valves are damaged.

Determinants of RF and RHD disease burden

Despite a documented decrease in the incidence of acute RF prevalence of RHD in developed countries during the past five decades, these cardiovascular sequel of GAS pharyngitis remain problems of public health significance in developing countries.

Major socioeconomic and environmental factors responsible for the disease include poverty, under-nutrition, overcrowding and poor housing. These factors cause rapid spread of GAS strains leading to higher incidence of pharyngitis and its suppurative complications. A constrained health care system, low expertise of health care providers, inadequacy of secondary prophylaxis and lack of awareness among community regarding these diseases further complicates the situation.

2.1. Global Overview

On a global scale, *S. pyogenes* or GAS is an important cause of morbidity and mortality. It is the most common bacterial cause of acute pharyngitis, accounting for 15%–30% of childhood cases and 10% of adult cases (15). These cases place a high burden on the health care system and society as a result of doctor's visits, treatment costs, and the loss of working days (16). A number of epidemiological factors including age of patient, season of the year and geographical area play a major role in GAS infections especially pharyngitis.

In developed world, GAS related diseases, i.e., ARF had steadily decreased throughout the 20th century but in the 1980's and 1990's, a resurgence was seen (17). These resurgences have made this organism again an important pathogen. The WHO global burden of disease estimates indicates that GAS diseases continue to be a public health problem in most of the developing countries.

A survey conducted by WHO between 1986-1990 indicated that in developing countries, around 2.2 out of every 1000 school going children suffer from RF/RHD (18) whereas in developed countries, this disease had become rare. According to a report by the WHO (2004), at least 12 million people suffer from RHD and 3, 32,000 deaths annually are attributable to RF/RHD. An estimated 6.6 million Disability Adjusted Life Years (DALYs) are lost per year worldwide due to RF/RHD (19) .

Another WHO report released in 2005 estimated that there are about 15.6 million cases of RHD world-wide. A vast majority of these are in developing countries. About 2, 82,000 new cases of RHD occur every year, and 2, 33,000 people die due to RHD each year. Over 4,70,000 new cases of RF occur each year (14).

The burden of invasive GAS diseases is also high, with at least 6, 63,000 new cases and 1, 63,000 deaths each year (14). As previously reported by the Centers for Disease Control and Prevention Active Bacterial Core (ABCs) surveillance system estimated that the rate of invasive GAS disease in the United States during 1995–1999 was 3.1–3.8 cases per 100,000 population, resulting in 9000–11,000 cases and 1000–1700 deaths per year, with a case fatality ratio of 11.7%–14.8% (20). From 2002-2004, the average incidence of invasive GAS diseases was 3.5 per 100,000 with 735 deaths per year (case fatality ratio 13.7 %). The Strep-EURO program, which analyzed data gathered in 11 participating countries, reported the epidemiology of severe *S pyogenes* disease in Europe during 2000s (21). A crude rate of 2.46 cases per 100,000 individuals was reported in Finland, 2.58 in Denmark, 3.1 in Sweden, and 3.31 in the United Kingdom. In contrast, the rates in the more central and southern countries, the Czech Republic, Romania, Cyprus, and Italy were substantially lower (0.3-1.5 per 100,000 individuals), perhaps due to poor diagnostic microbiological investigative methods in these countries.

Surveillance for invasive GAS disease is not well developed in developing countries. A Kenyan study found that the incidence of GAS bacteraemia in children <15 years was 13 per 100,000 with a comparatively high mortality rate of 25%. Aboriginal Australians are at particularly high risk of invasive infections. Crude hospital-based incidence rates of invasive GAS disease were 23.8 and 82.5 per 100,000 in the Northern Territory and in north Queensland respectively (22). Invasive GAS infections are more common in adults with other co-morbidities although many cases (almost all in children) occur in otherwise healthy individuals.

Rodriguez-Iturbe *et al* (2008) reviewed the global burden of acute glomerulonephritis (AGN) (23). The incidence of AGN ranged from 9.5-28.5 new cases per 100,000 individuals per year. Globally, AGN accounted for 2.6% to 3.7% of all primary glomerulopathies from 1987-1992, but a decline has been noticed between 1992 and 1994. In China and Singapore, the incidence of AGN has decreased in the past 40 years. In Chile, the disease has virtually disappeared since 1999, and in Maracaibo, Venezuela, the incidence of sporadic AGN decreased from 90-110 cases per year from 1980-1985 to 15 cases per year from 2001-2005. In Guadalajara, Mexico, the combined data from two hospitals showed a reduction in cases of AGN from 27 in 1992 to only 6 in 2003.

Overall there are at least 5, 17,000 deaths each year due to severe GAS diseases (includes ARF, RHD, AGN, and invasive infections). The prevalence of severe GAS disease is at least 18.1 million cases, with 1.78 million new cases each year (14).

In a meta-analysis Sheikh *et al* (2010) found a significant heterogeneity among the estimates from the reported data on the prevalence of GAS among children with sore throat (24). The prevalence of GAS was 36%. Sensitivity analysis revealed that prevalence of GAS was very similar when the analysis was restricted to studies that were conducted in the United States or Canada (37%). Studies were also included that presented data on GAS carriage among asymptomatic children who were younger than 18 years. On stratified analysis, prevalence of GAS carriage was found to be lower in studies that included only children who were younger than 5 years as compared with studies that included children of all ages. The pooled prevalence of GAS carriage was found to be 12%.

The incidence of GAS infections was compared between developing countries like India and Australia (25). The etiology of pyoderma differs between developing and industrialized nations. Pyoderma is endemic in children in many developing countries with prevalence rates averaging 7%. A study by Nandi *et al.* (2001) shows that the incidence of GAS culture-positive pharyngitis in school-aged children ranges from 0.95 per child-year in an urban slum area of northern India to 0.13 per child year in urban Melbourne (22, 26). Also, the GAS impetigo is more common (6.9 per 100 child visits) in the tropical climate of south India.

Regarding the prevalence of serotypes based on *emm*-typing, the global *emm* type distribution in different regions show similarities in *emm* type distribution among the high-income countries, Asia, the Middle East, and Latin America in contrast to the distribution in Africa and the Pacific region (25). In high-income countries, 25 *emm* types accounted for 90·3% of all isolates, and 146 types

contributed the remaining 9·7%. In Africa, 26 *emm* types accounted for 62·5% of all isolates, and 65 contributed remaining 37·5% of the isolates. Twenty six *emm* types accounted for 61·8% of all isolates from the Pacific region, and 74 types contributed the remaining 38·2% of the isolates.

Steer *et al.* (2009) further suggested that *emm*1 and *emm*12 were the two most common *emm* types in high-income countries, Asia, and Latin America, and the second and third most common *emm* types in the Middle East, accounting for between 26·1% and 40·0% of all isolates in these regions (25). By contrast, *emm*1 was ranked fifth in Africa and 13th in the Pacific region, accounting for 3·6% and 2·0% of isolates, respectively. The *emm*12 did not appear in the 25 most common sequence types in the Pacific region. Other than *emm*1 and *emm*12, there were several other common *emm* types found in high-income countries, Asia, the Middle East, and Latin America; these included *emm*4 and *emm*6, which were ranked among the eight most common *emm* types in all four regions. By contrast, *emm*4 was ranked 32nd in the Pacific region and it was not reported in any of the African studies included in the database, whereas *emm*6 was ranked 29th in Africa and it was not reported in any of the Pacific studies. There was greater diversity of *emm* types in Africa and the Pacific than in other regions, as indicated by the smaller proportions of isolates accounting for the first 25 *emm* types in these regions.

A vaccine has been developed against GAS that comprises of 4 recombinant proteins adsorbed to aluminum hydroxide containing N-terminal peptides from streptococcal protective antigen and M proteins of 26 common pharyngitis, invasive, and/or rheumatogenic serotypes. It was believed that this 26-valent vaccine could have a significant impact on the overall burden of streptococcal disease (27). These 26-valent vaccines are undergoing clinical trial in USA (28). This tentative 26-valent M-protein-based GAS vaccine covers all isolates or the clinical disease state (includes *emm* types 1, 2, 3, 5, 6, 11, 12, 14, 18, 19, 22, 24, 28, 29, 33, 43, 59, 75, 76, 77, 89, 92, 94, 101, 114) (29). Recent studies of GAS disease in North America found that *emm* types in the 26-valent vaccine accounted for 79% of all invasive isolates from ten sites in the USA between 2000 and 2004, and 85% of pharyngitis isolates from 13 sites in the USA and Canada between 2000 and 2007 (30). However, the efficacy of this vaccine against most prevalent GAS emm types in India remains to be investigated. Recently, a 30-valent vaccine has been designed and studied for efficacy which contains M protein peptides from GAS serotypes prevalent in North America and Europe (31).

2.2. Indian Scenario

Over the past century, as living conditions have become more hygienic and less crowded, and nutrition and access to medical care have improved, RF and RHD have become rare in developed countries. But, in developing countries like India, in the Middle-East and sub-Saharan Africa this disease is still the commonest preventable cardiac disease in children and young adults with a public health significance (32).

In India, incidence of GAS sore throat is more common among 5-15 years age group. The prevalence of GAS pharyngitis and carriage ranges from 4.2% to 13.7% and 1.3% to 20% respectively (26, 33-34). The incidence of GAS culture positive pharyngitis among 5-15 year old urban slum children near Chandigarh in northern India was 0.95 episodes per child per year (26). GAS impetigo is also quite common in India.

The earliest report of RHD in India dates back to Nineteenth century. A professor of pathology in Calcutta Medical College reported a single case of RHD in Indians among 4800 post-mortem records of 37 years (35). However, Kutumbiah (1958) reported that RHD accounted for 40% of heart cases in males and 52% in females in 1935 (36)

Even during the 1980s, hospital admission data suggested that RF/RHD accounted for nearly one-half to one-third of the total cardiac admissions at various teaching hospitals in India (37). A recent survey across various tertiary care hospitals also found that hospital admission rates of RHD vary from 5%–26% of all cardiac admissions (38). A report from Cuttack in Orissa suggested that the number and proportion of RF/RHD did not decline significantly over a 20-year period. RF and RHD cases accounted for 45% of total cardiac cases even during 1991–2000 (39).

Epidemiological surveys on RF/RHD have been conducted in selected population groups in India. A house-to-house survey of a random sample of 33,361 subjects (all ages), comprising one-third of the total urban population of Chandigarh, showed the prevalence of chronic RHD and RF to be 1.23/1000 among males and 2.07/1000 among female subjects. In this survey, of the 48 cases of RHD, 62% gave a history suggestive of RF (40). A population study in 1993 reported a prevalence of 0.9/1000 for RHD in a rural area of Raipur Rani in Haryana (41). A cross-sectional study carried out in rural areas of Aligarh, Uttar Pradesh covering a total population of 3760 drawn from 11 villages showed the total number of confirmed cases of RHD was 24 with a prevalence rate of 6.4 per 1000

general rural population. It was found that the prevalence of RHD increased with age until the age of 25 years and females were more prone RHD as compared to males (42).

Most of the epidemiological studies in India are school-based surveys. After World War II, several school surveys have been reported. Between 1940 and 1983, school surveys estimated the prevalence of RHD to be between 1.8 and 11 per 1000 (average 6 per 1000) in school children. While from 1984 to 1995, lower prevalence (1 to 3.9 per 1000) has been reported, but the evidence for a decline in RF/RHD has not been conclusive, as these cross sectional surveys covered different populations. As regards ARF, the prevalence was estimated to be 0.05 to 1.7 per 1000 (from 1940-1983) and 0.18-3.0 per 1000 (from 1984-1995) as reported by Padmavati (1995) (43). Recent epidemiologic studies of RHD prevalence have used clinical screening along with echocardiographic confirmation of the suspected cases and report very high prevalence (44). The prevalence of RHD was estimated to be 4.54 per 1000 individuals by Padmavati (2001)(45). A survey from Shimla (46) showed that the prevalence of RF/RHD was 2.9/1000 children in 5-15 years age group. A total of 15,080 children were screened and the prevalence was found to be significantly greater in rural schools (4.8/1000) than in urban schools (1.98/1000). Recently a review indicated that the prevalence of RHD estimates range from 0.5/1000 in Gorakhpur to 0.67/1000 school children in Vellore (47).

Recent surveys have used auscultation to screen for murmurs which later use echocardiography for diagnosis of RHD (48). Echocardiography has also been used for screening. In schools of Bikaner city, 1059 children aged 6–15 years screened for RHD by echocardiographic study reported that the prevalence of rheumatic heart disease was 51 per 1,000 (49). Another study carried out in Ballabgarh reported RHD prevalence of 20.4/100 in school children (49a). This indicates indicate high burden of RHD in the population which is not detectable by the usual clinical methods (auscultation). The detection of large number of subclinical RHD lesions by echocardiography in these studies suggests the importance of investigating the natural course of these subclinical lesions through large prospective studies in different parts of the world.

Shet *et al* (2004) reviewed the epidemiology of GAS diseases in India (50). According to them if one assumes that 0.3% of the streptococcal sore throat episodes in endemic situation and 3% during epidemics develop into ARF(51) , there would be between 50,000 and 500,000 new cases of ARF in India every year. Approximately 60% of the acute RF episodes may progress to damage the heart valves causing RHD. However, considering a median RF incidence of 0.5/1000 Shrivastava, (2007)

estimated that approximately 1,31,000 children suffer from RF every year in India (52). Considering the lowest and the highest reported prevalence of RHD in the population/schoolchildren, the number of RHD cases in India could range from 0.44 to 3.37 million (47).

The bottom line is that the burden of RF/RHD continues to be high in India, hence, RHD should be detected early and secondary prophylaxis needs to be implemented. If a safe RF vaccine becomes available, it will be a boon for control of this disease (45).

The diversity of *emm* types in developing countries is quite high, and new *emm* types emerge frequently. Therefore, while M type-specific vaccines may hold promise in affluent communities, these may prove to have limited effectiveness in developing countries and other settings with high rates of GAS diseases. A recent study from Karnataka showed the comparison of various studies which clarify that distinct differences do exist among the *emm* types identified among GAS isolated from Bangalore, Chennai and Chandigarh (53). Interestingly, types 12, 49, 71 and 74 and to some extent type 1 are common to the above regions which confirm the high diversity among Indian GAS isolates as well as significant regional differences among the distribution of *emm* types.

Considering the high heterogeneity among the GAS isolates and distinct differences existing among them in different parts of India, the concept of a multivalent GAS vaccine may not work and further studies are needed to identify alternate candidate antigens (single or multiple or a combination) for vaccine development.

2.2.1. ICMR Studies

ICMR's study between 1972 to 1975 included 1,33,000 children in age group of 5 to 14 y in schools at Agra, Allepy, Bombay, Delhi and Hyderabad whereas that between 1984 to 1987 included population of 2,17,000 with 53,986 children in age group of 5 to 14 y in schools at Delhi, Varanasi and Vellore The prevalence rate of RHD observed in these studies ranged from 0.8/1000 to 11/1000 in 1970s to 1.0/1000 to 5.6/1000 in 1980s.

The studies on primary and secondary prophylaxis have shown the efficacy of these methods (54). Implementation of primary prevention is very difficult as it has to be given either to all cases of sore throat or in children from whom GAS are isolated. Since isolation of GAS is almost impossible due to lack of culture facilities in most health institutions before initiation of antibiotic treatment, primary

prevention is difficult to practice. Moreover, majority of patients with sore throat do not visit clinic. Hence, secondary prophylaxis remains the cornerstone for prevention of RF.

Most of the earlier ICMR studies have been conducted in areas well served by health services in better income populations. The burden of RF/RHD in some of the under developed states such as Bihar, UP, Jharkhand, Orissa, MP, North Eastern regions and Jammu & Kashmir State could be quite high, hence, registry-based secondary prevention RF/RHD control program needs to be initiated. Surveillance studies are also needed to track time trends and emergence of new or more virulent strains. Efforts for development of vaccines using Indian strains of GAS also need to be accelerated.

3. Epidemiology of Group A Streptococci

3.1. Introduction

During the past decades lot of Group A ß hemolytic Streptococcus (GAS) related epidemiological data has been generated (55). Worldwide burden of GAS diseases has been estimated (14). At least 5,17,000 persons die every year due to severe GAS infections and over 616 million new cases of GAS pharyngitis occur in a year (14). It is estimated that 0.3% of the streptococcal sore throat episodes in endemic situations and 3% during epidemics develop into ARF and 60% of the RF episodes may cause RHD (51).

Although ARF and RHD have declined remarkably in the developed countries, due to the improved socioeconomic conditions, timely diagnosis and treatment of streptococcal pharyngitis and an unexplained decrease in the virulence of group A Streptococcus, but it still remains a leading cause of cardiovascular morbidity and mortality in developing countries like India (56).

Epidemiological data from developing countries is scarce. Prevalence of GAS pharyngitis and carriage in children in different countries varies from 9% to 34.1% (57-59). Incidence of streptococcal pharyngitis has been reported to be 8-18 episodes per week per 1000 children in the age group of 5-15 years in India. According to Bisno *et al.* (1996), GAS pharyngitis from 15% to 20% or more was found in 5-15 years age group, depending upon the epidemiological factors including age of patient, season and geographic area; however it was less common among children in first 3 years of life (60).

In India, prevalence of GAS pharyngitis and carriage ranges from 4.2% to 13.7% and 1.3% to 20% respectively (26, 33, 50, 61, 62). Sore throat among rural school children in Varanasi ranged from 16% to 27% showing age dependent variation (63). Similarly Jasir *et al*. (2000) showed 34.1% isolation rate of GAS in children with pharyngio-tonsillitis as compared to 20% in adults (59).

GAS impetigo is also common in India (62). In aboriginal communities of northern territory of Australia, the incidence of GAS pyoderma was reported to be in almost 40% of children at least once, and the prevalence was greatest during dry season (22).

Initially GAS was characterized by M protein serotyping but that method is not widely used now because of the non-availability of sera commercially. Identification based on nucleotide sequence of

the *emm* gene encoding M protein, i.e., *emm* typing has become successful these days. On that basis more than 200 *emm* types have been isolated. There is a probability that *emm* types prevalent in India are different from those reported elsewhere.

Group C and G streptococci, genetically close relatives of GAS, are now considered to be capable of causing a range of clinical signs and symptoms just similar to those seen with GAS such as pharyngitis, epidemic acute nephritis as well as invasive diseases (64). It has also been hypothesized that non- GAS infections may be the driving forces behind ARF in the aboriginal communities of Australia (65) . Hence, human GCS and GGS should also be included while studying the epidemiology of *S. pyogenes* infections.

Strain prevalence rather than the innate virulence potential is considered to be a major factor for the observed increase in serious GAS infections (66). Some GAS serotypes are much more common than others within a population in different geographical locations (67). In the absence of GAS type distribution data, true propensity of any M type to cause a specific clinical manifestation still remains controversial. Moreover, the eventual introduction of vaccines, especially those based on multiple M protein protective epitopes, require better understanding of GAS types. Hence, epidemiological surveillance of the GAS was initiated in different regions of India in the present study.

3.2. Objectives

The main objectives of the project were:

a) To find out the prevalence of GAS sore throat and skin infections in children aged 5 to 14 yrs
b) To identify GAS carrier rates in the children (5-14 years)
c) To define the prevalent strains of GAS by emm-typing.

3.3. Methodology

The epidemiology of GAS was studied in four phases at several centers in India from 2000 to 2007. Throat and skin swabs were collected using standard procedures.

3.3.1. Study Areas

In the first phase (2000-2002), school surveys were carried out by PGIMER, Chandigarh and CMC, Vellore. A cross-sectional survey was carried out among rural school children (5-15 years) in the

Raipur Rani block of Panchkula district in Haryana state and Kaniyambadi Block of Vellore district in Tamil Nadu. A sub-sample of children was also followed up fortnightly for one year.

In the second phase (2002-2007), school surveys were carried out as part of the RF/RHD registry at in Rupnagar district of Punjab near Chandigarh and from several schools in the Vellore Health Unit District. Then, in the third phase (2007-10) three satellite centers were set up at Shimla in Himachal Pradesh, Jammu in Jammu & Kashmir and Jodhpur in Rajasthan coordinated by PGIMER, Chandigarh, and one center was set up in Dibrugarh in Assam which was coordinated by CMC, Vellore and one centre in urban area of Mumbai in Maharashtra was set up which was coordinated by AIMS, Kochi (Figure. 3.1).

3.3.2. Staff Training

Before the commencement of the study, newly appointed staff was trained for collection and processing of samples along with isolation, identification and preservation of GAS. A manual of standard operating procedures (SOPs) was prepared by PGIMER, Chandigarh for all the centers. The manual also outlined the schedule of activities that each center should follow before the start of the project.

Laboratory training included instrument handling and maintenance, collection and transport of throat swab and skin swab, preservation of GAS collection, culturing of throat swab and skin swab, preparation of media (blood agar plates), processing of samples, identification and purification of Beta Hemolytic Streptococci (BHS) from mixed culture, isolation of DNA from GAS, grouping by streptex kit, agarose gel electrophoresis to visualize DNA, demonstration of PCR technique, amplification of *emm* gene by PCR agarose gel electrophoresis for visualization of PCR product.

In order to standardize the protocol and procedures among the Nodal Centers, a workshop was held in the Christian Medical College, Vellore in 2001 which was attended by investigators from CMC Vellore, PGI Chandigarh and Amrita Institute of Medical Sciences, Kochi. Diagnostic criteria, case definitions, inclusion and exclusion criteria and the proformae to be used in this registry for investigating GAS epidemiology were discussed and agreed. The system of collection and transportation of throat swabs, process of inoculation, culturing and typing were observed in the laboratory in order to standardize the process across all centers.

Another training program for satellite centers was also held at the Christian Medical College, Vellore in August 2007. Some of the important aspects covered in the training program included selection of

partners, networking, implementation, protocols for RF, RHD diagnosis, school surveys, monitoring and challenges. Separate sessions were conducted on the Microbiology, Cardiology and Field Components of the project. In addition to investigators from the satellite centers, the training program was also attended by investigators from the nodal centers and scientists from ICMR and members of the project steering committee.

3.3.3. Processing of the Specimen

In the first (2000-2002) and second phase (2002-2007) of study, all the samples collected from Raipur Rani Block of Panchkula district were brought to the laboratory at Experimental Medicine and Biotechnology, Post Graduate Institute of Medical Education and Research, Chandigarh, and from Kaniyambadi Block of Vellore district in Tamil Nadu to laboratory at Department of Microbiology, Christian Medical College, Vellore. Early transportation of the samples was made to the lab to maintain the viability of the organism. In the third phase of study (2007-2010), samples were collected and processed at the satellite centers. All the confirmed GAS strains were sent to the respective coordinating centers for reconfirmation of GAS and *emm* typing.

Throat and skin swabs were inoculated on blood agar plate (Columbia agar base with 5-7% defibrinated sheep blood). Streaking was done over the plate with a sterile loop following a quadrant method to obtain well-isolated colonies. The loop was stabbed several times into the medium to grow the organism under low oxygen tension. Plates were incubated overnight at 37°C with 5% CO_2 in incubator/candle jar.

3.3.3.1. Presumptive Identification of Group A Streptococcus

Typical beta hemolytic colonies (producing complete hemolysis) with circular and entire edge and 0.5 to 2mm in diameter were sub-cultured on blood agar plate for further isolation and purification. Bacitracin sensitivity of all the suspected beta hemolytic colonies was checked on blood agar plate with bacitracin disc (0.05U/disc).

3.3.3.2. Confirmation of Group A Streptococcus

All the bacitracin sensitive strains were further processed for grouping (Fig. 3) by Latex agglutination by Streptex kit (Murex Biotech Ltd, UK). Strains were preserved by storing at −70°C in glycerol stocks (Todd Hewitt broth + 20% glycerol) at respective coordinating centers.

3.3.4. *emm* Typing

The *emm* typing was done at coordinating centers, i.e., at CMC, Vellore and PGIMER, Chandigarh.

3.3.4.1. Preparation of Genomic DNA

Genomic DNA was prepared manually by the method of the modified SDS-phenol method. Bacterial cells were harvested from 1.5 ml saturated culture of GAS in Todd-Hewitt broth and re-suspended in 567μl of TE buffer (pH 7.8). It was followed by addition of 30μl of 10% SDS to a final concentration of 1% and 3μl of proteinase K (20mg/ml) to final concentration 100μg/ml. The cells were incubated at 37^0C for 1 hour and lysed with 5M NaCl and 10% CTAB/NaCl mixture at 65^0C for 10 minutes. Finally, extraction was done with chloroform/isoamyl alcohol followed by phenol-chloroform-isoamyl alcohol. DNA was precipitated with 0.6 volume of alcohol and the pellet collected by centrifugation was washed twice with 70% ethanol. The pellet was then dried and dissolved in 30μl of TE buffer and stored at -20^0C for future use. Genomic DNA isolation was also standardized using commercially available kits in order to save time and resources.

3.3.4.2. Quantification of Genomic DNA

The DNA was quantitated using UVIKON spectrophotometer (Pharmacia). The DNA samples were diluted and absorbance was read at 260 nm and 280 nm. The purity of DNA was checked by measuring the ratio of A_{260} to A_{280}. The concentration of DNA solution was calculated using formula: DNA concentration (in μg/ml) = A_{260} X 50 X dilution factor.

A_{260} of 1 corresponds to DNA concentration of 50 μg/ml of H_2O.

3.3.4.3. Agarose Gel Electrophoresis

Genomic DNA was visualized on agarose gel. The percentage of the gel varied from 0.8-1.5% depending on size of DNA fragments. Gels were run in 0.5X TBE buffer at 5-10 V/cm. 6X gel loading dye was used for loading samples (final concentration 1X). Ethidium bromide (10mg/ml) was used at a final concentration of 0.5μg/ml for staining gels. The gels were then visualized on Chemilmager™ 4400 (System and Control).

3.3.4.4. Storage of DNA

Stock DNA was kept at -20°C for long time storage. Small aliquot of DNA was kept at 4ºC for short term analysis.

3.3.4.5. *emm* typing by Polymerase Chain Reaction

The *emm* gene of *S. pyogenes* encodes a major virulent factor, the M protein. The variable 5´sequences of the majority of the *emm* genes confer established distinguishable M serotypes to *S. pyogenes* isolates. Following primers were used.

Primer	Sequence (5'-3')
emm F	ATAAGGAGCATAAAAATGGCT
emm R	AGCTTAGTTTTCTTCTTTGCG

Reaction was performed in a total volume of 50 µl. Each reaction mix contained 1X buffer, 5µl; Primer (Forward & Reverse), 4.0µl each; 200µM each of deoxyribonucleotide triphosphate (dATP, dCTP, dGTP, dTTP); 1.0 unit of Pwo DNA polymerase (high fidelity enzyme); template DNA, depending on the concentration of the DNA. The final volume was made to 50 µl with sterile double distilled water.

PCR conditions were as follows: 94^0C-5min (94^0C-1min, 55^0C-1min, 72^0C-1.30min)× 35 cycles, 72^0C- 7 min and then at 4^0C till the PCR product was purified.

3.3.4.6. Agarose Gel Electrophoresis

PCR product was visualized on 1% agarose gel. Gels were run in 0.5X TBE buffer at 5-10 V/cm. 6X gel loading dye was used for loading samples (final concentration 1X). Ethidium bromide (10mg/ml) was used at a final concentration of 0.5µg/ml for staining gels. The gels were then visualized on Chemilmager™ 4400 (System and Control).

3.3.4.7. Purification of PCR Product

The PCR product was purified by Qiagen PCR purification kit as described by the manufacturer.

3.3.4.8. Sequencing of *emm* gene

Sequencing of *emm* gene was carried out in an ABI prism automated DNA sequencer. Big dye terminator reaction kit version 3.1 was used for the sequencing of PCR products according to the manufacturer's instructions. Briefly, 2 µl of ready reaction mix (containing polymerase, dNTPs and ddNTPs) provided in the kit, template, depending on the concentration of the DNA, forward primer (1pM) 1.6 µl, sequencing buffer (1x) 1.0 µl were added. The final volume was made to 10 µl with

sterile double distilled water. The conditions of the sequencing reaction were: 96^{0}C-10 sec, (96^{0}C-10 sec, 50 ^{0}C-0.5 sec, 60^{0}C-4 min) x 25 cycles, 4^{0}C till the reaction mix was purified.

3.3.4.9. Purification of Sequencing Reaction Mix

To remove the unincorporated dye, unused primer and unused dNTPs, reaction mix was purified by standardized protocol. The procedure included the following steps. 12 µl of master mix l (10 µl of milli Q water + 2 µl of 125 mM EDTA) was added to 10µl of sequencing reaction followed by addition of 52µl of master mix ll (2µl of 3 M sodium acetate pH 4.6 and 50 µl of ethanol). Contents were mixed and incubated at room temperature for 15 min and then centrifuged at 12000xg for 20 min to obtain DNA pellet. The pellet was washed twice in 70% ethanol and air-dried. Finally, the DNA precipitate was dissolved in 12-15µl Hi Di formamide and denatured by heat (at 95^{0}C for 4-5 min) and chilling and was kept in the instrument for sequence read.

3.3.4.10. Sequence Analysis of the Amplified *emm* gene

Sequence obtained with forward primer of *emm* gene was subjected to homology search against CDC reference strains (http://www.cdc.gov/ncidod/biotech/strep/strepblast.htm) as well as by Blast Search Analysis (http://www.ncbi.nlm.nih.gov/BLAST/Blast.cgi) and *emm* type and subtype was designated to each strain by CDC formulations.

3.3.5. Quality Control

Strict quality control measures were observed. All the chemicals and media used were of analytical grade. All standardized protocols were documented and strictly followed and carried out along with positive and negative control. All media were first checked for sterility and tested with a reference strain of GAS. All the GAS strains isolated at satellite centers were checked and reconfirmed at the coordinating centers.

Records were maintained for all the chemicals, media and protocols. These were tested on a regular basis. Similarly, the protocol for *emm* PCR and sequencing were documented. All samples were run with positive and negative control. All components of PCR reaction mixture were stored at -20^{0}C in small aliquots to avoid repeated freezing and thawing. Log book was maintained for all the instruments.

3.4. Results

In the initial period of the project, cross-sectional as well as cohort studies were conducted at Chandigarh (2000-02) and Vellore center (2001-02). Registry-based GAS epidemiological studies

were conducted in Chandigarh (2002-07), Mumbai (2007-10), Dibrugarh (2007-10), Jodhpur (2007-10), Shimla (2007-10) and Jammu (2007-10) center.

3.4.1. Cross-Sectional Study (2000-02)

3.4.1.1. GAS Isolates from Throat Swabs

Table 3.4.1 presents GAS isolates from throat swabs from cross sectional study. In a rural community near Chandigarh, out of 579 sore throat swabs, Group A and Group G streptococci were found in 16 (2.8%) and 2 (0.3%) children respectively; whereas out of the 3,385 throat swabs collected from children without any sore throat, GAS was found in 44 (1.3%) samples. However, no Group G & C streptococci were identified in children who did not have sore throat. In Vellore, out of 657 sore throat swabs, Group A, B, C and Group G streptococci were found in 74(11.3%), 12(1.8%), 27(4.1%) and 62 (9.4%) children respectively; whereas out of the 3,357 throat swabs collected from children without any sore throat, Group A, B, C and Group G streptococci were found in 418(12.5%), 77(2.3%),100(3.0%) and 317 (9.4%) children respectively.

3.4.1.1.1. emm Types from Throat Swabs

Table 3.4.2 represents the distribution of *emm* types of GAS isolates from throat swab in cross-sectional study (2000-02). Out of the 8 different *emm* types identified *emm* 77, *emm* 81 and *emm* 11 were most common *emm* types in the rural community near Chandigarh whereas in Vellore out of the 175 different *emm* types identified, *emm* 112, *emm* 11 and *emm* 82 were most common. The strains from rural community near Chandigarh and Vellore showed prevalence of 14 and 52 different emm types.

3.4.1.2. GAS Isolates from Skin Swabs

Table 3.4.3 presents the details of GAS isolated form skin swabs of children in cross-sectional studies. From rural communities near Chandigarh, 28 impetigo swabs were collected and only 2 (7.1%) GAS was isolated from these swabs whereas out of the 4,221 skin swabs taken from children without impetigo, not even a single GAS specimen could be isolated. In contrast from Vellore, 205 impetigo swabs were collected and 56(27.3%) GAS, 3(1.5%) GBS, 2 (1.0%) GCS were isolated whereas out of the 366 skin swabs taken from children without impetigo, 29(7.9%) GAS, 4(1.1%) GBS were isolated.

3.4.1.2.1. *emm* Types of GAS isolates from Skin Swabs

Table 3.4.4 shows a wide variety of *emm* isolates from skin swabs from Chandigarh and Vellore. The *emm* 77 and *emm* 44 were reported from Chandigarh whereas in Vellore, 59 different *emm* types were found. Out of 52 *emm* types, *emm* 100 and *emm* 112 were most common.

3.4.2. Cohort Study (2000-02)

3.4.2.1. GAS Isolates from Throat Swabs

Table 3.4.5 shows the results of GAS isolates obtained from throat swabs of children in cohort study (2000-02). In rural communities near Chandigarh, out of the 761 samples collected from children having sore throat, 18 (2.4%) GAS were isolated. Twenty six (1.3%) GAS were isolated from 2,016 samples collected from children having no sore throat and no Group C and Group G streptococci were isolated.

Vellore reported 31(7.9%) GAS from 391 sore throat swabs and 347(11.4%) GAS from 3,044 throat swabs taken from children who did not have sore throat. Other groups reported were Group B (18 in sore throat and 45 in no sore throat); Group C (14 in sore throat & 99 in no sore throat); Group G (35 in sore throat & 242 in no sore throat).

3.4.2.1.1. emm Types of GAS Isolates from Throat Swabs

Table 3.4.6 presents different *emm* types of GAS isolates form throat swabs collected in cohort study. In Chandigarh, out of the 27 isolates, 11 different *emm* types of GAS were present; *emm* 81, *emm* 77 and *emm* 71 being most common. In Vellore, out of the 100 GAS isolates, 42 different *emm* types were reported; most common types among these were *emm* 112, *emm* 110 & *emm* 82.

3.4.2.2. GAS Isolates from Skin Swabs

Table 3.4.7 shows GAS isolates from skin swabs of children obtained from the cohort study. In Chandigarh, out of the 75 samples of impetigo, only 2(2.7%) GAS were isolated, whereas out of the 2,312 skin swabs from children without impetigo only 1(0.04%) GAS was isolated. In Vellore, out of the 938 skin swabs from impetigo cases, 236 GAS (25.2%), 22 GBS, 15 GCS and 3 GGS were isolated, whereas out of 2,493 specimens collected from children without impetigo, 56 GAS (2.2%), 14 GBS, and 1 GCS were isolated.

3.4.2.2.1. *emm* Types of GAS Isolated from Skin Swabs

In Chandigarh, one GAS isolate identified from skin sore was *emm* type 77. Twelve different *emm* types were identified from 21 GAS strains in Vellore; e*mm* 100 and e*mm* 112 being the most common types (Table 3.4.8).

3.4.3. GAS Epidemiology in Registry Project (2002-10)

3.4.3.1. GAS Isolates from Throat Swabs

Tables 3.4.9 presents GAS isolates from throat swabs collected in the registry project (2002-10). Chandigarh, Mumbai, Dibrugarh, Jodhpur, Shimla and Jammu centers carried out the surveillance for GAS in registry project areas. In these centers the prevalence of GAS in pharyngitis cases ranged from 0.1% to 8.3% whereas among non-pharyngitis children the prevalence was 0% to 3.3%. Group C and Group G were also isolated from both pharyngitis and non-pharyngitis cases in Mumbai, Shimla and Jammu.

3.4.3.2. *emm* Types of GAS Isolates from Throat Swabs

Table 3.4.10 shows the *emm* types of 148 GAS isolates from throat swabs from the registry project. A total of 148 GAS were *emm* typed from different centers: Chandigarh (26), Mumbai (35), Dibrugarh (1), Jodhpur (38), Shimla (47), and Jammu (1). Out of these 49 different *emm* types were identified. The most prevalent *emm* type found was *emm* 12 followed by *emm 4*2, *emm* 1, *emm* 81, and *emm* 57.

3.5. Discussion

Different terminologies have been used by scientists from all over the world for streptococcal infection like carriers, infection, colonization etc. making it difficult to distinguish between streptococcal carriage and true infection with GAS.

In this study, GAS prevalence in sore throat cases ranged from 2.4% (Chandigarh) to 7.9% (Vellore) in different regions whereas among those who were not having sore throat, the prevalence varied from 1.3% (Chandigarh) to 11.4% (Vellore). The prevalence of GAS carriage was high in Vellore and lowest in Chandigarh center. Other centers showed the GAS prevalence in the range of 0.1% (Jammu) to 7% (Shimla) in sore throat cases and from 0% (Jammu) to 3.3% (Jodhpur) among those who did not have sore throat. GAS pharyngitis predominates in temperate countries and peaks in late winter and early spring months. Crowded conditions and poor indoor air environment favor its spread.

GAS in impetigo cases (studied only in two centers) ranged from 2.7% in Chandigarh to 25.2% in Vellore. Skin carriage was 0.4% in Chandigarh and 2.2% in Vellore**.** Impetigo predominates in sub-tropical environments, such as in India and among aboriginals in the northern territories of Australia.

GAS were isolated from the throat and skin, using similar methods, in every region of India – north, west, south and east - which have different climatic conditions (sub-tropical to tropical). Out of the 174 isolates from all the regions, 56 different *emm* types were obtained indicating considerable heterogeneity. Isolates from South (tropical climate) were more heterogeneous compared to the northern isolates (sub-tropical climate).

Most prevalent *emm* types (*emm* 81, *emm* 77) during cross sectional study are same as in the cohort study. This shows that pattern of prevalent *emm* types does not change during short period of time of one year. However, most prevalent *emm* types – *emm* 112, *emm* 110 and *emm* 82 of Southern region differ from the most prevalent isolates in northern region. There was not even a single *emm* type which was common in all the centers. This suggests that distant geographic regions have different *emm* types.

The data from this study indicates that *emm* 1 and *emm* 12 which are the most predominant *emm* types in western countries are also prevalent in India. These types were not common according to earlier reports on emm typing from North India (68). Seven *emm* 1 isolates were from Vellore, Jodhpur and Shimla. In addition to the presence of *emm* 1-2, this study for the first time noticed *emm* 1-4 from Indian community. Both *emm* 1-2 and *emm* 1-4 are distinct *emm* types (i.e., not a subtype of *emm* 1).

The distribution of *emm* types of GAS has been well studied in several countries. There are more than 200 *emm* types (based on the sequence of M protein, a major surface protein of GAS) circulating in different geographical regions (69) as an individual GAS serotype enters and leaves a community fairly quickly. Hence inter-site and time variations in *emm* typing are common.

Traditionally particular GAS M types were considered to be either rheumatogenic or nephritogenic, but no such correlation has been drawn recently, rather replacement of rheumatogenic strains with non rheumatogenic types for acute pharyngitis have been observed, the reason for this remain to be

elucidated (70). The e*mm* 1, *emm* 1-2, and *emm* 57 which are commonly reported to be associated with glomerulonephitis were prevalent in this study.

With an exception of few *emm* types, the GAS types identified in India are generally different from the ones taken into consideration while developing multivalent vaccines in USA, implying that the efficacy of currently available vaccine based on N terminal variable region sequence found in the western world will have doubtful efficacy in India.

In this study children's close contacts have not been examined, hence, transmission dynamics among different members of the family could not be examined. It seems prudent to have more family data to understand the dynamics of streptococcal carrier states and infections.

Low socio-economic conditions and overcrowding are favorable environments for GAS infections. Hence the improved living standards, awareness towards one's health, proper treatment facilities in primary health care systems may reduce the burden of GAS diseases in Indian communities. However, the additional types of GAS having rheumatogenic potential, and new types emerging every other day emphasize that epidemiological surveillance of this bacteria in different zones of the country should be continued to have precise information to design a vaccine strategy.

The genetically close relatives of GAS, i.e., Group C Streptococcus (GCS) and Group G Streptococcus (GGS) were also found to be common in throat swabs particularly in Vellore and Mumbai centers (64). These organisms, traditionally considered as commensals, are now considered to be capable of eliciting a range of clinical manifestations. Being designated as minor human pathogens, their virulence attributes were less extensively studied. Recently it has been observed that non- GAS infections may be the driving forces behind RF in the aboriginal communities of Australia (71). It is also becoming more evident that these organisms may have acquired known GAS virulence factors like M protein, fibronectin binding proteins, streptokinase & C5a peptidase through genetic transfers (72). Hence a comprehensive examination of presence of human GCS and GGS in the community should be included while studying epidemiology of GAS diseases. From Vellore itself the isolation rate of group C and G streptococcus was quite high in comparison to GAS which further indicates that future studies should include GCS and GGS epidemiology and their pathogenesis.

In conclusion, GAS sore throat and skin infections are common in India, and *emm* types vary a lot from one region of the country to another region. Therefore, it is important to conduct surveillance in different part of country periodically to study whether *emm* types change over time.

4. Epidemiology of Rheumatic Fever/Rheumatic Heart Disease

4.1. Introduction

Rheumatic fever is initiated by GAS throat infection which may lead to RHD (54). The consequences of RF/ RHD include damage to heart valves, repeated hospitalizations increasing disability and premature deaths.

WHO estimated global due to RHD has a prevalence of at least 15.6 million cases, with 2,82,000 new cases and 2,33,000 deaths each year (14). Children and adolescents of the developing countries are especially susceptible to this disease. Overcrowding, poor socioeconomic status and illiteracy contribute to the high prevalence of RF/RHD. In developed countries RF/RHD has become an uncommon health problem during past two decades (73). However prevalence of RF/RHD reported from some nations of Asia are highest, yet many countries in the region do not have national RF/RHD control programs (74).

The prevalence of RF/RHD in India has been reported to be varying from very infrequent to very high levels depending upon the source of information (50). According to recent epidemiological surveys among school children, the prevalence RHD in India varies from 1- 5.4 per 1000 children in 5-15 years of age. This imposes a tremendous national burden since it mainly affects children and young adults, leading to significant social and economic losses.

RHD is one of the preventable chronic disorders of the heart. The current focus of global efforts at prevention of RHD is on secondary prevention (regular administration of penicillin to prevent recurrence of RF), although primary prevention (timely treatment of streptococcal pharyngitis to prevent RF) is also important in populations in which it is feasible. A RF/RHD control program can be sustained within the primary health care system, and the case registry can be utilized not only for monitoring the program but also to gain insight into the epidemiology of the disease (75).

4.2. Objectives

a) To establish a registry of rheumatic fever and rheumatic heart disease
b) To estimate the prevalence of rheumatic heart disease among school children in the 5-14 year age group.

4.3. Methodology

4.3.1. Study Area

Table 4.3.1 presents the profile of study area, i.e., total population, children in 5-14 years, population density, education and occupation. The population covered includes rural as well as urban population in most centers except Mumbai and Indore, where only urban population was included.

4.3.2. Project Duration

Chandigarh and Vellore centers were the initial centers where the project starting date was year 2001-02, later on Kochi (2003), Indore (2004) and Wayanad (2006) centers were added. In year 2006-07 the project was also started in Mumbai, Dibrugarh, Jodhpur, Shimla, & Jammu.

4.3.3. Project Preparatory Activities

A situational analysis was done to prepare a profile of the district, to identify the facilities available for diagnosis and management of RF/RHD patients, type of prophylaxis/ treatment being practiced, usual place of referral of RF/RHD cases, and estimated number of RF/RHD cases (suspected or confirmed) in last one year.

4.3.4. Partnerships with State Health Directorate and Education Department

A meeting with Director, Health and Family Welfare and Education Secretary of the state was held to seek formal approval for project implementation at district level and for carrying out School Health Survey including training of school teachers. Civil Surgeon and District Education Officers of Secondary and Primary Schools of district were briefed by the project investigator regarding the objectives of the project and its implementation strategy. A project advisory committee was constituted to decide policy issues. The civil surgeon of district was nominated as nodal officer. A project implementation committee was also formed for taking decisions related to implementation and monitoring. Formal inauguration of the project in a gathering of officials of health department and key people of the district was done at most of centers.

4.3.5. RF/RHD Registry

After orientation training, registries (and sub-registries) were set up in each study center. ASO test kits, injection benzathine penicillin and registers with monitoring forms were supplied to all the health institutions of the district where RF/RHD registries were set up.

4.3.5.1. Registration Procedures

In a registry**,** a patient could come from either a general OPD or referred by general physician, health worker or school teacher. On examination if a doctor suspected RF or RHD, he/she followed a standard procedure for registration of a case. A suspected patient of RF was sent for ASO test in the laboratory and the report was obtained. If the patient fulfilled Jones criteria then he/she was registered and a unique identification number was allotted. Similarly on auscultation if the doctor was sure about RHD then the case was registered. If echocardiography was required then patient was sent to a cardiology center with referral card on a fixed day. After echocardiography confirmation of RHD, patient was registered and secondary prophylaxis was prescribed.

A case registration sheet was filled and retained at registry and patient's card was given to the patient. This card was used to record secondary prophylaxis, i.e., each injection of benzathine penicillin or oral penicillin tablets. Patient was also given a folder for health education.

4.3.5.2. Reporting System

The reporting system comprised of sending a monthly report on a format from a health institutions to registry (office of civil surgeon) by 5th of every month. A compiled report of all the registries was sent to principle investigator by 15th of every month. By 25th a feedback was sent to the registry from project office of each center.

4.3.6. School Health Survey

4.3.6.1. Study Area

The study area for school health survey comprised all areas in the district where RF/RHD registry was established. Permission from health and education authorities was obtained to conduct the school health survey in the district. A list of all the schools in the district with number of students in each class was obtained from education department.

4.3.6.2. Sampling

Systematic random sampling of schools was done to select 25,000 children in Chandigarh, Vellore, Kochi, Indore and Wayanad centers, whereas in all other centers sample comprised of 10,000 children.

4.3.6.3. School Health Procedure

School health team consisted of a medical officer (MO) and a social worker. On reaching the school social worker introduced the team to principal/ in-charge teacher and enquired about the number of school children. MO sought active cooperation of class teachers for school health examination. School children were assembled in open space preferably, along with class teachers. Social worker also delivered a health talk on RF/RHD and distributed IEC material amongst school children and teachers.

The name, age, sex and address of students were recorded in a school health form and a unique identification number was allotted with active cooperation of class teacher. Any other relevant general information such as height and weight measurements of students was also recorded. MO examined student clinically (auscultation sounds and recording of blood pressure) and entered the findings in the school health form.

For cases having any audible murmur on auscultation, MO filled up the echocardiography referral card and allocated a date and day for echocardiography test in consultation with social worker. Parents of suspected cases were counseled in the school itself. The parents were explained utility of echocardiography test by MO. Any apprehensions of parents were dispelled by MO and social worker. Repeated attempts were made to do echocardiography in all cases with murmur. Throat swab specimen of students was also taken by the Medical Officer in a sub-sample of school children.

4.3.7. Estimation of the RF/RHD Prevalence

The case registrations in the RF/RHD registry followed passive surveillance methods, i.e., cases that reported to health institutions were registered, hence, under-registration is expected. Therefore, the incidence/prevalence of RF/RHD estimated from the registry can only be considered as minimum (upper level not known). On the other hand the prevalence of RHD in school survey provides a reliable estimate only in 5-14 years age group.

A correction factor based on the proportion of RHD cases in older age group (15+ years) compared to 5-14 year olds, usually varying from 5-7, was used to estimate the prevalence of RF/RHD in the population (14). The number of cases in the 5-14 year age group (a) = prevalence of RF/RHD in 5-14 years age group from school survey x number of children in the study site in 5-14 years. The number of cases of RF/RHD in >15 year olds (b) = number of cases in the 5-14 year olds x 5.5 (correction

factor). Thus, total number of cases in the study site were estimated to be a + b. RF/RHD prevalence estimated per 100,000 population was (a + b/ population of the site) x 100,000.

4.4. Results

4.4.1. RF/RHD Registrations

Table 4.4.1 shows the start and end date of the project at various study sites along with the total number of RF/RHD cases registered in each center. Five thousand five hundred and ninety cases of RF/RHD (RF 654 & RHD 4936) were reported from all centers. Maximum numbers of cases were reported in Vellore (1144) and Chandigarh (813) which started registries in year 2001-02 whereas the number of cases registered at Shimla (634), Indore (583), Mumbai (522), Wayanad (463), Kochi (449), Jammu (379), Dibrugarh (373) and Jodhpur (220) were less, as these centers were started later. Similar trend was seen for RF and RHD cases at various centers.

Table 4.4.2 shows total number of RHD cases at different centers according to the year of registration. During the initial years of the project significantly higher registration was noticed as prevalent cases were registered. In the last years of project, all center showed decline in registration.

Table 4.4.3 presents the total number of RF cases at different centers according to the year of registration. Number of cases registered is higher in Chandigarh and Vellore centers as these centers had started registrations early.

During the initial years of project significant increase was found in RF registration except in Jodhpur & Shimla center where registration reported was very less as compared to other centers and in last years of project, all centers showed declination in RF registration but Shimla center showed increase in RF registration.

4.4.1.1. Age and Sex Distribution of RHD and RF Cases

Table 4.4.4 presents age and sex-wise distribution of RHD cases. Very few RHD registrations were reported in age group 0-4 years. RHD registrations peaked in the age group of 5-14 years in some of the centers whereas in others the peak was in adults (35-39 years); the numbers of registration in older people were low.

Table 4.4.5 shows the age and sex-wise distribution of RF cases which shows that very few RF registration cases were reported in age group 0-4 years, and highest numbers of RF registrations were reported in the 5-9, 10-14 and 15-19 years age group. In other age groups, i.e., after 20-24 years there were very few registrations in all the centers.

Figure 4.4.1 & 4.4.2 present the distribution of RF and RHD cases by age.

4.4.1.2. Clinical Manifestation of Registered RF cases

Clinical manifestations of registered RF cases are presented in Table 4.4.6. As shown in table carditis was most common in Shimla (65.5%), Jammu (60.0%) and Jodhpur (50.0%). It was reported in 48.2% cases in Mumbai, 50.9% cases in Indore, 25.6% cases in Chandigarh, and in 13.8% cases in Wayanad, whereas Vellore, Kochi and Dibrugarh did not have carditis alone in their registered RF cases.

Arthritis was reported in 39.3% to 75.9% cases. It was higher in Shimla (75.9%), Vellore (75.8%), Chandigarh (69.5%), Wayanad (69.0%), Dibrugarh (66.7%), Kochi (64.3%) and Indore (58.2%). However, reports from Mumbai (39.3%) were on lower side and Jodhpur & Jammu centers did not show arthritis in any RF cases.

Chorea was reported in Indore (30.9%), Mumbai (12.5%), Chandigarh (4.9%) and Shimla (3.45%) respectively. Vellore, Kochi, Wayanad, Dibrugarh, Jodhpur and Jammu did not report any case of chorea during the study period.

Subcutaneous Nodules were reported only in Jodhpur (25.0%), Shimla (24.1%), and Indore (14.5%) centers. Erythema marginatum was reported only in Indore (1.0%) center.

Carditis and Arthritis was reported more often in Shimla (41.4%), Dibrugarh (33.3%) & Kochi (35.7%). Wayanad (10.3%) and Vellore (5.5%) also reported this combination in some cases. Arthritis and chorea were together reported in only in Vellore (1.1%). Carditis along with chorea was reported in Jodhpur (25.0%), Wayanad (6.9%) and Shimla (3.5%).

4.4.2. School Health Survey

Table 4.4.7 presents age and sex-wise distribution of children included in the School Health Survey. Table 4.4.8 shows number of children examined in 5-9 years and 10-14 years age group who were

suspected of having heart murmurs, and in whom echocardiography was done. Table 4.4.9 gives the reason for not examining some of the children in school survey.

4.4.2.1. RHD Prevalence in School Children

Table 4.4.10 presents RHD prevalence among school children in the age group of 5-15 years. Highest prevalence per 1000 children was reported from Vellore (1.2) and lowest in Kochi, Dibrugarh & Wayanad (0.1).

4.4.3. Prevalence of RF/RHD in the Registry Area

It is important to note that all cases of RF/RHD do not get into the registry, hence, the incidence/prevalence rate estimates from the registry can only be considered as the minimum. Hence, prevalence was estimated using the school survey data, assuming that number of cases in the 15+ year age group is 5.5 times than that in the 5-14 years age group. Prevalence estimates arrived at by using this assumption is presented in Table 4.4.11. The prevalence of RF/RHD ranged from 10 to 161 per 100,000 population in various centers. Prevalence was highest in Vellore and Jodhpur followed by Chandigarh, Shimla, Mumbai, Jammu, Indore and Wayanad, and it was lowest in Kochi. Median prevalence of RF/RHD was 84 per 100,000 population.

4.5. Discussion

RF/RHD prevalence estimate ranged from 10 in Kochi to 161 per 100,000 population in Vellore (median 84). One has to keep in mind that these estimates are based on the school surveys conducted in these areas. We did not use registry data to estimate RF/RHD burden as it is well known that in (passive) surveillance many cases do not get registered. However, passive surveillance shows that RF/RHD continues to affect a substantial number of children and adults, in relatively economically developed regions of India. Even larger number of children may have been affected in economically under developed states. RF peaked in most of the study sites in the 5-14 years age group though RHD peak in some sites was seen in older age groups (Figure 4.4.1 and 4.4.2).

One of the reasons for less number of registrations in the registry could be that mild RHD cases may not feel the need for presentation to a medical institution. Some of the cases may also present to private institutions. One of the registries set up in the private sector in Rupnagar District did indicate that some of the cases of RF/RHD were indeed cared by the private medical practitioners. Wealthier sections of the population are more likely to use private medical practitioners but RF/RHD rates are

lower in them. RHD prevalence was higher in children studying in government schools compared to the private schools which generally cater to higher socioeconomic class.

Since the surveillance effort was dependent on the medical and paramedical staff of the government health services alone, it was not possible to register all cases of RF/RHD. The proportion of RF/RHD cases registered in the 5-14 years age group is far less than the estimated numbers from the school surveys in the registry sites. Others have documented that despite best efforts, all cases of RF/RHD do not get notified in the public health system (76). However, surveillance system set up in the public sector institutions despite its limitations can be used for monitoring disease trends.

Higher proportion of RHD cases were registered among females especially after the age of 20 years, though prevalence of RHD among boys and girls was found to be similar in school surveys. This could be due to differential care seeking for chronic RHD. Males may be seeking care from private sector doctors whereas females may have continued to rely on public sector institutions. Pregnancy related changes may also increase the severity of otherwise mild RHD leading to higher rate of RHD detection among females during antenatal examinations. This indicates that antenatal examinations could be an important source of RHD surveillance in the population.

The clinical presentation of RF and RHD in various districts was similar to other studies (77-78), most of the centers did not detect erythema marginatum and subcutaneous nodule, and the proportion of carditis was also lower in some centers than reported earlier. Other hospital-based studies from India report higher rates of carditis but rates of erythema marginatum and subcutaneous nodules are low (77-78).

School surveys are considered to be valid methods for estimating RHD burden in the community. RF/RHD prevalence in school surveys ranged from 0.1 to 1.8 per 1000 children. However, even school surveys may also be under-estimating the disease burden, because of out-of- school children generally belonging to lower socio-economic group, which are known to have higher RHD rates. Further, some of the murmurs may have been missed as ideal conditions for auscultation (a quiet room) are generally not available in school setting.

Due to limited resources available to us, we have used clinical methods (auscultation) for initial screening for heart murmurs and echocardiography for confirmation of RF/RHD. A recent Australian study has observed “doctor identification of any murmur had 38.2% sensitivity, 75.1% specificity and

5.1% PPV, and the corresponding values for doctor detection of suspicious or pathological murmurs were 20.6%, 92.2% and 8.3%. For all auscultation approaches, negative predictive value was more than 97%" when compared to echocardiography-based screening (79). Echocardiography is also useful in differentiating doubtful cases of RHD from Congenital Heart Disease. Introduction of Echocardiography and Doppler (E&D) in the evaluation of carditis with acute rheumatic fever has identified the presence of subclinical carditis (SCC), that is, presence of cardiac involvement which cannot be diagnosed clinically. Studies suggest that SCC occurs in upto 30 percent children with acute rheumatic fever. The Utah epidemic in USA between 1985-94 found that clinically identifiable carditis was present in 68 percent with clinically unidentifiable disease in 16 percent giving an overall frequency of carditis in 84 percent children. Studies in normal school children have identified 19 to 44 percent asymptomatic, unknown SCC. The data indicate that the estimates obtained in our ten centre study based on clinical evaluation are underestimating the prevalence by a big margin. RHD burden could be much more than what is generally believed. Studies are underway to estimate the prevalence of SCC to estimate the burden of hidden, clinically undiagnosed rheumatic heart disease in our country. Recently conducted school surveys have used echocardiography for screening in India also. School surveys based on echocardiography have found RHD prevalence about 10-15 times higher than the screening method employed by us (49, 49a).

Whether secondary prophylaxis will be beneficial in sub-clinical cases of RHD, detected by echocardiography, needs to be investigated by long term follow-up studies of the sub-clinical cases detected by echocardiography.

Some investigators have opined that RF/RHD has been declining in India (39, 80). They have based their assessment on the proportion of hospital admissions due to RHD and or school surveys that have been conducted over a period of several decades in various geographic regions of India. These comparisons could be biased as over the years treatment seeking pattern might have changed and survey design, populations sampled, especially clinical assessment methods may also have differed. Now several peripheral level health institutions provide care for RF and RHD whereas such facilities were earlier available only in few tertiary care institutions. Findings from this study present a variable picture of RF/RHD trends. In some districts the age distribution still shows a peak in the 5-14 years age group rather than in the middle age whereas in some districts (such as Kochi, Indore, Shimla) show peak in middle age. A peak in the later age group indicates a decline in the incidence of RF/RHD in children (5-14 year) population, i.e., lower prevalence of RHD in children and adolescents compared to the adults. However, it is possible that in some centers under-reporting was more

common in younger age group, hence, one cannot infer from these data that there is a declining trend of RF/RHD. Surveillance data from registries can provide trend of RF/RHD as school surveys are usually not repeatedly conducted in the same populations using same study design and clinical methods.

Based on this study, it appears that the burden of RF/RHD could be similar to the cancer burden in India. However, India still does not have a national RF/RHD control program, whereas a national cancer control program is functioning for several decades, despite the fact that RHD is a preventable disease of children and adolescents which primarily affects poorer segments of population. Management of RHD is a costly affair and does not offer a permanent cure.

To conclude, RF/RHD continues to be an important public health problem in the selected districts of India which have relatively higher socio-economic status than many other districts of India and other developing countries. Higher prevalence of RHD in younger age groups in many districts indicates that disease is not showing significant declining trend in most parts of India. Prospective surveillance in registry-based programs, set up within the existing health infrastructure for controlling RHD, can discern disease trends and provide opportunities for implementation of secondary prevention programs to prevent recurrence of RF and progression of RHD.

5. Prevention and Control of RF/RHD

5.1. Introduction

RF and RHD are non-supurative complications of GAS pharyngitis due to a delayed immune response. Although RF/RHD is rare in developed countries, they are still major public health problems among children and young adults in developing countries (81-84). The economic effects of the disability and premature death caused by these diseases are felt at both the individual and national levels through higher direct and indirect health-care costs.

ARF is often clinically diagnosed based on the Jones Criteria. These criteria include major manifestations, i.e., carditis, polyarthritis, chorea, erythema marginatum and subcutaneous nodules, and minor manifestations, i.e., fever, arthralgia and laboratory findings of elevated erythrocyte sedimentation rate, C-reactive protein, and prolonged PR interval on ECG. For making a diagnosis of ARF, two major or one major and two minor manifestations must be accompanied by supporting evidence of antecedent GAS infection in the form of positive throat culture or elevated or rising anti-streptolysin titer (ASO). The updated guidelines also highlighted a subgroup of 'exceptions to Jones Criteria' for patients with chorea, indolent carditis and previous history of RF or RHD. Role of echocardiography has not been defined in these modifications but may be important, as clinical detection of soft murmurs may be difficult due to tachycardia (10). Indicators of GAS infection such as a DNAase or ASO serology test must confirm the GAS infection (85).

RHD, non-inflammatory sequelae of ARF, is the most common acquired heart disease among children worldwide. The consequences of RHD include: continuing damage to the heart, increasing disabilities, repeated hospitalization and premature death usually by 35 years or even earlier. The severity of RHD and the prognosis depend on the extent of the carditis. Endocarditis can develop with aseptic vegetations along the valve closure lines, particularly on the mitral valve. Chronic RHD mostly affects the mitral valve which can become thickened with calcification of the leaflets. Some of the most common symptoms of RHD are: breathlessness, fatigue, palpitations, chest pain, and fainting attacks.

A consolidated effort is necessary to generate awareness regarding all the factors that predispose to GAS infection as well as about the signs and symptoms of GAS sore throat to encourage its treatment for prevention of attacks of RF/RHD. Epidemiological studies have demonstrated that appropriate antibiotics given early in the course of streptococcal infections prevent the subsequent

development of RF. Data from a study by Wannamaker *et al.* (1951) indicated that penicillin therapy of acute streptococcal infections almost completely prevents the subsequent occurrence ARF (86). The GAS infection can usually be eradicated by a single intramuscular injection of benzathine benzyl penicillin or by ten days treatment with oral penicillin. Failure to eradicate GAS from throat occurs more frequently with oral penicillin than with Injection Benzathine Penicillin G. For patients allergic to penicillin, erythromycin is an acceptable alternative.

Efforts to ensure primary prevention of RF are focused on education of general community regarding proper treatment for sore throat and also of health personnel regarding early diagnosis and effective treatment of streptococcal pharyngitis. Till date, no effective vaccine is available against streptococcal diseases.

Secondary prophylaxis involves regular administration of an antibiotic usually penicillin to a patient who has had RF or RHD in order to prevent colonization or infection of the upper respiratory tract with GAS and the subsequent development of recurrent attacks of RF. Secondary prophylaxis has been shown to reduce recurrences, morbidity and mortality. Even with optimal patient adherence, the risk of recurrence is higher in individuals receiving oral prophylaxis than in those receiving intramuscular benzathine penicillin G. World Health Organization has recommended secondary prophylaxis as cost-effective and practical approach even in the poorest countries which can be most effectively delivered within a coordinated program using a registry of patients.

Since the late 1940s several RF/RHD prevention and control programs have been implemented in different countries including establishment of RF/RHD registers, follow-up and secondary prophylaxis, as well as some comprehensive programs on the prevention of RF/RHD integrated into the health care system. It should be emphasized that secondary prophylaxis is useful even if not given according to a completely regular schedule, though its efficacy declines as fewer injections are given. Patients out of secondary prophylaxis have a high recurrence rate (5.5 to 25.0% of patient-years) and severe RHD (41, 81, 87-92, 94-97).

A number of countries in the South East Asian region have been able to develop or strengthen national RHD registers. These registers allow for more effective delivery of secondary prophylaxis, the mainstay of disease control. Primary prevention of RF and screening for RHD are important adjunctive strategies. **A** pilot RF and RHD control project was started in 1988 in Raipur Rani Block of district Ambala in Haryana to test the feasibility of early detection, treatment and secondary

prophylaxis for rheumatic fever/rheumatic heart disease cases. School teachers, students and health workers were trained to identify and refer suspected cases of RF/RHD to the community health center where physicians examined the suspected cases and monthly secondary prophylaxis was provided to the confirmed cases. A survey of registered cases was done in 1999 to determine the compliance rate of secondary prophylaxis and to describe clinical and epidemiologic features of the registered cohort of rheumatic fever/rheumatic heart disease patients. A total of 257 patients had been registered till the end of 1999 with 1263 person-years of follow-up and compliance to secondary prophylaxis was 92% during past 12 years (98). This strategy required testing at a larger scale before recommending its implementation at national level.

5.2. Objectives

a) To train medical and paramedical staff for prevention and control of RF/RHD
b) To generate awareness in the community about prevention and control of RF/RHD
c) To provide secondary prophylaxis to registered patients
d) To establish RF/RHD registry at district level in selected states of India.

5.3. Methodology

State and District Health Authorities were sensitized for initiation of RF/RHD prevention and control programs in one district having about one million population. State health department implemented the project through the existing health infrastructure with the technical support of the medical institution.

5.3.1. Capacity-building

The RF/RHD centers organized training of different categories of the project staff. To ensure similar pattern of functioning at all the centers, doctors and research staff from all centers participated in the training. Content of training were ongoing research on RF/RHD at ICMR, epidemiology and management of RF/RHD, management information system (MIS), registration, reporting, and analysis formats. Field visits were also organized for trainings.

5.3.2. Preparation of Training and Health Education Materials

On the basis of the situation analysis, health education and training material was prepared and finalized. These modules were pre-tested in the field and finalized in a “Workshop on RF/RHD control” after incorporating suggestions from district health officers who had participated in the workshop. Training of medical and paramedical personnel, and community education for primary

prophylaxis was also a component of the project. Several training modules and health education materials were developed.

A training of trainer's workshop was organized at RF/RHD centers in beginning of project so that master trainers (from the district health organization) were trained about the aims and objectives of project, various components of project as well as role of different personnel working in the project at district level.

Trainings of health workers, pharmacists, school teachers and medical officers were periodically carried out at all centers by the master trainers with the aim of improving the awareness regarding RF/RHD and the project.

5.3.3. Information Education and Communication (IEC)

In all centers, leaflets (in local language), folders and posters regarding signs and symptoms of RF/RHD were distributed in schools as well as during all trainings. A specially designed colored teaching aid poster was distributed to all registries and was used for training purposes. It was displayed at monthly meetings of health workers in all registries.

Wall paintings were also done in some centers to display the signs and symptoms of RF/RHD and penicillin availability was made at the civil hospitals and primary health centers of the districts. This was to propagate the aims and objectives of project and awareness about the disease.

Announcements through involvement of religious places regarding RF/RHD project were made by reading the information leaflet by priest at village level in some districts at some of the centers.

Health talks on RF/RHD by faculty of the RF/RHD center were broadcasted on All India Radio at some of the centers. Radio broadcast messages about the signs and symptoms and treatment of RF/RHD and cable advertisement displaying the information about the signs and symptoms, treatment and the availability of the injection benzathine penicillin at the civil hospitals and primary health centers of the district was relayed all over district at some centers.

A short video film on RF/RHD was also prepared during the course of project depicting various components of project and on field activities by some of centers.

Participation in health and science fairs was also done at some of centers. Teachers were informed about the clinical signs and symptoms of RF/RHD, use of referral card and role of teachers in the program. They were given health education material to be displayed in their respective schools.

A knowledge attitude and practice study was done to assess the impact of health education strategy in one of the centers.

5.4. Results

Table 5.4.1 reports the start and end year of the project in various centers. Case registrations had started earlier in Chandigarh and Vellore.

Table 5.4.2 reports the orientation trainings conducted in RF/RHD control program. Chandigarh and Jodhpur centers conducted refresher trainings also whereas all other centers had conducted only initial training.

Table 5.4.3 shows the number of material utilized in RF/RHD control program at various centers. ASO kits for diagnosis of GAS infection and medicine for secondary prophylaxis (injection benzathine penicillin /oral penicillin tablets) were supplied to all health institutions during the project period in all the centers.

Table 5.4.4 presents diagnostic categories of RF and RHD cases. The registrations started earlier at Chandigarh and Vellore; hence, these centers had recorded higher number of cases than other centers. Vellore center registered 1144 cases, followed by Chandigarh (813), Shimla (605), Indore (583), Mumbai (522), Wayanad (463), Kochi (449), Jammu (389), Dibrugarh (373) and Jodhpur (220).

The number of RF in 1A (with carditis) and 1B (without carditis) categories were: 171 in Chandigarh, 102 in Vellore, 14 in Kochi, 55 in Indore, 29 in Wayanad, 56 in Mumbai, 27 in Dibrugarh, 3 in Jodhpur, 29 in Shimla and 10 in Jammu.

RHD cases in 2A (RHD) and 2B (RHD with rheumatic activity) categories were 610 in Chandigarh, 1042 in Vellore, 371 in Kochi, 511 in Indore, 393 in Wayanad, 126 in Mumbai, 346 in Dibrugarh, 213 in Jodhpur, 576 in Shimla and 378 in Jammu.

Some of the cases registered had past history of rheumatic fever, few of them had documentation of RF diagnosis while others did not have documentation but were on secondary prophylaxis.

Table 5.4.5 shows the type of valvular involvement in registered RHD cases. Mitral valve involvement was highest in Chandigarh (74.4%) and lowest in Mumbai (25.0%). Aortic valve was involved in 0.7% (Mumbai) to 5.1% (Wayanad).

Mitral and aortic valve involvement ranged from 13.8% in Chandigarh to 37.1% in Wayanad. Mitral and tricuspid valve involvement was highest in Mumbai (29.3%) and lowest in Chandigarh (3.3%). Aortic and tricuspid valve involvement was reported only in few cases.

Mitral, aortic and tricuspid valve involvement was highest in Mumbai (24.3%) and lowest in Jammu (0.8%). Mitral, aortic, tricuspid and pulmonary valves were involved in few cases only.

Table 5.4.6 presentation the data of RHD cases who required interventions during the project period. Cases requiring interventions were 233 in Indore, followed by Vellore (197), Jodhpur (170), Jammu (56), Chandigarh (42) and Dibrugarh (23) whereas other centers did not report this data.

RHD cases who received intervention were 218 in Kochi followed by Indore (160) and Shimla (105), Wayanad (52), Jodhpur (39), Vellore (18), Dibrugarh (11) and Jammu (3) whereas other center did not report this data.

The numbers of surgical intervention done at Jodhpur were 170, followed by Shimla (85), Indore (57), Mumbai (39), Chandigarh (14) and Dibrugarh (11); other centers did not record data on surgical interventions. Percutaneous interventions were reported from Indore (95), Shimla (20) and Chandigarh (12) whereas other centers did not report data of percutaneous interventions.

Table 5.4.7 presents the reasons of not receiving intervention of registered RHD cases. Cases who did not receive intervention due to poor financial problem were 90 at Jodhpur followed by Indore (84), Vellore (61), Dibrugarh (12) and Chandigarh (10). Cases who do not received intervention as they died before interventions were 23 in Jodhpur followed by Shimla (12), Vellore (8) and Chandigarh (2). The reasons for not receiving interventions were ‘not known’ in 34 cases at Vellore, followed by Jodhpur (18), Indore (5) and Chandigarh (4).

Secondary prophylaxis compliance data was available only from few centers. Only Chandigarh, Vellore, Indore, Dibrugarh and Jodhpur centers reported the secondary prophylaxis compliance. Kochi, Wayanad, Mumbai, Shimla and Jammu did not record secondary prophylaxis compliance. Secondary prophylaxis compliance was 95% in Chandigarh, 75% in Vellore, 92% in Indore, 93% Dibrugarh. Vellore, Kochi and Wayanad centers had provided secondary prophylaxis with oral penicillin whereas all other centers had used Injection Benzathine Penicillin.

Various reasons to stop secondary prophylaxis are presented in Table 5.4.8. Highest number of cases who stopped taking injection due to loss to follow up were reported from Kochi (78) followed by Vellore (52), Jodhpur (25), Shimla (14) & Indore (3). Migration was the main reason for not taking secondary prophylaxis. Maximum cases that stopped taking secondary prophylaxis at the advice of doctors were reported in Indore (187), Shimla (187), Kochi (55) and Jodhpur (44). The number of cases who stopped taking injection themselves were higher in Indore (47) and Chandigarh (29) followed by Vellore (8), Kochi (7), Dibrugarh (5) and Mumbai (1).

Table 5.4.9 presents the number of cases that were lost during follow up due to migrations or had died and or left at the end of project. Lost to follow up without any reason were high in Mumbai (82) whereas Shimla (14) and Indore (3) reported very less loss of cases. Migration cases were highest in Mumbai (154), followed by Chandigarh (75), Vellore (42), Jodhpur (2), Shimla (2) and Dibrugarh (1).

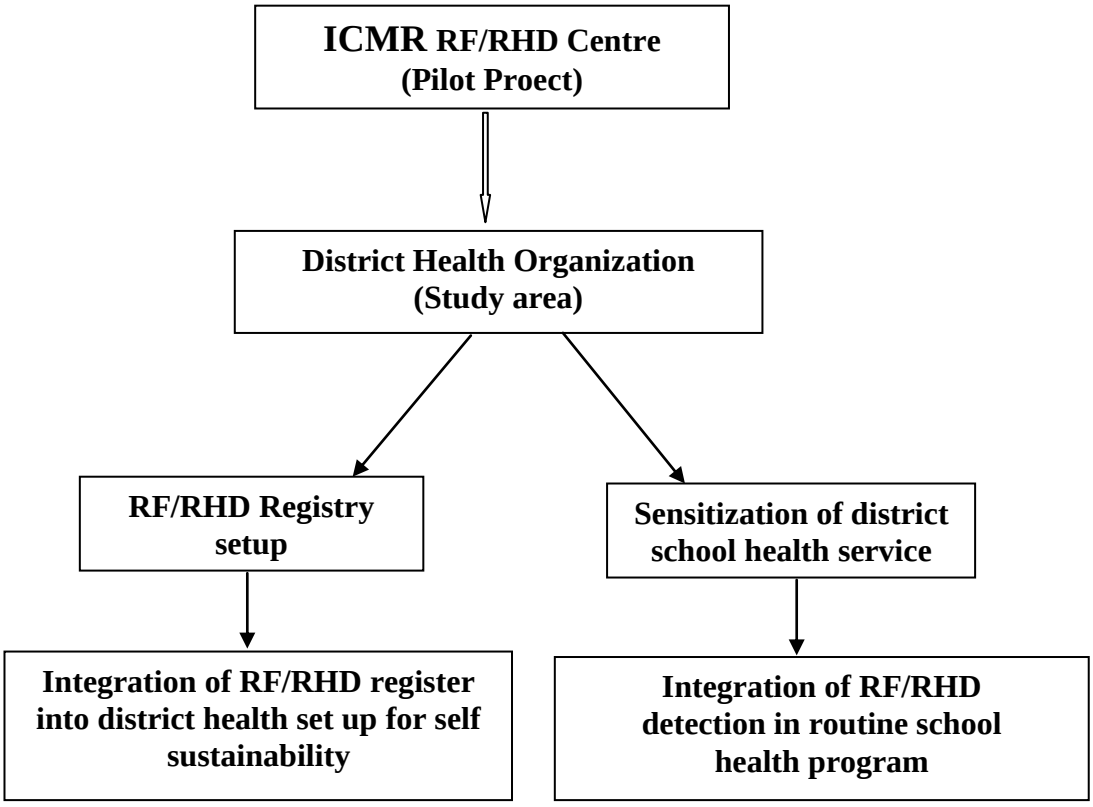
Maximum number of deaths cases were reported from Chandigarh (46) followed by Vellore (46) and Jodhpur (23), Kochi (12), Indore (12), Shimla (12), Dibrugarh (7), and Jammu (1).. Death due to RHD were reported from Chandigarh (31), Indore (12), Shimla (12), Dibrugarh (6), Mumbai (5) and Jammu (1), whereas in Vellore, Kochi, Wayanad and Jodhpur exact causes of death were not known. One death was reported following Injection Benzathine Penicillin in Chandigarh center.

5.5. Discussion

The RF/RHD control project, based on registration of patients and providing secondary prophylaxis free of cost, was successfully implemented through the existing district health organization. District health authorities monitored the RF/RHD registry. The medical officers at district level were sensitized to the registration process and referral to tertiary care centers for echocardiography and other diagnostic tests. Additionally the sensitization of district school health teams for the detection of RF/RHD case during school health examination led to a strengthening of the school health system in the study areas of all the centers. A schematic diagram showing implementation of RF/RHD

control project is given below. The successful maintenance of registry by the existing health services with minimum inputs from investigators at the academic institutions in terms of logistics and manpower requirements indicates that RF/RHD programs can be replicated in other parts of India using the existing infrastructure.

Schematic diagram showing implementation of RF/RHD control project



Most centers used monthly injections of benzathine penicillin for secondary prophylaxis, however, in some of the centers (Vellore, Kochi, Wayanad) oral penicillin was used due to a fear of anaphylactic reactions. The state governments do not allow use of penicillin injection in peripheral health institutions. The risk of anaphylactic reaction, though very low, exists. Hence, all the centers utilizing Injection Benzathine Penicillin G ensured that the resuscitation equipment and drugs were available in the injection room. One day per week was fixed for injections and the presence of a medical officer was made compulsory for the management of any anaphylactic reaction if required. A few cases of sudden death following injections were observed but it was not possible to establish whether the deaths occurred due to severe heart disease or due to an anaphylactic reaction. The risk of sudden death is high in patients with severe RHD due to atrial fibrillation, other arrhythmias or

pulmonary embolism. A multi-country study on secondary prophylaxis using **Injectible Benzathi**ne penicillin reported that after 32,430 injections during 2736 patient years of observation, 57 of the 1790 patients (3.2%) had an allergic reaction, 4 had anaphylaxis, an incidence of 0.2% (1.2/10,000 injections), all in patients over 12 years of age. one patient died, a fatality incidence of 0.05% (0.31/10,000 injections). (99) However, benefits of Injection Benzathine Penicillin are more than the risks as even with optimal patient adherence, the risk of recurrence is higher in individuals receiving oral penicillin prophylaxis than in those receiving intramuscular benzathine penicillin G. Failure to eradicate GAS from throat occurs more frequently with oral penicillin than with Injection Benzathine Penicillin G (100).

A large number of patients with RHD needing interventions were registered at most of the centers, but the high cost of treatment was cited as the commonest reason for not availing the medical or surgical interventions. Adherence to secondary prophylaxis was reported by some centers. Since compilation of data required tracking of each case, complete information was not possible at every center due to limited resources. However, most centers reported high rates of secondary prophylaxis (75% to 95%). Only few patients discontinued prophylaxis on their own. Migration was mentioned as the major reason for lack of information regarding compliance. Several deaths occurred among registered patients during the study, identifying the severity of RHD reducing the life expectancy. Prevention of RF/RHD by treatment of GAS sore throat with oral antibiotics for 10 days as an alternate strategy was included in the project. Failure to eradicate GAS from throat occurred more frequently with oral penicillin than with Injection Benzathine Penicillin G. Streptococcal sore throat can be asymptomatic or mild enough and difficult to differentiate clinically from viral pharyngitis. Due to poor school health services, it is possible that many children do not get the required treatment. Acute RF cases continued to occur at all the centers during the study.

Prevention of RF by raising the standard of living or reducing overcrowding is going to take decades, hence, vaccine development should be a priority. However, considering that several *emm* types of GAS circulate in India, use of M-protein as a base for vaccine development is a challenge. The vaccine is not likely to be available for quite some time. Hence, currently, establishment of a registry and secondary prophylaxis is the most feasible strategy for controlling RF/RHD in India. Clinical decision charts/scores can be used for the diagnosis and treatment of GAS sore throat with appropriate antibiotics. National Rural Health Mission should adopt this strategy as RF more often affects poor rural children who have already crossed the most risky period of the first five years of life and have a better chance of survival. Strengthening of school health services would go a long

way in implementing RF/RHD control program. Implementation of right to education program is likely to increase enrollment rates in the schools.

Some of the centers were able to integrate the project into a state level program. Punjab School Heart Disease Control program was launched on 4th November 2008. It was funded by Govt. of Punjab under NRHM. Guidelines have been sent to Civil Surgeons of all the districts of Punjab for the recognition of RHD and congenital heart disease (CHD) patients at PHC and CHC levels. The registration, provision of free medical and surgical treatment to the students of Govt. and Govt. aided schools of Punjab who are suffering from Rheumatic heart disease or Congenital heart disease is being done under the project. Shimla center has advocated successfully for an extension of the RF/RHD control to few more districts of Himachal Pradesh.

However, despite the reports of high disease burden, most state governments still do not have RF/RHD control programs. Rheumatic fever/ rheumatic heart disease continues to be a neglected public health priority. Primary and secondary prophylaxis based prevention strategies implementation within the existing primary health care setting has been demonstrated to be a cost-effective strategy to control RHD in developing countries (75, 85, 101). One of the major reasons for sluggish scale up of these programs perhaps has been the belief that with improvement in socio-economic status RF/RHD will decline in developing countries as it has happened in the developed countries. General perception is that in India RF/RHD is on a decline. However, resurgence of rheumatic fever has been observed in middle class families in the USA (73). Registry data shows peak of RF/RHD in many centers in the 5-14 year age group indicating that RF/RHD is still continuing as a public health problem in India, and the decline may be occurring only in some areas (such as Kerala).

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Figures and Tables

Figure 3.1. Location of Jai Vigyan Mission Mode Project Centers

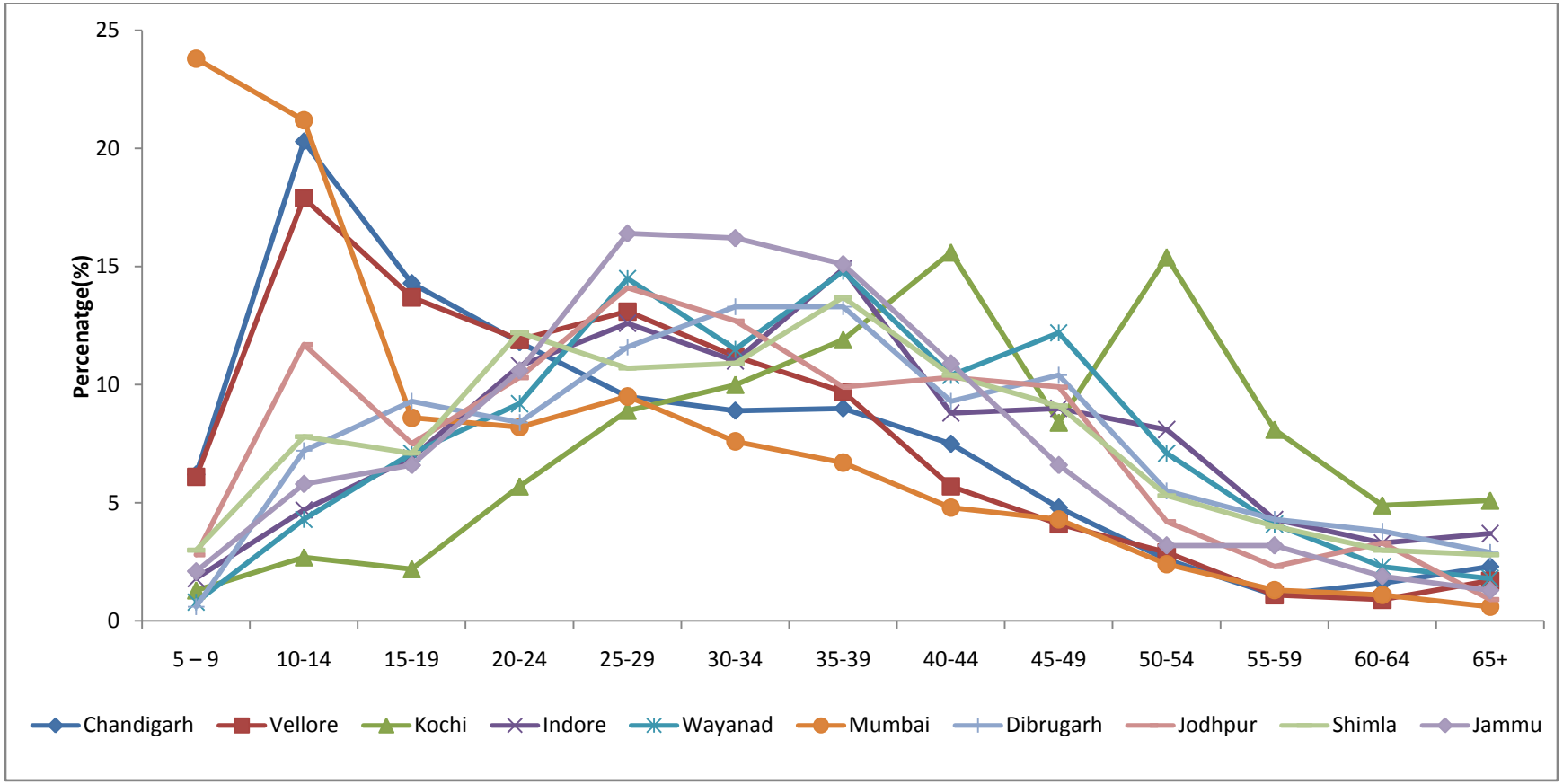


Figure 4.4.1: Age-wise distribution of RHD cases

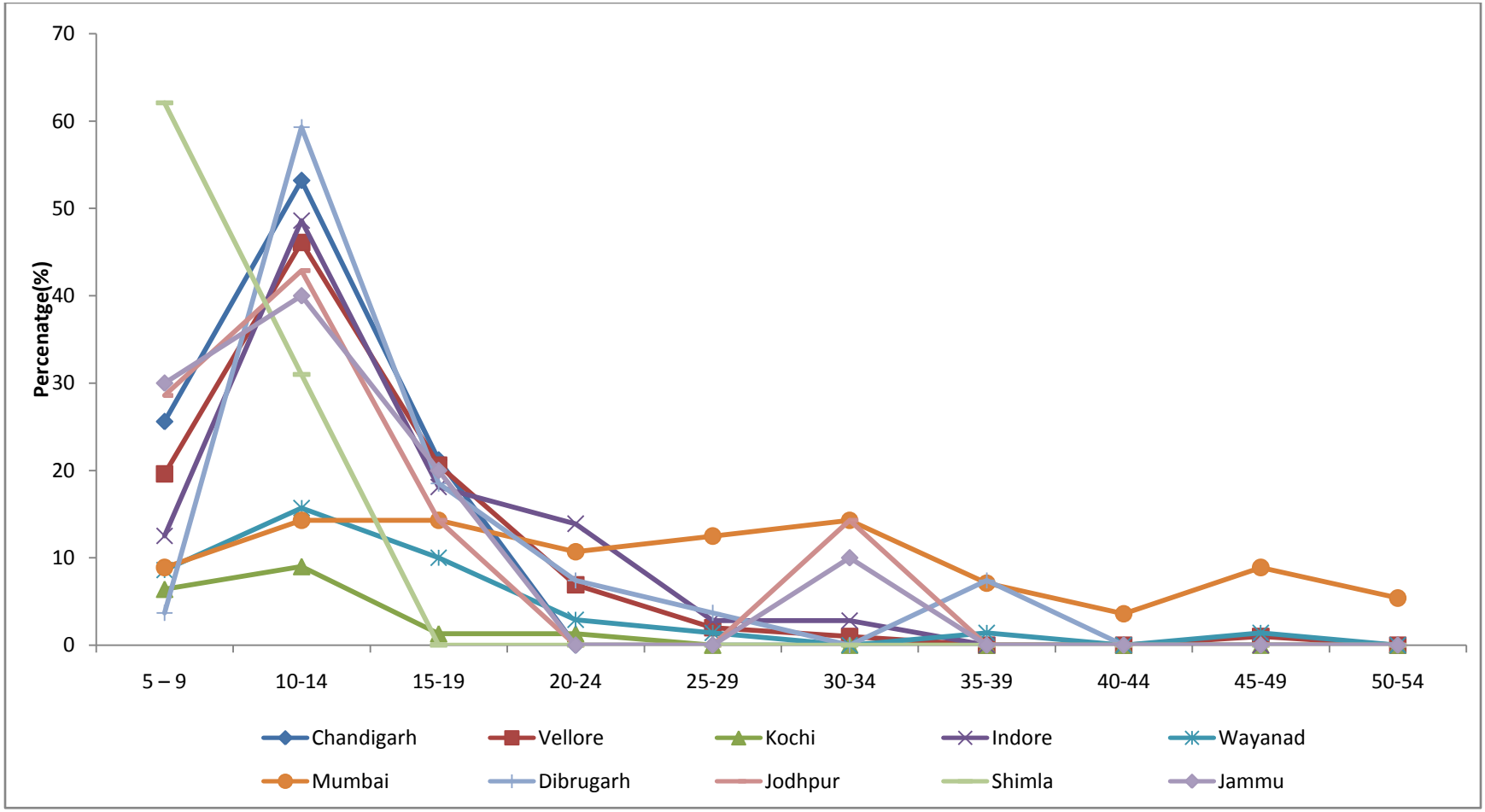


Figure 4.4. 2: Age-wise distribution of RF Cases

Tables

Table 3.4.1: Beta hemolytic streptococci (BHS) from throat swabs of 5-15 years children in cross-sectional study (2000-02)

Center's Name	Symptom	No. of swabs	BHS	Group			
				A	B	C	G
Chandigarh (2000-2002)	Sore throat	579	149	16 (2.8)	0	0	2 (0.3)
	No sore throat	3385	520	44 (1.3)	0	0	0
Vellore (2001-2002)	Sore throat	657	176	74 (11.3)	12 (1.8)	27 (4.1)	62 (9.4)
	No sore throat	3357	928	418 (12.5)	77 (2.3)	100 (3.0)	317 (9.4)

Data in parenthesis is percentages

Table 3.4.2: Distribution of *emm* types of GAS isolates from throat swabs in cross-sectional study (2000-02)

emm type	Chandigarh	Vellore	Total
11	8	10	18
112		18	18
77	14	3	17
81	11		11
82		9	9
110		8	8
85		6	6
105		6	6
108		6	6
1		5	5
18	2	3	5
49		5	5
66		5	5
69	3	2	5
113		5	5
55		4	4
63		4	4
92	1	3	4
111		4	4
28		3	3
53		3	3
56		3	3
58		3	3
74		3	3
75	1	2	3
100		3	3
St212		3	3
New type		3	3

emm type	Chandigarh	Vellore	Total
9		2	2
12		2	2
15		2	2
60		2	2
65		2	2
78		2	2
86		2	2
93		2	2
104		2	2
St 2147		2	2
St2460		2	2
Stns 292		2	2
Stns554		2	2
3		1	1
33		1	1
44		1	1
54		1	1
68		1	1
70		1	1
73		1	1
88		1	1
102		1	1
103		1	1
116		1	1
118	1	0	1
st 1389		1	1
St 5282		1	1
St62		1	1
St11014		1	1
St1731		1	1

emm type	Chandigarh	Vellore	Total
Std432		1	1
Total	41	175	216

Table 3.4.3: Beta hemolytic streptococci (BHS) from skin swabs of children in cross-sectional study (2000-02)

Center's Name	Symptom	No. of swabs	BHS	Group			
				A	B	C	G
Chandigarh	Impetigo	28	2	2 (7.1)	0	0	0
	Without Impetigo	4221	0	0	0	0	0
Vellore	Impetigo	205	61	56 (27.3)	3 (1.5)	2 (1.0)	0
	Without Impetigo	366	36	29 (7.9)	4 (1.1)	0	0

Data in parenthesis is percentages

Table 3.4.4: Distribution of *emm* types of GAS isolates from skin swabs in cross-sectional study (2000-02)

emm type	Chandigarh	Vellore	Total
112		10	10
44	1	3	4
100		4	4
82		3	3
105		3	3
111		3	3
28		2	2
49		2	2
56		2	2
66		2	2
77	1	1	2
102		2	2
108		2	2
113		2	2
st 1389		2	2
11		1	1
15		1	1
25		1	1
36		1	1
53		1	1
69		1	1
75		1	1
St 2147		1	1
New type		1	1
Total	2	52	54

Table 3.4.5: Beta hemolytic streptococci (BHS) from throat swabs of children in cohort study (2000-02)

Center's Name	Symptom	No. of swabs	BHS	Group			
				A	B	C	G
Chandigarh	Sore throat	761	70	18 (2.4)	0	0	0
	No sore throat	2016	112	26 (1.3)	0	0	0
Vellore	Sore throat	391	98	31 (7.9)	18 (4.6)	14 (3.6)	35 (9.0)
	No sore throat	3044	713	347 (11.4)	45 (1.5)	99 (3.3)	242 (8.0)

Data in parenthesis is percentages

Table 3.4.6: Distribution of *emm* types of GAS isolates from throat swabs in cohort study (2000-02)

emm type	Chandigarh	Vellore	Total
1	0	3	3
9	0	2	2
11	2	2	4
12	0	2	2
15	0	1	1
18	0	2	2
28	0	2	2
33	0	1	1
44	2	1	3
53	0	1	1
54	0	1	1
55	0	4	4
58	0	3	3
63	0	2	2
65	0	2	2
66	0	4	4
68	1	1	2
69	0	1	1
71	4	0	4
73	0	1	1
74	0	2	2
75	1	0	1
77	5	3	8
78	0	2	2
81	7	0	7
82	0	7	7
85	0	3	3
87	1	0	1
88	1	0	1
92	0	1	1

emm type	Chandigarh	Vellore	Total
100	0	3	3
102	0	1	1
105	0	4	4
108	0	2	2
110	0	8	8
111	0	3	3
112	0	10	10
113	0	3	3
116	0	1	1
118	1	0	1
N type	0	2	2
st NS 29	0	1	1
st 62	0	1	1
st 212	0	3	3
st D432	0	1	1
st 854	2	0	2
st 1731	0	1	1
st 2460	0	1	1
st 11014	0	1	1
Total	27	100	127

Table 3.4.7: Beta hemolytic streptococci (BHS) from skin swabs of children in cohort study (2000-02)

Center's Name	Symptom	No. of swabs	BHS	Group			
				A	B	C	G
Chandigarh	Impetigo	75	2	2 (2.7)	0	0	0
	Without Impetigo	2312	2	1 (0.04)	0	0	0
Vellore	Impetigo	938	276	236 (25.1)	22 (23.0)	15 (1.6)	3 (0.3)
	Without Impetigo	2493	71	56 (2.2)	14 (0.6)	1 (0.04)	0

Data in parenthesis is percentages

Table 3.4.8: Distribution of *emm* types of GAS isolates from skin swab in cohort study (2000-02)

emm type	Chandigarh	Vellore	Total
77	1	0	1
100	0	3	3
111	0	2	2
82	0	2	2
102	0	1	1
66	0	1	1
ST138	0	1	1
105	0	1	1
44	0	1	1
28	0	2	2
112	0	5	5
15	0	1	1
49	0	1	1
Total	**1**	**21**	**22**

Table 3.4.9: Distribution of beta hemolytic streptococci (BHS) from throat swabs in registry project (2007-10)

Centre's Name	Pharyngitis	No. of swab	BHS	Group			
				A	B	C	G
Chandigarh (2007-10)	Yes	656	103 (15.7)	13 (1.9)	-	-	-
	No	2920	366 (12.5)	14 (0.5)	-	-	-
Mumbai* (2007-10)	Yes	3516	543 (15.4)	293 (8.3)	0	286 (8.1)	
	No	7324	767 (10.5)	209 (2.9)	2 (0.03)	556 (7.6)	
Dibrugarh (2007-10)	Yes	0	0	0	0	0	0
	No	1384	106 (7.7)	18 (1.3)	4 (0.3)	6 (0.4)	21 (1.51)
Jodhpur (2007-10)	Yes	443	45 (10.1)	28 (6.3)	0	3 (0.7)	14 (3.6)
	No	769	42 (5.5)	25 (3.3)	0	0	17 (2.2)
Shimla (2007-10)	Yes	371	68 (18.3)	26 (7.0)	0	9 (2.5)	7 (1.9)
	No	1849	90 (4.9)	28 (1.5)	0	0	3 (0.2)
Jammu (2007-10)	Yes	1875	69 (2.8)	1 (0.1)	0	10 (0.5)	05 (0.3)
	No	634		0 (0.0)	0	5 (0.8)	0.0

*Data for Group C and G is not separately available. Data in parenthesis is percentages.

Table 3.4.10: Distribution of *emm* types of GAS isolates from throat swab: Registry project (2007-10)

emm Type	Chandigarh	Mumbai	Dibrugarh	Jodhpur	Shimla	Jammu	Total
1	0	3	0	3	3	0	9
1-2	0	0	0	1	0	0	1
1-4	0	0	0	1	0	0	1
2	0	0	0	0	4	0	4
9	1	3	0	0	0	0	4
11	1	0	0	4	0	0	5
12	0	1	0	1	18	0	20
15	3	0	0	0	0	0	3
18	0	0	0	2	5	0	7
22	0	1	0	0	0	1	2
25	0	2	0	2	0	0	4
27	1	0	0	0	1	0	2
28	0	0	0	1	0	0	1
39	0	0	0	1	0	0	1
42	1	3	0	4	4	0	12
44	0	0	0	0	1	0	1
49	1	1	0	1	1	0	4
55	1	0	0	1	1	0	3
57	5	3	0	0	0	0	8
60	0	5	0	0	0	0	5
63	0	0	0	1	0	0	1
65	0	0	0	2	0	0	2
66	1	0	0	2	1	0	4
68	3	0	0	1	0	0	4
76	0	0	0	0	1	0	1
77	0	0	0	0	2	0	2
81	5	7	0	0	0	0	12

emm Type	Chandigarh	Mumbai	Dibrugarh	Jodhpur	Shimla	Jammu	Total
87	0	1	0	0	0	0	1
89	0	0	0	1	0	0	1
92	0	0	0	1	0	0	1
98	0	1	0	0	0	0	1
103	1	0	0	3	0	0	4
107	0	0	1	0	0	0	1
109	0	0	0	1	0	0	1
112	1	0	0	1	0	0	2
405	1	0	0	0	0	0	1
stC58	0	0	0	0	1	0	1
st 1448	0	0	0	0	1	0	1
st4722.0	0	0	0	0	1	0	1
st1389	0	0	0	1	0	0	1
st4532	0	0	0	1	0	0	1
st HK.O	0	0	0	1	0	0	1
st KB3.2	0	0	0	0	1	0	1
st HK precursor	0	0	0	0	1	0	1
st 9505	0	1	0	0	0	0	1
st 2111.1	0	1	0	0	0	0	1
st 2904.1	0	1	0	0	0	0	1
st Kn b6	0	1	0	0	0	0	1
Total	26	35	1	38	47	1	148

Table 4.3.1: Profile of study population

Centre Name	Chandigarh (2002-10)	Vellore (2002-06)	Kochi (2003-06)	Indore (2004-07)	Wayanad (2006-09)	Mumbai (2007-10)	Dibrugarh (2007-10)	Jodhpur (2007-10)	Shimla (2007-10)	Jammu (2007-10)
Population	11,16,108	16,48,350	13,68,715	25,85,000	7,87,000	10,68,000	11,85,072	10,20,000	7,21,745	15,00,000
Urban	3,62,407	2,98,011	6,06,340	18,49,536*	30,693	10,68,000	2,28,438	83 ,000	1,66,833	300,000
Rural	7,53,701	13,50,339	7,62,374	7,35,464*	7,56,307	-	9,56,634	9.,37,000	5,54,912	12,00,000
Children 5-14 years										
Male	-	1,77,375	49.62%	-	51.02%	-	-	91,000	63,744	1,98,203
Female	-	1,72,425	50.38%	-	48.99%	-	-	1,05,000	59,099	1.76,797
Total	2,44,872	3,49,800	2,02,710	-	1,30,352	-	2,86,000	1.96,000	1,22,843	3,75,00
Population density person/km^2	524	646	3,146	839**	367.18	46,500	351	126	141	507
Education (%)										
Male	84.4%	86.96%	95.95%	89.2**	90.28%	-	-	67.6%	87.72%	84.92
Female	71.74%	72.43%	90.96%	74.9**	80.80%	-	-	25.16%	70.68%	68.75
Total	78.07%	79.65%	93.42%	82.3**	85.52%	-	68.96%	47.21%	79.12%	77.30
Major Occupation	Agriculture	Agriculture, Service, Small & Large Industry	Trading, fishing, industry	Farming, trading, industries	Agriculture	-	Cultivation	Agriculture	Agriculture	Service, farming, trading, industries
No. of schools	997	1150	377	1664	297	105	1631	932	2278	2614
Primary	785	843	231	1492	228	-	1185	778	1616	1087
Secondary	212	307	146	1561	69	-	446	154	195	950

* 2001 census, ** 2011 census

Table 4.4.1: Registration of RF/RHD cases

Centre Name	Project date		RF			RHD			Total		
	Start	End	M	F	Total	M	F	Total	M	F	Total
Chandigarh	01/12/2002	31/12/2009	104	99	203	224	386	610	328	485	813
Vellore	Feb/ 2002	Sept/ 2006	53	49	102	363	679	1042	416	728	1144
Kochi	15/01/2003	30/11/2006	29	49	78	143	228	371	172	277	449
Indore	01/09/2004	31/08/2007	32	40	72	176	335	511	208	375	583
Wayanad	1/6/2006	31/3/2009	38	32	70	110	283	393	148	315	463
Mumbai	01/06/2007	31/05/2010	21	35	56	224	242	466	245	277	522
Dibrugarh	01/06/2007	28/02/2010	14	13	27	123	223	346	137	236	373
Jodhpur	30/03/2007	29/03/2010	3	4	7	89	124	213	92	128	220
Shimla	January/ 2007	March/ 2010	17	12	29	201	404	605	218	416	634
Jammu	May/ 2007	31/03/2010	5	5	10	159	220	379	164	225	389
Total	-	-	316	338	654	1812	3124	4936	2128	3462	5590

Table 4.4.2: Year-wise registration of RHD cases

Centre	2001-02			2002-03			2003-04			2004-05			2005-06			2006-07			2007-08			2008- 09			2009-10			Total		
Name	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Chandigarh (2002-10)	36	44	80	66	102	168	35	51	86	18	35	53	20	29	49	22	71	93	8	12	20	19	42	61	-	-	-	224	386	610
Vellore (2002-06)	12	15	27	35	64	99	51	89	140	32	56	88	32	52	84	22	47	69										363	679	1042*
Kochi (2003-06)	-	-	-	39	57	96	39	62	101	61	99	160	4	10	14	-	-	-	-	-	-	-	-	-	-	-	-	143	228	371
Indore (2004-07)	-	-	-	-	-	-	-	-	-	-	-	175	-	-	65	-	-	271	-	-	-	-	-	-	-	-	-	-	-	511
Wayanad (2006-09)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60	165	225	34	83	117	16	35	51	110	283	393
Mumbai (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	89	67	156	92	98	190	68	52	120	249	217	466
Dibrugarh (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	93	153	246	70	30	100	163	183	346
Jodhpur (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	41	45	86	31	43	74	17	36	53	89	124	213
Shimla (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	60	159	219	91	124	215	39	107	146	201	404	605
Jammu (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	10	-	-	110	-	-	256	-	-	3	-	-	379

* Information on year-wise distribution was not available for all the cases of Vellore center

Table 4.4.3: Year-wise registration of RF cases

Centre	2001-02			2002-03			2003-04			2004-05			2005-06			2006-07			2007-08			2008-9			2009-10			Total		
Name	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T	M	F	T
Chandigarh (2002-10)	12	12	24	25	27	52	27	28	55	12	10	22	4	3	7	6	1	7	5	6	11	11	10	21	-	-	-	104	99	203
Vellore (2002-06)	7	3	10	10	13	23	15	12	27	8	2	10	5	9	14	4	3	7	-	-	-	-	-	-	-	-	-	49	42	91 *
Kochi (2003-06)	-	-	-	18	26	44	7	14	21	4	8	12	0	1	1	-	-	-	-	-	-	-	-	-	-	-	-	29	49	78
Indore (2004-07)	-	-	-	-	-	-	-	-	-	-	-	32	-	-	18	-	-	22	-	-	-	-	-	-	-	-	-	-	-	72
Wayanad (2006-09)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	26	20	46	7	9	16	5	3	8	-	-	-	38	32	70
Mumbai (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4	6	10	15	23	38	2	6	8	21	35	56
Dibrugarh (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	10	11	21	4	2	6	14	13	27
Jodhpur (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	0	3	3	2	1	3	1	0	1	3	4	7
Shimla (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	6	1	7	3	2	5	8	9	17	17	12	29
Jammu (2007-10)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	3	3	6	2	2	4	5	5	10

* Year-wise distribution of some cases was not available

Table 4.4.4: Age & sex wise distribution of RHD cases

Center	Age	0-4	5 – 9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65 +	Total
Chandigarh	M	.	23	66	39	19	19	8	16	10	8	4	2	5	5	224
	F	.	15	58	48	53	39	46	39	36	21	12	5	5	9	386
	T	.	38	124	87	72	58	54	55	46	29	16	7	10	14	610
Vellore	M	1	35	95	69	28	30	26	22	18	15	8	7	0	9	363
	F	0	29	91	74	96	106	91	79	41	28	22	4	9	9	679
	T	1	64	186	143	124	136	117	101	59	43	30	11	9	18	1042
Kochi	M	0	5	6	5	9	11	8	12	23	18	24	9	6	7	143
	F	0	0	4	3	12	22	29	32	35	13	33	21	12	12	228
	T	0	5	10	8	21	33	37	44	58	31	57	30	18	19	371
Indore	M	2	5	6	17	15	23	18	23	14	12	20	9	4	8	176
	F	0	4	18	18	40	41	38	53	31	34	21	13	13	11	335
	T	2	9	24	35	55	64	56	76	45	46	41	22	17	19	511
Wayanad	M	0	1	6	12	10	16	7	16	9	13	10	5	5	0	110
	F	0	2	11	16	26	41	38	42	32	35	18	11	4	7	283
	T	0	3	17	28	36	57	45	58	41	48	28	16	9	7	393
Mumbai	M	2	59	50	20	20	17	14	12	12	8	2	3	3	2	224
	F	1	51	48	20	18	27	21	19	10	12	9	3	2	1	242
	T	3	110	98	40	38	44	35	31	22	20	11	6	5	3	466
Dibrugarh	M	1	1	16	17	7	15	14	11	7	15	7	6	4	2	123
	F	0	1	9	15	22	25	32	35	25	21	12	9	9	8	223
	T	1	2	25	32	29	40	46	46	32	36	19	15	13	10	346
Jodhpur	M	0	2	10	6	11	10	8	9	9	12	6	2	3	1	89
	F	0	4	15	10	11	20	19	12	13	9	3	3	4	1	124
	T	0	6	25	16	22	30	27	21	22	21	9	5	7	2	213
Shimla	M	0	10	20	26	23	22	22	24	16	12	10	9	2	5	201
	F	0	8	27	17	51	43	44	59	47	43	22	15	16	12	404
	T	0	18	47	43	74	65	66	83	63	55	32	24	18	17	605

Center	Age	0-4	5 – 9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65 +	Total
Jammu	M	0	6	8	17	15	22	33	20	16	11	4	5	1	1	159
	F	2	2	14	8	25	40	28	37	25	14	8	7	6	4	220
	T	2	8	22	25	40	62	61	57	41	25	12	12	7	5	379
	Total	9	263	578	457	511	589	544	572	429	354	255	148	113	144	4936

Table 4.4.5: Age & sex wise distribution of RF cases

Center Name	Age (Year)→ ↓ Sex	0-4	5 – 9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	Total
Chandigarh	M	-	31	50	22	-	-	-	-	-	-	-	103
	F	-	21	58	21	-	-	-	-	-	-	-	100
	T	-	52	108	43	-	-	-	-	-	-	-	203
Vellore	M	2	12	26	9	3	0	1	0	0	0	0	53
	F	1	8	21	12	4	2	0	0	0	1	0	49
	T	3	20	47	21	7	2	1	0	0	1	0	102
Kochi	M	0	3	2	1	1	0	0	0	0	0	0	29
	F	0	2	5	0	0	0	0	0	0	0	0	49
	T	0	5	7	1	1	0	0	0	0	0	0	78*
Indore	M	1	4	14	7	6	0	0	-	-	-	-	32
	F	0	5	21	6	4	2	2	-	-	-	-	40
	T	1	9	35	13	10	2	2	-	-	-	-	72
Wayanad	M	0	3	7	2	1	1	0	0	0	0	0	38
	F	0	3	4	5	1	0	0	1	0	1	0	32
	T	0	6	11	7	2	1	0	1	0	1	0	70*
Mumbai	M	-	2	4	6	2	2	2	2	1	0	0	21
	F	-	3	4	2	4	5	6	2	1	5	3	35
	T	-	5	8	8	6	7	8	4	2	5	3	56
Dibrugarh	M	0	0	8	3	1	0	0	2	0	0	0	14
	F	0	1	8	2	1	1	0	0	0	0	0	13
	T	0	1	16	5	2	1	0	2	0	0	0	27
Jodhpur	M	0	1	1	1	0	0	0	0	0	0	0	3
	F	0	1	2	0	0	0	1	0	0	0	0	4
	T	0	2	3	1	0	0	1	0	0	0	0	7
Shimla	M	0	11	7	0	0	0	0	0	0	0	0	18
	F	2	7	2	0	0	0	0	0	0	0	0	11
	T	2	18	9	0	0	0	0	0	0	0	0	29

Center Name	Age (Year)→ ↓ Sex	0-4	5 – 9	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	Total
Jammu	M	-	2	1	2	-	-	0	-	-	-	-	5
	F	-	1	3	0	-	-	1	-	-	-	-	5
	T	-	3	4	2	-	-	1	-	-	-	-	10
Total		6	118	244	95	28	13	12	7	2	7	3	654

* Information of some cases of RF was not available

Table 4.4.6: Clinical manifestations of registered rheumatic fever cases

Centre Name	Carditis	Arthritis	Chorea	Nodules	Erythema Marginatum	Carditis+ Arthritis	Arthritis+ Chorea	Carditis+ Chorea
Chandigarh	52(25.6)	141(69.5)	30(14.8)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Vellore	0(0.0)	69(75.8)	0(0.0)	0(0.0)	0(0.0)	21(5.5)	1(1.10)	0(0.0)
Kochi	0(0.0)	9(64.3)	0(0.0)	0(0.0)	0(0.0)	5(35.7)	0(0.0)	0(0.0)
Indore*	28(50.9)	32(58.2)	17(30.9)	8(14.5)	1(1.0)	0(0.0)	0(0.0)	0(0.0)
Wayanad	4(13.8)	20(69.0)	0(0.0)	0(0.0)	0(0.0)	3(10.3)	0(0.0)	2(6.9)
Mumbai	27(48.2)	22(39.3)	7(12.5)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Dibrugarh	0(0.0)	18(66.7)	0(0.0)	0(0.0)	0(0.0)	9(33.3)	0(0.0)	0(0.0)
Jodhpur	2(50.0)	0(0.0)	0(0.0)	1(25.0)	0(0.0)	0(0.0)	0(0.0)	1(25.0)
Shimla	19(65.5)	22(75.9)	1(3.45)	7(24.1)	0(0.0)	12(41.4)	0(0.0)	1(3.45)
Jammu	6(60.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	0(0.0)

Figures in parenthesis are percentage. * Out of total 55 patients with rheumatic fever from the project study area.

Table 4.4.7: Age & sex wise distribution of children included in school health survey

Centre Name	Age (Year)→ ↓ Sex	5-9	10-14	15-19	Total
Chandigarh	M	19939	6230	0	26169
	F	16595	5813	0	22408
	T	36534	12043	0	48577
Vellore	M	6680	8477	0	15157
	F	6874	6553	0	13427
	T	13554	15030	0	28584
Kochi	M	4045	6311	970	11326
	F	3546	8832	1329	13707
	T	7591	15143	2299	25033
Indore	M	5855	6066	1019	12940
	F	5670	6214	852	12736
	T	11525	12280	1871	25676
Wayanad	M	2983	2024	359	5366
	F	3085	2279	442	5806
	T	6068	4303	801	11172
Mumbai	M	2159	2679	559	5397
	F	2350	2769	324	5443
	T	4509	5448	883	10840
Dibrugarh	M	3360	2075	0	5435
	F	2753	1988	0	4741
	T	6113	4063	0	10176
Jodhpur	M	2615	2627	0	5242
	F	2320	2449	0	4769
	T	4935	5076	0	10011
Shimla	M	1918	2706	408	5032
	F	1994	2989	174	5157
	T	3912	5695	582	10189

Centre Name	Age (Year)→ ↓ Sex	5-9	10-14	15-19	Total
Jammu	M	2500	2500	0	5000
	F	2500	2500	0	5000
	T	5000	5000	0	10000

Table 4.4.8: Echocardiographic confirmation of suspected heart murmurs in school survey

Centre Name	Age (Year)→ ↓ Sex	Children Examined		Suspected Murmurs		Echo done		ECHO positive (RHD)		ECHO negative (not RHD)	
		5-9 yrs	10-14 yrs	5-9 yrs	10-14yrs	5-9 yrs	10-14 yrs	5-9 yrs	10-14 yrs	5-9 yrs	10-14 yrs
Chandigarh	M	19939	6230	131	81	131	81	26	3	105	78
	F	16596	5813	80	32	80	32	17	5	63	27
	T	36354	12043	211	113	121	113	43	8	168	105
Vellore	M	6680	8477	36	74	20	40	9	15	11	25
	F	6874	6553	57	30	34	13	13	6	21	7
	T	13554	15030	93	104	54	53	22	21	32	32
Kochi	M	4045	6311	43	58	34	43	1	0	33	43
	F	3546	8832	40	78	33	62	0	2	33	58
	T	7591	15143	83	136	67	105	1	2	66	102
Indore	M	5844	6066	76		76		4		70	
	F	5580	6214	67		67		4		61	
	T	11424	12280	143		143		8		131	
Wayanad	M	2983	2024	24	13	16	9	0	0	16	9
	F	3085	2279	22	18	14	13	0	1	14	12
	T	6068	4303	46	31	30	22	0	1	30	21
Mumbai	M	2159	2679	47	39	35	30	2	1	33	29
	F	2350	2769	32	35	30	25	0	1	30	24
	T	4509	5448	79	74	65	55	2	2	63	53
Dibrugarh	M	3360	2075	48	51	43	42	0	1	43	41
	F	2753	1988	43	32	39	28	0	0	39	28
	T	6113	4063	91	83	82	70	0	1	82	69
Jodhpur	M	2615	2627	32	40	6	7	2	2	30	38
	F	2320	2449	23	15	7	10	2	3	16	12
	T	4935	5076	55	55	13	17	4	5	51	50
Shimla	M	1918	2706	69	69	69	69	3	3	66	66
	F	1994	2989	55	82	55	80	3	3	52	77

	T	3912	5695	124	151	124	149	6	6	118	143
Jammu	M	2500	2500	23	23	23	23	2	1	21	22
	F	2500	2500	28	28	28	28	3	0	25	28
	T	5000	5000	51	51	51	51	5	1	46	50

Table 4.4.9: Reasons for not examining children in school survey

Centre Name	No. of schools	No. of children examined	No. of children not examined	Reasons				
				1	2	3	4	5
Chandigarh	306	51381	913	96	373	96	248	0
Vellore	1150	28584	2888					2888
Kochi	-	25362	329	-	-	-	-	-
Indore	80	25676	3	-	-	-	-	Absentees
Wayanad	-	11888	716	-	-	-	-	-
Mumbai	46	10,840	42	17	0	13	12	0
Dibrugarh	99	10176	765	No	Yes	No	Yes	Yes
Jodhpur	201	10011	0	-	-	-	-	-
Shimla	138	10015	Data not recorded		-	-	-	Absentee
Jammu	-	-	-	-	-	-	-	-

1= Migration of family, 2 = Participation in festivals, 3= Shifted to private schools, 4= Not at village & 5= Any other

Table 4.4.10: RHD prevalence/ 1000 in school children

Center	Gender	No. examined	RHD cases by Echo	Prevalence per 1000
Chandigarh	M	25752	29	1.1
	F	28638	22	0.8
	T	54390	51	0.9
Vellore	M	13233	24	1.8
	F	21904	19	0.9
	T	35137	43	1.2
Kochi	M	10356	1	0.1
	F	12378	2	0.2
	T	22734	3	0.1
Indore	M	12940	4	0.3
	F	12736	4	0.3
	T	25676	8	0.3
Wayanad	M	5007	0	0.0
	F	5364	1	0.2
	T	10371	1	0.1
Mumbai	M	4928	3	0.6
	F	7798	1	0.1
	T	12726	4	0.3
Dibrugarh	M	5348	1	0.2
	F	6816	0	0.0
	T	12164	1	0.1
Jodhpur	M	5242	4	0.8
	F	4769	5	1.0
	T	10011	9	0.9
Shimla	M	4907	6	1.2
	F	7689	6	0.8
	T	12596	12	1.0
Jammu	M	5000	3	0.6
	F	5000	3	0.6
	T	10000	6	0.6

Table 4.4.11: RF/ RHD prevalence estimates from school surveys

Centre Name	RF/RHD prevalence 5-14 years in school survey /1000	Estimated number of children in 5-14 year*	No. of RF/RHD Children in 5-14 year population	No. of RF/RHD case in adult population (15 year +)	Total estimated Population	Estimated RF/RHD prevalence per 100000 population
	A	B	C=(A/1000) x B	D=C x 5.5	E	(C+D)/ E x100000
Chandigarh	1.1	244872	269	1480	1116108	157
Vellore	1.2	715737	859	4725	3477317	161
Kochi	0.1	470604	47	259	3105798	10
Indore	0.3	294884	83	457	1282108	42
Wayanad	0.1	142415	14	77	780619	12
Mumbai	0.3	549811	165	908	1068000	100
Dibrugarh	0.1	286303	29	160	1185072	16
Jodhpur	0.9	791184	712	3916	2886505	160
Shimla	1.0	149801	150	825	722502	135
Jammu	0.6	343465	206	1133	1588772	84

*Source: census 2001

Table 5.4.1: Profile of study sites

Centre Name	Chandigarh (2002-10)	Vellore (2002-06)	Kochi (2003-06)	Indore (2004-07)	Wayanad (2006-09)	Mumbai (2007-10)	Dibrugarh (2007-10)	Jodhpur (2007-10)	Shimla (2007-10)	Jammu (2007-10)
Population	11,16,108	16,48,350	13,68,715	25,85,000	7,87,000	10,68,000	11,85,072	10.20 Lac	7,21,745	15,00,000
Urban	3,62,407	298011	44.3%	18,49,536*	3.9%	10,68,000	2,28,438	0.83 Lac	1,66,833	300,000
Rural	7,53,701	1350339	55.7%	7,35,464*	96.1%	-	9,56,634	9.37 Lac	5,54,912	12,00,000
Children 5-14 years										
Male	-	1,77,375	49.62%	-	51.02%	-	-	0.91 Lac	63,744	1,98,203
Female	-	1,72,425	50.38%	-	48.99%	-	-	1.05 Lac	59,099	1,76,797
Total	244872	3,49,800	2,02,710	-	1,30,352	-	2,86,000	1.96 Lac	1,22,843	3,75,000
No. of schools	997	1150	377	1664	297	105	1631	932	2278	2078
Primary	785	843	231	1492	228	-	1185	778	1616	1087
Secondary	212	307	146	1561	69	-	446	154	195	950
Health Institutions	-	-	-	-	64	06	1	-	2	2
No. of Hospitals	7	5 Govt. hospitals	155	60***	?	35	113	1	10	1

Centre Name	Chandigarh (2002-10)	Vellore (2002-06)	Kochi (2003-06)	Indore (2004-07)	Wayanad (2006-09)	Mumbai (2007-10)	Dibrugarh (2007-10)	Jodhpur (2007-10)	Shimla (2007-10)	Jammu (2007-10)
Dispensaries/ Health centers	PHC=6, Mini PHC=17, Subsidiary HC=62, Sub HC =128	35 PHCs	-	31***	-	117	Dispensaries=11 PHC=6 CHC=4 Sub centers=240	34	373	CHC=08 SDH=01 PHC=47 UHC=07 UHP=15 Sub Centre=204

* 2001 census, ** 2011 census

Table 5.4.2: Orientation training in RF/RHD control program

Centre Name	Training	Medical Officers	Pharmacists	Lab. Technicians	MPHW (Female)	MPHW (Male)	LHV/Sanitary / Health worker inspector	Block Extension Educator	Any others		
									SHG	School Teaches/ AWW/ Nursing Students	Others
Chandigarh (2002-10)	Initial	167	118	32	303	194	90	8	0	0	1105[#]
	Refresher	78	25	3	72	27	16	3	0	0	0
Vellore (2002-06)	Initial	73	35	0	231	150	150	10	0	6415	0
	Refresher	-	-	-	-	-	-	-	-	-	-
Kochi (2003-06)	Initial	409	-	-	1236	-	787	-	3169	503+47	0
	Refresher	-	-	-	-	-	-	-	-	-	-
Indore (2004-07)	Initial	536	41	75	82	24	13	-	-	-	65
	Refresher	-	-	-	-	-	-	-	-	-	-
Wayanad (2006-09)	Initial	95	0	0	0	0	919	0	1295	75	0
	Refresher	-	-	-	-	-	-	-	-	-	-
Mumbai (2007-10)	Initial	75	0	0	0	0	0	0	0	500	0
	Refresher	-	-	-	-	-	-	-	-	-	-
Dibrugarh (2007-10)	Initial	197	484*	0	0	0	0	0	0	0	286
	Refresher	-	-	-	-	-	-	-	-	-	-
Jodhpur (2007-10)	Initial	61	0	0	119[1]	0	0	0	0	0	0
	Refresher	87	0	0	221[2]	0	0	0	0	0	0
Shimla (2007-10)	Initial	566	36	Nil	554	0	0	17	0	670	0
	Refresher	-	-	-	-	-	-	-	-	-	-
Jammu (2007-10)	Initial	373	33	61	62	34	4	0	0	1329	0
	refresher	-	-	-	-	-	-	-	-	-	-

MPHW: Multiple Purpose Health Workers, LHV: Lady Health Visitor * Includes all the paramedical staff of the PHC & 1,2=(inclusive Female HW, Lab Tech and pharmacists), #Training for Panches and Sarpanches

Table 5.4.3: Number of training modules, registry forms and health education material utilized

Centre Name	Physician Module	Para-Medical Worker Module	Referral Cards	Clinical& Follow up forms	Patients cards	RF/RHD Registers	Teaching Aid Poster	Folders	Flash cards	News-paper insert	Project Brochure	Jones criteria chart	Any other
Chandigarh (2002-10)	850	1310	11303	3715	3149	41	59	49577	36	49577	662	131	Poster =12704, 1=Radio Broadcast, Cable Advertisement
Vellore (2002-06)	98	750	8000	30000	1000	33	0	40	0	-	0	-	Cable TV, audio cassette
Kochi (2003-06)	1200	1400	1200	1500	-	2	23	1500	?	10	2000	1200	Documentary-1 Bit notices – 5000
Indore (2004-07)	500	500	2400	1700	500	500	17	2000	16	25000	24800	-	RHD support Group,-11, Public education camp -167, Documentary film-1,Posters
Wayanad (2006-09)	350	-	900	2400	-	8	-	300	-	6	-	-	Cable TV advt. Documentary Greeting cards- 1200
Mumbai (2007-10)	650	-	600	300	300	16	2500	10000		01	-	-	-
Dibrugarh (2007-10)	197	180	1970	-	888	-	2800	1970	-	-	197	197	-
Jodhpur (2007-10)	350	1050	11000	-	300	2	550	-	-	-	900	-	12000
Shimla (2007-10)	550	1100	1650	1550	5700	70	4200	1200	30,100	0	5000	0	0
Jammu (2007-10)	350	1000	4000	800	600	20	22000	-	-	10000	-	9200	Local channel, Local FM Radio, Broad cast local newspaper, Display boards, Poster, pamphlets for teacher, AWWs, paramedical

Table 5.4.4: Diagnostic categories of RF/RHD cases at registration

Center Name	RF (1A+1B)			RHD (2A+2B)			Past h/o RF (3A+3B)			Total		
	M	F	T	M	F	T	M	F	T	M	F	T
Chandigarh (2002-10)	90	81	171	224	386	610	14	18	32	328	485	813
Vellore (2002-06)	53	49	102	363	679	1042	0	0	0	416	728	1144
Kochi (2003-06)	7	7	14	143	228	371	22	42	64	172	277	449
Indore (2004-07)	21	34	55	176	335	511	11	6	17	208	375	583
Wayanad (2006-09)	14	15	29	110	283	393	24	17	41	148	315	463
Mumbai (2007-10)	31	25	56	53	73	126	17	11	28	101	109	210
Dibrugarh (2007-10)	14	13	27	123	223	346	0	0	0	137	236	373
Jodhpur (2007-10)	1	2	3	89	124	213	2	2	4	92	128	220
Shimla (2007-10)	18	11	29	183	393	576	6	17	23	201	404	605
Jammu (2007-10)	5	5	10	158	220	378	1	0	1	164	225	389

1A :with carditis; 1B :without carditis; 2A : RHD; 2B: RHD with rheumatic activity

Table 5.4.5: Valvular involvement in registered RHD cases

Centre Name	Mitral alone	Aortic alone	Tricuspid alone	Mitral+ Aortic	Mitral+ Tricuspid	Aortic +Tricuspid	Mitral+ Aortic+ Tricuspid	Mitral+ Aortic+ Tricuspid+ Pulmonary	Total	Not Known	All
Chandigarh	454(74.4)	8(1.3)	0(0.0)	84(13.8)	20(3.3)	8(1.3)	36(5.9)	0(0.0)	610(100.0)	0	610
Vellore	162(32.0)	14(2.8)	9(1.8)	82(16.2)	145(28.6)	1(0.2)	85(16.8)	8(1.6)	506(100.0)	1	507
Kochi	111(29.9)	9(2.4)	0(0.0)	93(25.1)	73(19.7)	1(0.2)	82(22.1)	2(0.05)	371(100.0)	0	371
Indore	342(66.9)	9(1.8)	0(0.0)	89(17.4)	52(10.2)	0(0.0)	19(3.7)	0(0.0)	511(100.0)	0	511
Wayanad	147(38.2)	22(5.7)	3(0.8)	143(37.1)	30(7.8)	1(0.3)	38(9.9)	1(0.3)	385(100.0)	8	393
Mumbai	35(25.0)	01(0.7)	2(1.4)	27(19.3)	41(29.3)	(0.0)	34(24.3)	0(0.0)	140(100.0)	326	466
Dibrugarh	180(52.9)	13(3.8)	0(0.0)	112(32.9)	22(6.5)	3(0.9)	10(2.9)	0(0.0)	340(100.0)	6	346
Jodhpur	115(54.0)	5(2.3)	0(0.0)	37(17.4)	26(12.2)	1(0.5)	29(13.6)	0(0.0)	213(100.0)	0	213
Shimla	181(32.6)	31(5.6)	0(0.0)	139(25.0)	99(17.8)	10(1.8)	95(17.1)	0(0.0)	555(100.0)	50	605
Jammu*	298(62.2)	4(0.8)	1(0.2)	151(31.5)	20(4.2)	1(0.2)	4(0.8)	0(0.0)	479(100.0)	0	479

Figures in parenthesis are percentage, * 100 cases from outside Jammu also added.

Table 5.4.6: RHD cases requiring interventions

Centre Name	Requiring intervention	Surgical intervention	Percutaneous intervention	Cases received intervention	Cases not able to get intervention
Chandigarh(2002-10)	42	14	12	0	16
Vellore(2002-06)	197	0	0	18	103
Kochi(2003-06)	-	-	-	218	-
Indore(2004-07)	233	57	95	160	89
Wayanad (2006-09)	-	-	-	52	-
Mumbai(2007-10)	-	39	-	39	-
Dibrugarh(2007-10)	23	11	-	11	12
Jodhpur (2007-10)	170	170	0	39*	131**
Shimla (2007-10)	-	85***	20	105	0
Jammu (2007-10)	56	0	0	3	53

*36 were already operated before registration; ** Facility Not available at Jodhpur; ***30 (CMV) & 55(Valve replacement)

Table 5.4.7: RHD cases received intervention

Centre Name	Cases received intervention	Cases not able to get intervention	Reasons of not receiving intervention		
			Poor financial status	Death	Not Known
Chandigarh (2002-10)	0	16	10	2	4
Vellore (2002-06)	18	103	61	8	34
Kochi (2003-06)	218	-	-	-	-
Indore (2004-07)	160	89	84	0	5
Wayanad (2006-09)	52	-	-	-	-
Mumbai (2007-10)	-	-	-	-	-
Dibrugarh (2007-10)	11	12	12	0	-
Jodhpur (2007-10)	39 *	131 **	90	23	18
Shimla (2007-10)	105	0	0	12	0
Jammu (2007-10)	3	53	0	0	0

*36 were already operated before registration; ** Facility Not available at Jodhpur

Table 5.4.8: Reasons to stop secondary prophylaxis in registered cases

Centre Name	No. of registered cases	Lost to follow up	Migrated	Died	Stopped by doctors	Stopped themselves	Other reasons
Chandigarh (2002-10)	813	0	75	46	29	29	2
Vellore (2002-06)	503	52	43	14	14	8	9
Kochi(2003-06)	449	78	?	12	55	7	1
Indore (2004-07)	581	3	0	12	187	47	2
Wayanad (2006-09)	-	-	-	-	-	-	-
Mumbai(2007-10)	466	0	32	11	5	1	98
Dibrugarh(2007-10)	373	0	1	7	0	5	22
Jodhpur (2007-10)	220	25	2	23	44	0	0
Shimla (2007-10)	605	14	2	12	187	0	0
Jammu (2007-10)	380	0	0	1	0	0	0

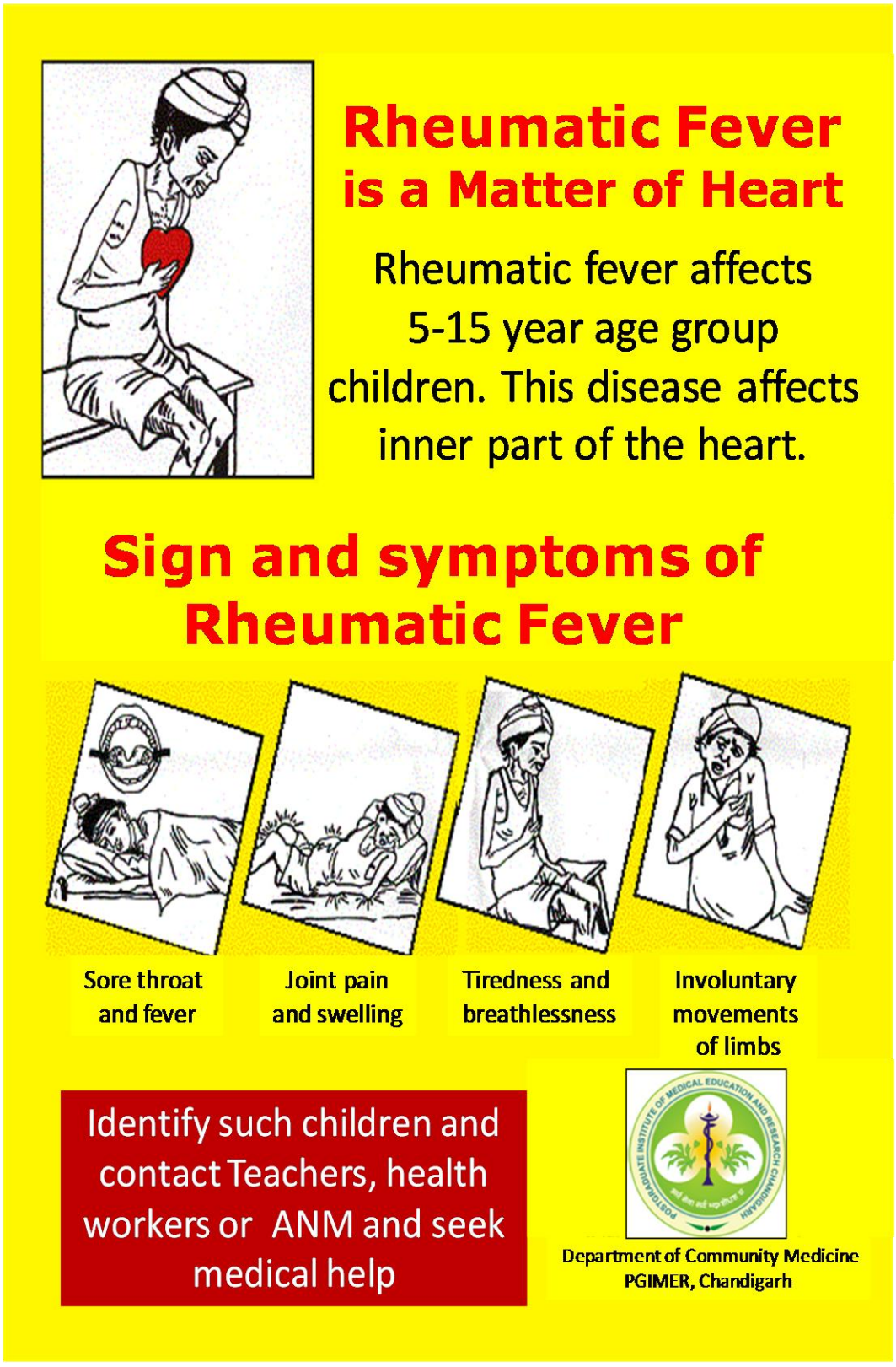
Table 5.4.9: Number of cases lost due to follow up in the registry

Centre Name	No. of cases registered	Lost to Follow-up	Migrated	Deaths	Deaths due to RHD	No. of cases at end of study
Chandigarh	610	0	75	46	31	490
Vellore	507	0	42	46	-	419
Kochi	449	0	0	12	-	437
Indore	583	3	0	12	12	568
Wayanad	393	-	-	-	-	-
Mumbai	466	82	154	24	5	201
Dibrugarh	373	0	1	7	6	359
Jodhpur	220	0	2	23	-	195
Shimla	605	14	2	12	12	565
Jammu	379	0	0	1	1	377

Annexures

Annexure I

RF/RHD Poster

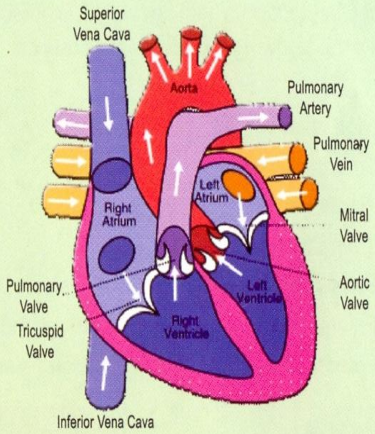


Annexure II

RF/RHD Folder

RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

IMPORTANT INFORMATION



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RHEUMATIC FEVER / RHEUMATIC HEART DISEASE

A. General Information:

A simple disease called sore throat (stringing sensation in the throat) caused by a specific group of bacteria (germs) called *streptococcus beta haemolyticus* can lead to rheumatic fever and development of rheumatic heart disease if it is not treated properly. Incidence of rheumatic fever following sore throat infection is 0.31 to 3.0% which usually occurs within 2 – 3 weeks. The age group < 15 years is most commonly affected. Suspicion for Streptococcus beta haemolyticus infection can be easily made if the following symptoms are present:

(i) High fever
(ii) Sore throat (Fig - 1)
(iii) Redness of throat (Fig - 1)
(iv) Pain during swallowing
(v) Swelling of tonsil with pus formation.
(vi) Enlargement of lymph node of throat and
(vii) Petechia (hemorrhagic spot) of soft palate

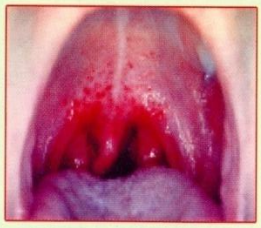

Fig -1

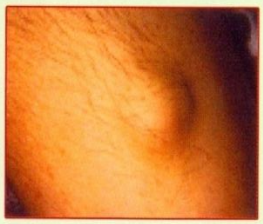

Fig -2

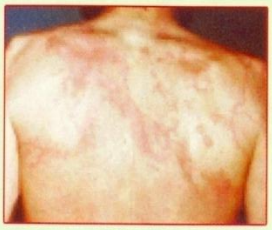

Fig -3

B. Rheumatic Fever:

The rheumatic fever has the following symptoms:

1. High fever.
2. Joint pain and swelling.
3. Abnormal movement of hands and legs (Rheumatic Chorea).
4. Difficulty in breathing during walking and running.
5. Subcutaneous nodule (Fig - 2)
6. Erythema Marginatum (Fig - 3)

C. Rheumatic Heart Disease:

Up to 60 - 80% of patients suffering from rheumatic fever may develop rheumatic heart disease if they are not treated. The disease is characterized by damage of the heart valves. Possibility of suffering from rheumatic heart disease may be suspected if the child presents with the following symptoms:

1. Difficulty on respiration
2. Palpitation
3. Easy fatigability and tiredness
4. Swelling on the legs
5. Coughing out of blood.

D. Important notes for prevention of Rheumatic Fever / Rheumatic Heart Disease:

Prevention of Rheumatic Fever/ Rheumatic Heart Disease is easy. If we follow some of the important guidelines mentioned below we can get rid of this dreaded disease:

(i) Identification of streptococcal sore throat infection (based on the above mentioned symptoms) and treatment with proper antibiotic agent.

(ii) The most suitable antibiotic is either single injection of Benzathine penicillin or Erythromycin tablet in appropriate dose for a period of 10 days.

(iii) Treatment of sore throat with antibiotic will help in the prevention of subsequent development of Rheumatic fever / Rheumatic Heart Disease.

(iv) ***Treatment of Rheumatic Fever:*** Once the disease develops, patient should be treated with either Benzathine penicillin injection or Erythromycin as indicated above to eliminate streptococcal infection. Other symptomatic and supportive treatment should be given. After this initial treatment long term treatment with Benzathine penicillin injection once in a month up to the age of sixteen years or for a period of five years (which ever is more) should be given. Children allergic to penicillin should be given Sulphadiazine tablet daily in recommended dose for the duration similar to penicillin.

(v) ***Treatment of Rheumatic Heart Disease:*** Patients suffering from chronic rheumatic cardiopathy, including those who have undergone cardiovascular surgery, should be kept on the preventive antibiotic regimen throughout their lives.

(vi) Children with RF/RHD who are registered under Rheumatic fever/Rheumatic Heart disease registry programme of Regional Medical Research Centre, Dibrugarh will be given antibiotic free of cost by RMRC, Dibrugarh till the project runs.

(vii) Full adherence to such treatment is very much needed to prevent recurrence of RF or development of Rheumatic heart disease or its complications.

E. Conclusion :

Prevention of RF/RHD has social and economic implications. Poor socioeconomic condition, overcrowding and living in bad hygienic conditions will promote the development as well as propagation of this disease. Every individual in a society has the responsibility to alleviate these factors in order to avoid this easily preventable but otherwise dreaded disease.

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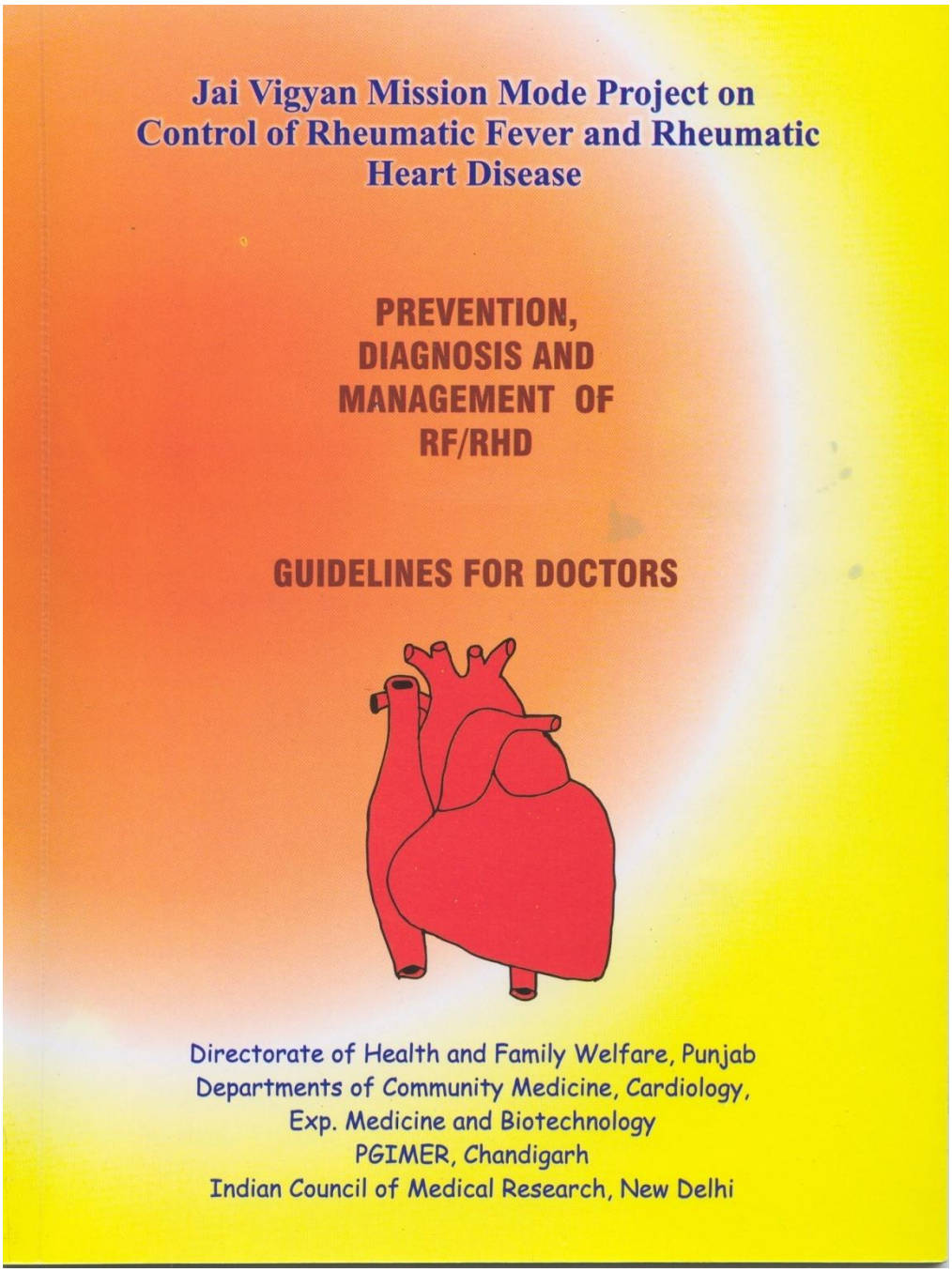
In connection with Jai Vigyan Mission Mode Project on
Establishment of Rheumatic Fever / Rheumatic Heart Disease
Registry in Dibrugarh District

Annexure III

Manual on Prevention, Diagnosis and Management of RF/RHD for Medics and Paramedics



Contents

1. Introduction

Rheumatic fever is initiated by Group A Beta Haemolytic Streptococcus (GAS) throat infection, which may lead to Rheumatic Heart Disease (RHD). The consequences of RF & RHD include: continuing damage to the heart, increasing disability, repeated hospitalisations, and premature death. RHD is one of the preventable chronic disorders of the heart.

1.1. Magnitude of the problem of RF/RHD

Worldwide: Studies conducted in the developing countries estimate a prevalence of 0.2 to 2.3 /1000 school children. In the developed countries, prevalence of RF/RHD has declined during the second half of last century. But during 1980s and 90s outbreaks of RF have been reported even from the developed countries.

India: Population based studies indicate prevalence of RHD to be about 2/1000 population. However, surveys conducted among school children in the age group of 5-16 years by ICMR gives an overall prevalence of 6/1000 (range: 1.8 to11/ 1000).

1.2. Causation of RF/RHD

The occurrence of Rheumatic fever /Rheumatic heart disease is an interplay of various factors, i.e., the agent, host and the environment.

1. **Agent:** Most serotypes of group GAS have been associated with the development of rheumatic fever. However, some stereotypes have been associated epidemiologically with rheumatic fever suggesting enhanced 'rheumatogenicity'.

   No "rheumatogenic substance' has yet been identified and confirmed in the laboratory, although several have been proposed. Other serological groups of beta-haemolytic streptococci (e.g., B, C, G, and F) have been associated with throat infections, but they do not cause rheumatic fever.

2. **Host:** The commonest age group involved is 5-15 years with no sex predisposition. The progression depends upon the frequency of subsequent pharyngitis by GAS, and the age of initial attack. Younger the age faster is the progression.

3. **Environmental:** RF is a disease linked to overcrowding in poor housing conditions (due increased droplet GAS infection). It declines sharply when the standard of living improves.

1.3. How can RF /RHD be prevented?

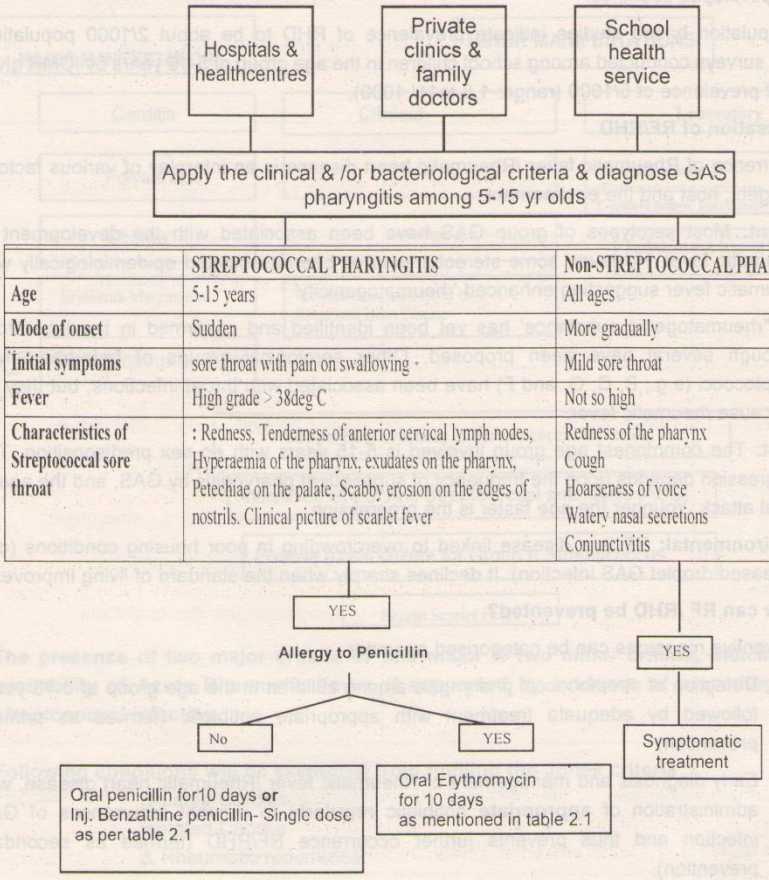
Preventive measures can be categorised as under

- Detection of streptococcal pharyngitis among children in the age group of 5-15 years followed by adequate treatment with appropriate antibiotic (termed as primary prevention)
- Early diagnosis and management of Rheumatic fever /Rheumatic heart disease, with administration of **appropriate** antibiotic **regularly** to prevent recurrences of GAS infection and thus prevents further occurrence RF/RHD (termed as secondary prevention).

2. Primary Prevention of RF/RHD

Primary prevention activities of RF/RHD involve an early diagnosis and treatment of Streptococcal Pharyngitis. Diagnosis is carried out by both clinical and bacteriological examination. Clinically, streptococcal pharyngitis has to be differentiated from non streptococcal pharyngitis by criteria as enumerated in flow diagram 1 given below. For bacterial confirmation of diagnosis, throat culture has to be done. On confirmation of diagnosis, patient of Streptococcal Pharyngitis has to be given injection Benzathine penicillin or tablet erythromycin if allergic to former. Recommended doses for the above is given in Table 2.1

Flow Diagram 1 : Detection, diagnosis and management of streptococcal sore throat



	STREPTOCOCCAL PHARYNGITIS	Non-STREPTOCOCCAL PHARYNGITI
Age	5-15 years	All ages
Mode of onset	Sudden	More gradually
Initial symptoms	sore throat with pain on swallowing	Mild sore throat
Fever	High grade > 38deg C	Not so high
Characteristics of Streptococcal sore throat	: Redness, Tenderness of anterior cervical lymph nodes, Hyperaemia of the pharynx, exudates on the pharynx, Petechiae on the palate, Scabby erosion on the edges of nostrils. Clinical picture of scarlet fever	Redness of the pharynx Cough Hoarseness of voice Watery nasal secretions Conjunctivitis

Table 2.1: Recommended treatment for acute streptococcal pharyngitis

Antibiotic	Mode of administration	Dose
Phenoxymethyl penicillin[a]	Oral	<20 kg body weight , 125mg, 4 times daily ≥20 kg body weight, 250mg, 4 times daily for 10 days.
Benzathine benzyl penicillin	Intramuscular after **antibiotic sensitivity test**	<30 kg body weight 6 lac units ≥30 kg body weight 12 lac units (given as a single injection)
Erythromycin	Oral (if allergic to penicillin)	≥25 kg body weight, 250 mg, 4 times a day for 10 days <25 kg body weight , 40mg/kg of body weight per day in 2-4 divided doses; the total daily dose should not exceed 1g

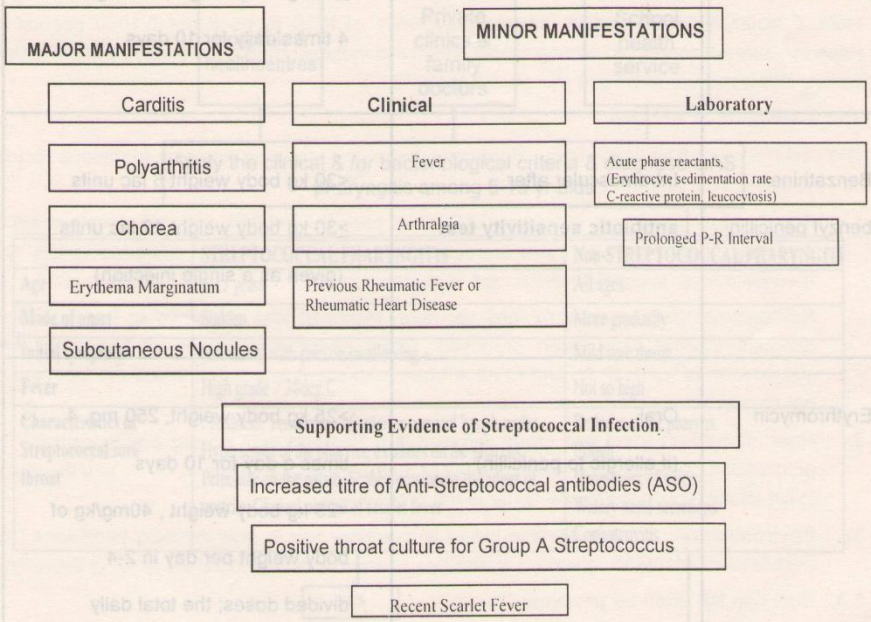
a. Phenoxymethyl penicillin is the preferred oral formulation because of its more reliable absorption; however, if it is not available, benzyl penicillin may be used.

3

How to diagnose Acute Rheumatic fever?

Cases with untreated, partially treated or recurrent streptococcal pharyngitis can result in acute Rheumatic fever. A set of major and minor manifestation was suggested by Dr. T.Duckitt Jones, subsequently revised by the American Heart Association in 1992 as given below. Major and minor manifestations have to be accompanied by evidence of preceeding group A streptococcal pharyngitis.

Flow diagram 2 : Guidelines for the clinical diagnosis of acute rheumatic fever. (Jones' criteria).



The presence of two major criteria or one major & two minor criteria, indicates a high probability of Acute Rheumatic Fever, if supported by evidence of preceding Group A streptococcal infection.

Following conditions will be exempted from fulfiling the Jones criteria

Isolated Carditis,
Isolated Chorea
& Rheumatic recurrence

3.1 Major Criteria for Diagnosis

Major Criteria:

Carditis. The rheumatic carditis is a pancarditis involving the pericardium, myocardium and the endocardium. It is an early manifestation of rheumatic fever so that by the time a patient seeks help he already has evidence of carditis.

Pericarditis: Pericarditis results in precordial pain, which may be quite severe. On auscultation a friction rub is present. The electrocardiogram may show ST and T changes consistent with pericarditis. A patient of rheumatic pericarditis always has additional mitral or mitral and aortic regurgitation murmur. If after the disappearance of the pericardial friction rub there are no murmurs, one can safely exclude rheumatic fever as the cause of pericarditis.

Myocarditis: The features diagnostic of myocarditis are: cardiac enlargement, soft first sound, congestive cardiac failure and Carey Coomb's murmur.

[Carey Coomb's murmur is a delayed diastolic mitral murmur heard during the course of acute rheumatic fever. It tends to disappear after the myocarditis subsides.]

Endocarditis: The endocarditis is represented by a pan systolic murmur of mitral regurgitation with or without an associated aortic regurgitation murmur. Pathologically mitral valve is involved in 100 per cent of cases of rheumatic fever that have carditis.

Arthritis: Rheumatic arthritis is a poly arthritis involving large joints like knees, ankles and elbows. Uncommonly smaller joints may also be involved. It is migratory poly arthritis with the affected joints showing redness, warmth, swelling, pain and limitation of movement.

The pain and swelling appear rather quickly, last 3-7 days and subside spontaneously to appear in some other joint. There is no residual damage to the joint.

Subcutaneous nodules: Subcutaneous nodules appear on bony prominences like elbows, shins, occiput and spine. They vary in size from pinhead to an almond. They are non-tender. Subcutaneous nodules are a late manifestation and appear around 6 weeks after the onset of rheumatic fever.

Chorea: Sydenham's chorea is also a late manifestation occurring about 3 months after the onset of acute rheumatic fever. It consists of purposeless jerky movements resulting in deranged speech, muscular incoordination, awkward gait and weakness. The affected child is emotionally disturbed and drops things he/she is carrying. It is 3-4 times more common in females as compared to males. Untreated it has a self-limiting course of 2-6 weeks.

Erythema Marginatum. The rash is faintly reddish, not raised above the skin and non-itching. Although considered to be more specific than other varieties of skin manifestations, it is known to be extremely rare in Indians.

3.2 Minor Criteria for Diagnosis :

The minor criteria have been sub-divided into (A) clinical and (B) laboratory manifestations.

A. CLINICAL.

(i) **FEVER:** Rheumatic fever is almost always associated with fever. The temperature rarely goes above 39.5°C(103 deg F). In the initial attack it is present in almost 90 per cent of the patients.

(ii) **ARTHRALGIA:** Arthralgia is defined as subjective pain, it is minor manifestation of rheumatic fever. Figures from India indicate that arthritis and arthralgia together occur in about 90 per cent of all patients.

(iii) **PREVIOUS RHEUMATIC FEVER OR RHEUMATIC HEART DISEASE.** This minor criterion is applicable only for a second attack of rheumatic fever.

B. LABORATORY MANIFESTATIONS

(i) ACUTE PHASE REACTANTS

Polymorphonuclear leucocytosis (10 to 15,000/mm3),

Increased sedimentations rate and

Presence of C-reactive protein (C-reactive protein is a beta globulin, which is increased uniformly in all patients of acute rheumatic fever. It subsides rapidly if a patient is on steroids. Absence of C-reactive protein is strongly against the diagnosis of acute rheumatic fever but the presence is not pathognomic of ARF).

(ii) PROLONGED PR INTERVAL IN THE ELECTROCARDIOGRAM

- Prolonged PR interval i.e. >0.2m sec. is also a non-diagnostic criterion since it can get prolonged in many infections. It is also not diagnostic of carditis.
- Artrioventricular block especially of the Wenckebach type. Prolongation of QTc (corrected QT interval) is also suggestive of mycocarditis.

3.3. Essential Criteria for Diagnosis:

Evidence of recent streptococcal infection detected by

1. ASO titre: increased titre indicates previous streptococcus infection. A four-fold rise in titre at a gap of three weeks or a titre of 250 units is significant.
2. Throat culture: Positive culture indicate streptococcal Group A infection.
3. Residua of Scarlet fever: Desquamation of skin of palms and soles indicate scarlet fever within previous two weeks. Scarlet fever cases are rarely seen in India.

[Scarlet fever -Streptococcal pharyngitis, with fever & generalised rash, which starts from trunk and spreads onto the entire body. It spares the palm and sole but, residua are seen only on palms and sole.]

4. Management of Rheumatic fever:

Management of Rheumatic fever entails early diagnosis and treatment. Treatment consist of

Bed rest

Anti -inflammatory drugs and

treatment to eliminate streptococcal infection. The doses, duration and tapering schedule of anti - inflammatory drugs have to be individualised according to the patient.

Flow Diagram 3: Management of Rheumatic Fever.

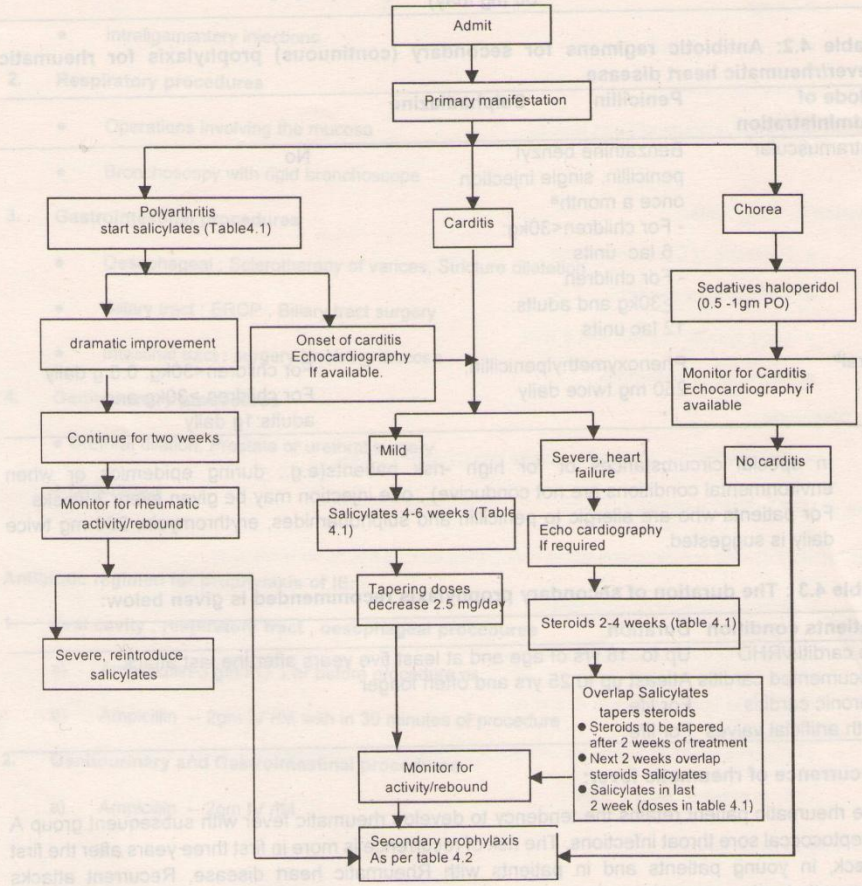


Table 4.1 Doses of anti-inflammatory drugs used in Rheumatic fever

Condition of patient	Drugs of choice	Dose	Frequency	Route of administration
Without carditis or mild carditis	Aspirin	(120 mg / kg /day) 500 mg up to 8 times a day	4 times a day	Oral
Moderate or serious carditis	Prednisone	1.5 to 2mg/kg/day (maximum 60 mg /day)	2-3 times a day	Oral

Table 4.2: Antibiotic regimens for secondary (continuous) prophylaxis for rheumatic fever/rheumatic heart disease

Mode of administration	Penicillin	Sulphadiazine
Intramuscular	Benzathine benzyl penicillin, single injection once a month[a] - For children<30kg: 6 lac units - For children ≥30kg and adults: 12 lac units	No
Oral[b]	Phenoxymethylpenicillin, 250 mg twice daily	For children<30kg: 0.5 g daily For children ≥30kg and adults:1g daily

a In special circumstances or for high -risk patients(e.g.: during epidemics or when environmental conditions are not conducive) , one injection may be given every 3 weeks

b For patients who are allergic to penicillin and sulphonamides, erythromycin, 250 mg twice daily is suggested.

Table 4.3 : The duration of secondary prophylaxis recommended is given below:

Patients condition	Duration
No carditis/RHD	Up to 18 yrs of age and at least five years after the last attack
Documented carditis	Atleast up to 25 yrs and often longer
Chronic carditis	For life
With artificial valves	For life

Recurrence of rheumatic fever:

The rheumatic patient retains the tendency to develop rheumatic fever with subsequent group A Streptococcal sore throat infections. The risk of recurrence is more in first three years after the first attack, in young patients and in patients with Rheumatic heart disease. Recurrent attacks frequently lead to progressive deterioration in valvular & myocardial function. Thus the need for ensuring adherence to prophylaxis in all patients is necessary.

4. How to diagnose RHD?

4.1.1. Criteria for diagnosis of RHD

Reliable auscultation is sufficient for diagnosis of RHD in most cases.
However, some cases may require confirmation by Echo.
Following criteria may be used for Diagnosis of RHD

Definite RHD:

- Isolated MS
- MS+ MR.
- MS or MR.+ AR
- Isolated MR with documented history of RF
- Isolated MR (by Echo)

Probable RHD

- Isolated AR
- Exclude bicuspid valve (by Echo)
  Marfan's syndrome (clinically characterized by tall stature, high arched palate, arm span more than height, and vascular deformities like Aortic dissection &aortic root dilation)

Suspected RHD

Rest of the cases referred to the cardiologist for confirmation (by Echo).

4.1.2. General signs & symptoms of RHD:

Valvular deformities are the hallmark of Rheumatic heart disease. The hemodynamic changes taking place because of them, result in alteration of blood flow across the valves. Heart undergoes changes due to pressure and volume overload, in the form of hypertrophy of myocardial fibres. Dilatation of heart chambers and pulmonary congestion lead to following signs & symptoms:

- Palpitation
- Dyspnoea
- Easy fatiguability
- Cough
- Chest pain
- Haemoptysis

Following classification given by New York Heart Association (NYHA) may be used to assess the functional status of the patient.

New York Heart Association (NYHA) Grades for Heart Failure

I. No limitation of physical activity. No symptoms with accustomed exertion.
II. Slight limitation of physical activity. Symptoms with accustomed exertion
III. Marked limitation of physical activity. Symptoms with less than accustomed exertion.
IV. Inability to carry out any physical activity without discomfort. Symptoms at rest.

4.1.3. Auscultatory & Other Findings of Common Cardiac Lesions of RHD

	Mitral Stenosis (MS)	Mitral Regurgitation (MR)	Aortic Stenosis (AS)	Aortic Regurgitation (AR)
S1	Loud	Soft or absent		Soft
S2	Loud P2	Widely split	Narrow to paradoxical split	A2 delayed or accentuated
S3		Low pitched (severe MR)	If Left Ventricle (LV) dilated	S3+Systolic ejection click
S4		If acute severe MR	Audible at apex when Left Ventricle Hypertrophy (LVH)	Rare
MURMUR Systolic/Diastolic	Opening snap followed by delayed diastolic murmur with pre-systolic accentuation	Systolic Holosystolic Crescendo/ De-Crescendo	Ejection mid systolic	High pitched blowing decrescendo Diastolic
Radiation of murmur		To the axilla	Towards carotid artery	
Best heard on precordium	At apex with patient in left lateral recumbent position	At the apex increases by iso metric strain decreased by Valsalva	Base of heart 2nd Inter costal space (ICS) (Rt)	Third ICS left sternal border increased by Patient leaning forward with breath held in expiration
Chest X Ray findings	Straightening of left heart border. Prominence of main pulmonary trunk. Dilatation of upper lobe pulmonary vein Kerley-B Lines	Left Atrium (LA) Enlargement. Pulmonary venous congestion. Interstitial oedema. Valve calcification	Rounding of cardiac apex. Post- stenotic dilatation of ascending aorta. Aortic calcification	Apex down and to the left. Ascending aorta and aortic knob may be moderately dilated
ECG findings	P-wave – LA enlargement. If severe MS – Right atrial dilatation RVH	LA enlargement AF may be present	LVH LV strain – ST segment depression. T-wave inversion in lead1 Avl and left precordial strain	LVH LV strain QRS prolonged LA dilatation
Medical Treatment	Penicillin prophylaxis	Penicillin prophylaxis	Penicillin prophylaxis	Penicillin prophylaxis
Surgical Treatment	Balloon Mitral Valvotomy (BMV) /Closed Mitral Valvotomy (CMV) Open heart valvotomy	Valve reconstruction. valve replacement	Valve replacement & aortocoronary bypass graft if co-existing coronary disease	Valve reconstruction. valve replacement

Note: Indications for referral

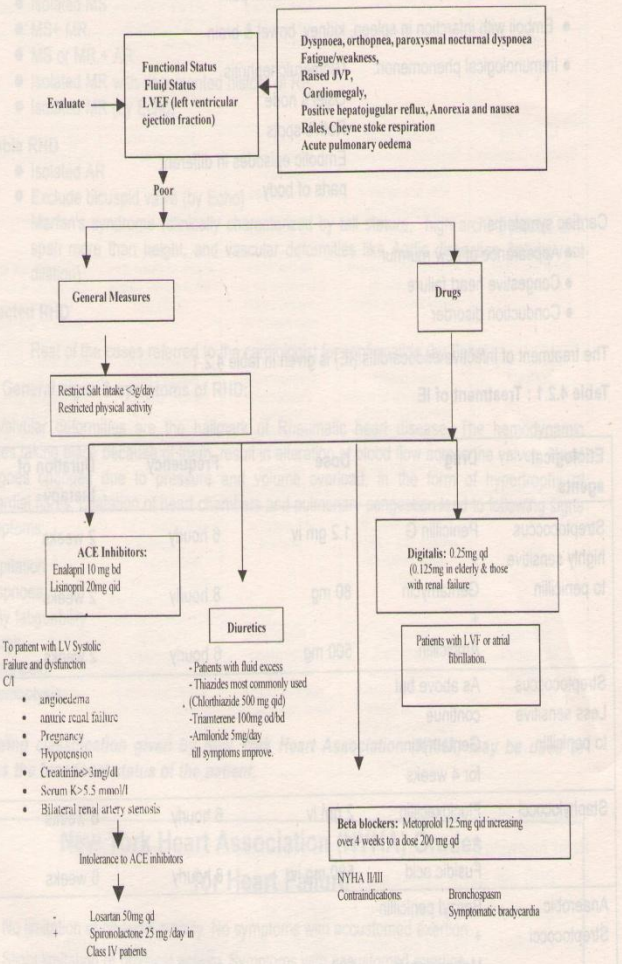
Refer following categories of patients to secondary or tertiary care centres

- RHD with NYHA class III and IV for management.
- Severe MS and pliable valves-for (BMV)/(CMV).
- Calcified valves and significant regurgitation-Mitral Valve Replacement (MVR).
- Isolated AS/AR or combination of both to be treated depending on the severity of aortic valve disease

4.2. COMPLICATIONS OF RHD

A patient of RHD can have many complications of which, Congestive Cardiac Failure and Infective Endocarditis are important. The management of both conditions are given as flow diagram below

Flow diagram 4 : Diagnosis and Management of Congestive cardiac failure.



4.2.2. INFECTIVE ENDOCARDITIS (IE)

Following signs & symptoms in a patient who has prolonged (unexplained) fever and valvular heart abnormalities indicate Infective Endocarditis.

Non-cardiac symptoms:

- Fever, myalgia, arthralgia, clubbing, splenomegaly
- Musculoskeletal symptoms of arthritis and back pain
- Emboli with infarction in spleen, kidney, bowel & brain
- Immunological phenomenon: Glomerulonephritis
  Osler's node
  Roth's spots
  Embolic episodes in different parts of body

Cardiac symptoms:

- Appearance of new murmur
- Congestive heart failure
- Conduction disorder

The treatment of infective endocarditis (IE) is given in table 4.2.1

Table 4.2.1 : Treatment of IE

Etiological agents	Drug	Dose	Frequency	Duration of therapy
Streptococcus highly sensitive to penicillin	Penicillin G +	1.2 gm iv	6 hourly	2 weeks
	Gentamycin +	80 mg	8 hourly	2 weeks
	Ampicillin	500 mg	6 hourly	2 weeks
Streptococcus Less sensitive to penicillin	As above but continue Gentamycin for 4 weeks			
Staphylococci	Flucloxacillin +	2 gm iv	6 hourly	6 weeks
	Fusidic acid	580 mg iv	8 hourly	6 weeks
Anaerobic Streptococci	Benzyl penicillin +			
	Metronidazole	500 mg PO/iv	8 hourly	4-6 weeks

PLACE OF PROPHYLAXIS IN IE:

1. **Dental procedures**
   - Extraction
   - Periodontal procedures cleaning causing gingival bleeding, implant placement, reimplantation of avulsed teeth or surgery beyond apex.
   - Intraligamentary injections.
2. **Respiratory procedures**
   - Operations involving the mucosa
   - Bronchoscopy with rigid bronchoscope
3. **Gastrointestinal procedures**
   - Oesophageal : Sclerotherapy of varices, Stricture dilatation
   - Biliary tract : ERCP , Biliary tract surgery
   - Intestinal tract : surgery involving mucosa
4. **Genitourinary procedures**
   - Urethral dilation, Prostate or urethral surgery
   - Cystoscopy

Antibiotic regimen for prophylaxis of IE:

1. **Oral cavity , respiratory tract , oesophageal procedures**
   a) Amoxycillin-3 gm PO 1 hr before procedure or
   b) Ampicillin -- 2gm IV /IM with in 30 minutes of procedure
2. **Genitourinary and Gastrointestinal procedures**
   a) Ampicillin -- 2gm IV /IM
   +
   Gentamicin 1.5 mg/kg with in 30 minutes of procedure, repeat Ampicillin 1gmIV/IM six hours later
   b) Vancomycin--- 1gm IV over 1-2 hours +Gentamicin 1.5 mg/kg with in 30 minutes of procedure

4.3. RHD IN PREGNANCY

Commonest cardiac lesion in pregnancy is rheumatic in origin of which mitral stenosis is most common (approximately around 80%).

Signs and Symptoms:

- Dyspnoea
- Cough
- Symptoms of cardiac failure
- Basal crepitations
- Change in grade of heart lesions

Criterion for Diagnosis:

- Presence of Diastolic murmur
- Cardiac enlargement
- Loud systolic murmur with a thrill
- Presence of Arrhythmia

Lab Diagnosis:

- Based on ECG, echocardiography and Doppler studies

Time of MTP in RHD patients:

If any of the following complications occur during pregnancy it has to be terminated.

- Primary pulmonary hypertension
- Pulmonary veno-occlusive disease
- Patients in NYHA Grade III and IV
- Patients in NYHA Grade I/II with previous history of cardiac failure in early months of pregnancy or in between pregnancies

Termination at 12 weeks:

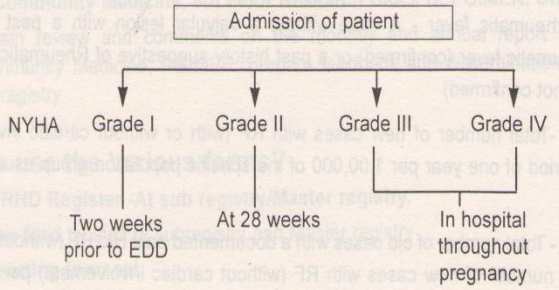
- Suction evacuation
- Conventional dilation and evacuation (termination by hysterectomy is contraindicated)

4.3.1 MANAGEMENT OF RHD IN PREGNANCY

Patient should be advised to undergo preconceptional valvotomy rather than undergoing the same procedure during pregnancy i.e. during 12th week.

The management of patient recommended is given in flow diagram below :

Flow diagram 5 : Managment of RHD in pregnancy :



MANAGEMENT OF RHD DURING LABOUR

1st stage	Bed rest, recumbent position, Oxygen, i.v. fluids, not more than 75ml/hr, Epidural anesthesia if required (contraindicated in AS)
2nd stage	Shorten by forceps or ventouse, pudendal or perineal block, Avoid i. v. Ergometrine at delivery of anterior shoulder Avoid lithotomy position
3rd stage	Conventional management Oxytocin if heavy bleeding i. v. Furosemide if fluid overload
Puerperium	Close observation for 24 hrs Hospitalization for 2 weeks If puerperal fever give antibiotics Breast feeding contraindicated only if CCF is there

Contraception:

Temporary : Barrier Method

Permanent : Minilap 1st week puerperium

: Vasectomy

Definitions (as laid down by World Health Organization)

- Rheumatic fever- A new (current) case with acute illness which fulfils the Jone's criteria (Revised 1992) (with or without cardiac involvement)
- Rheumatic heart disease* - A new or old case without rheumatic activity with a valvular lesion confirmed either by reliable auscultation or by echocardiography
- Past history of rheumatic fever - A case without a valvular lesion with a past history of documented rheumatic fever (confirmed) or a past history suggestive of Rheumatic fever, but undocumented (not confirmed)
- Incidence of RF -Total number of new cases with RF (with or without cardiac involvement) recorded in a period of one year per 1,00,000 of the specific population group usually school children.
- Prevalence of RF - Total number of old cases with a documented past H/o RF (without a valvular lesion) and total number of new cases with RF (without cardiac involvement) per 1000 in a selected area, period of time and specific population group usually school children.
- Prevalence of RHD -Total number of all cases with confirmed RHD and total number of new cases with RF (with cardiac involvement) per 1000 in a selected area ,period of time and specific population group usually school children.
- Prevalence of RF/RHD -Total no. of RF plus RHD cases per thousand population.
- Group A streptococcal throat infections - Cases with throat illness and a positive culture for GAS (confirmed)
- Compliance in prophylaxis -The patient who receives at least 90% of the long acting Benzathine Penicillin (LAP) injections due per year is considered compliant. Otherwise, the patient is non compliant. Centre compliance is reported as the percentage of total number of compliant patients/ the total number of patients registered.

*Reliable auscultation is sufficient for diagnosis of RHD in most cases. However, some cases may require confirmation by Echo.

Definite: Isolated Mitral Stenosis (MS); MS with Mitral Regurgitation (MR); MS or MR with Aortic Regurgitation (AR); Isolated MR with documented history of RF; Isolated MR (by Echo).

Probable: Isolated AR; Exclude bicuspid valve (by Echo); Exclude Marfan' s syndrome (clinically).

Suspected: Rest of the cases referred to the cardiologist for confirmation (by Echo).

PROJECT IMPLEMENTATION

JAI VIGYAN MISSION MODE PROJECT

ON CONTROL OF RF/RHD AT DISTRICT ROPAR.

The Indian Council of Medical Research (ICMR) is sponsoring the Mission Mode Project on control of Rhuematic fever/Rhuematic heart discease (RF/RHD) in assocation with Directorate of Health and family Welfare, Punjab and PGI MER, Chandigarh as partners in the programme. The Project is being carried out at two nodal centers on pilot basis-Ropar in North India and Vellore in the South. At these places the registration of RF/RHD patients will be carried out in the first phase in one district. In the second phase, each nodal centre will set up and monitor three satellite centers in districts of its neighbouring states.

OBJECTIVES:

The Following are the stated objectives of the operational research project:-

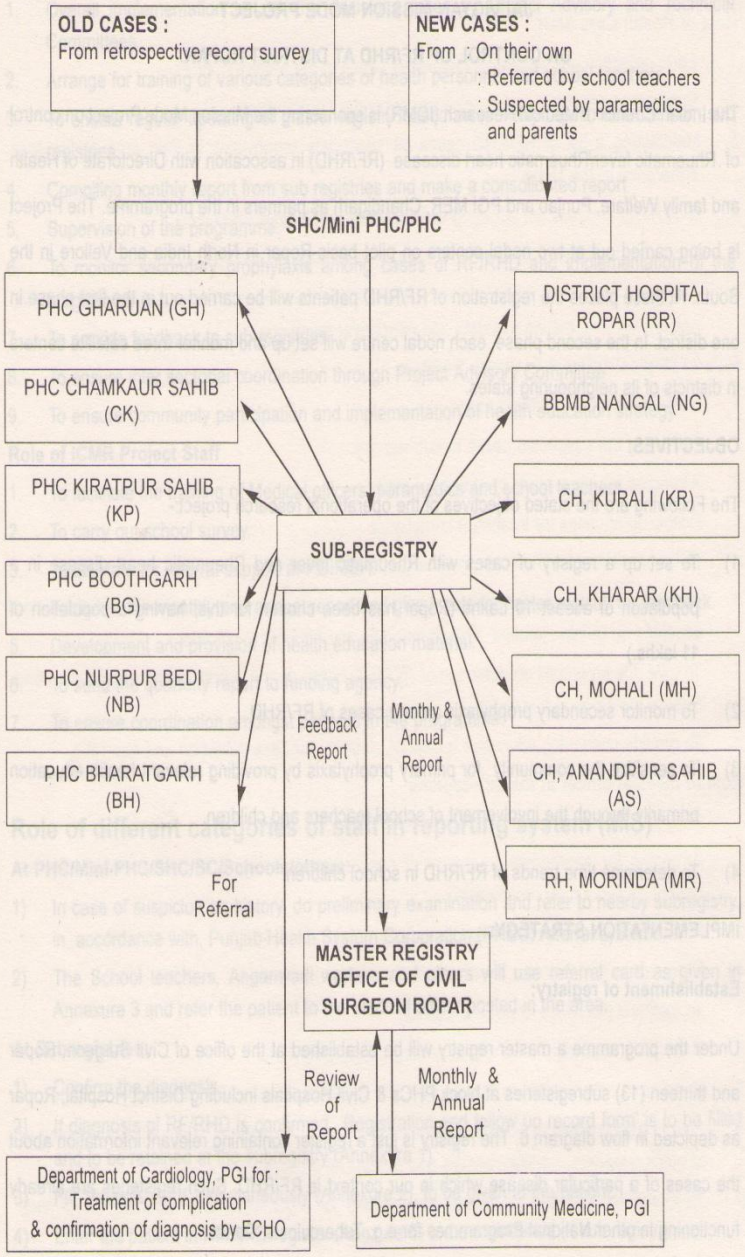
1) To set up a registry of cases with Rheumatic fever and Rheumatic heart disease in a population of atleast 10 Lakhs (Ropar has been chosen for this, having a population of 11 lakhs.)
2) To monitor secondary prophylaxis among cases of RF/RHD.
3) To sensitize the community for primary prophylaxis by providing relevant health education primarily through the involvement of school teachers and children.
4) To determine time trends of RF/RHD in school children.

IMPLEMENTATION STRATEGY:

Establishment of registry:

Under the programme a master registry will be established at the office of Civil Surgeon, Ropar and thirteen (13) subregisteries at block PHCs & Civil Hospitals including District Hospital, Ropar as depicted in flow diagram 6. The registry is just a register containing relevant information about the cases of a particular disease which in our context is RF/RHD. Such registeries are already functioning in other National Programmes for e.g. Tuberculosis, Cancer.

Flow diagram 6: Establishment of registry & Sub-registries with their codes given in brackets.



18

Job responsibilities of various categories of staff under the programme

Role of Health Care Staff

1. Early detection and referral of suspected cases to the Medical Officer.
2. Providing guidance to cases requiring secondary prophylaxis.
3. Maintaining a list of RF/RHD cases on secondary prophylaxis in their area and ensure adherence to the same.
4. Follow up of cases not adhering to secondary prophylaxis (defaulter).
5. Arranging for the education of school children through school health programme.
6. To ensure community participation by organizing health education sessions on RF/RHD for opinion leaders, mahila mandals and panchayat members.

Role of Medical Officers in Health Services

1. Early detection of RF/RHD cases.
2. Reporting the suspected cases to sub-registry.
3. Arranging for appropriate treatment of cases.
4. Follow up of cases for treatment compliance.
5. Refer cases for treatment of complications and follow them up.
6. Ensuring community participation in the programme by organizing health education sessions for opinion leaders, mahila mandals and panchayat officials.
7. To give due emphasis on detection of RF/RHD cases during school health examination and referral to nearby sub-registry.
8. To provide continuing education to school teachers for case detection and referral.

Role of medical officer at the sub-registry

1. Early detection and registration of RF/RHD cases.
2. Arranging for appropriate treatment of cases and maintaining a patient's card for each patient on secondary prophylaxis.
3. Follow up of cases for treatment compliance.
4. Refer cases for treatment of complications and follow them up.
5. To maintain the RF/RHD patient register.
6. To monitor secondary prophylaxis among cases of RF/RHD.
7. Sending monthly reports to Master RF/RHD Registry, Office of the Civil Surgeon, Ropar.
8. Ensuring community participation in the programme by organizing health education sessions of opinion leaders, mahila mandals and panchayat officials.
9. To ensure cooperation of private practitioners for registration and reporting of RF/RHD cases.

Role of in-charge Master-registry

1. Overall implementation as per the decisions taken by Project Advisory and Technical Committees.
2. Arrange for training of various categories of health personnel and school teachers.
3. To ensure regular updating of master registry based on monthly report recieved from sub registries.
4. Compiling monthly report from sub registries and make a consolidated report.
5. Supervision of the programme.
6. To monitor secondary prophylaxis among cases of RF/RHD and implementation of the programme.
7. To provide feedback to sub-registries.
8. To ensure inter sectorial coordination through Project Advisory Committee.
9. To ensure community participation and implementation of health education strategy.

Role of ICMR Project Staff

1. To facilitate the training of Medical officers, paramedics and school teachers.
2. To carry out school survey.
3. To facilitate for referral support at PGIMER.
4. To review the monthly and annual report and give inputs to master registry for feedback.
5. Development and provision of health education material.
6. To send the quarterly report to funding agency.
7. To ensure coordination amongst partners in the programme.

Role of different categories of staff in reporting system (MIS)

At PHC/Mini PHC/SHC/SC/Schools/others:

1) In case of suspicion on history, do preliminary examination and refer to nearby subregistry, in accordance with, Punjab Health System Corporation (PHSC) referral system.
2) The School teachers, Anganwadi workers and others will use referral card as given in Annexure 3 and refer the patient to the Medical officer posted in the area.

At Subregistries:

1) Confirm the diagnosis
2) If diagnosis of RF/RHD is confirmed, 'Registration and follow up record form' is to be filled and to be retained at the subregistry (Annexure 1)
3) Fill 'Patients Card' simultaneously (Annexure 2), to be given to the patient.
4) Enter the patient in RF/RHD register (Annxure 6) to be maintained at sub registry.

5) To generate monthly/annual report in duplicate, one to be retained at sub registry and other to be sent to Master Registry along with registry form giving details of the patients i.e. to, **Master RF/RHD registry at Office of Civil Surgeon Ropar, Punjab.**

At Master registry

1. Training of Medical Officers and Paramedical workers about MIS.
2. Compilation of report received from sub registries.
3. Propare a monthly progress report (Annexure 4) and annual report (Annexure 5) in duplicate. One to be retained at Master Registry and Other to be sent to **Prof. & Head, Department of Community Medicine, 5th Floor Research Block B, PGIMER, Chandigarh.**
4. Obtain review and comments on the monthly and annual report from Department of Community Medicine, PGIMER, prepare feedback and dissemination of the same to the subregistry.

How to use the Various forms?

1. **RF/RHD Register -At sub registry/Master registry.**

   To be filled by staff of subregistry and Master registry

2. **Reporting form set**

   Monthly report- to be filled by medical officer in-charge of sub registry/Master Registry.

   Registry form- To accompany the monthly report similar to RF/RHD register format, and will help in updating of master register.

   Annual report-To be sent by Medical Officer incharge of Sub registry/Master registry.

3. **Registration and follow up record form and Patient's Card**
   - Both to be filled by Medical officer at sub registry.
   - Registration follow up record form to be retained at sub registry
   - Patient's Card to be given to the patient

   Sub registry codes to be used in the forms are given in flow diagram 6.

4. **Referral Card-** To be used by school teachers, Anganwadi workers and others, to refer the patient to Medical Officer.
5. **School survey form -** To be filled by project staff.

Note:-	**Monthly/Annual report should reach Master, RF/RHD Registry by 5th of every month at - Office of Civil Surgeon, Ropar, Punjab.**
	- **Monthly/Annual report from Master registry to Prof. & Head Department of Community Medicine, 5th Floor , Research Block B, PGI MER, Chandigarh, by 15th of every month.**
	- **Feedback from Master Registry to sub registry by 25th of every month. It should be accompanied by the main registry number for updating of Registration and Follow Up Record Form & Patient Card.**

Annexure IV

Indian Council of Medical Research, New Delhi
Jai Vigyan Mission Mode Project on Control of
Rheumatic Fever/Rheumatic Heart Disease

PARAMEDICAL WORKER'S MODULE

Directorate of Health and Family Welfare,Punjab
Department of Community Medicine,
Cardiology, Experiment Medicine and Biotechnology.
Post Graduate Institute of Medical Education and Research,
Chandigarh

1.0. Learning objectives

Upon completion of the training the health care staff should

1. Know what causes RF and RHD
2. Know the common signs and symptoms for early recognition of i) Streptococcal sore throat, ii) Rheumatic Fever, iii) Rheumatic Heart Disease
3. Be aware of primary and secondary prophylaxis against Rheumatic Fever /Rheumatic Heart Disease and where to direct patients for it
4. Be aware of the main objectives of the Registry project
5. Be aware of the referral pathways

2.0 Project Objectives

2.1 This is an operational research project with the following main objectives:

1. To set up a registry of cases with rheumatic fever and rheumatic heart disease in a population of at least 10 lakhs; in the Ropar District.
2. To determine time trends of RF/RHD in school going children
3. To sensitize the community for primary prophylaxis by providing relevant health education, primarily through the involvement of school teachers and children.
4. To monitor secondary prophylaxis among cases of RF/RHD

2.2 Specific task for the health care staff in the PHCs/CHCs/SHC/SC

1. Early detection of Sore throat,Rheumatic Fever andRheumatic Heart Disease patients as well as early referral to Medical Officer of PHC.
2. Those patients who require secondary prophylaxis must be advised medical check-up.
3. To educate schools regarding identification of Rheumatic Fever sign and symptoms through School Health Education.
4. To compile a list of patients on secondary prophylaxis at Health Institution.
5. To follow up a patient for compliance of secondary prophylaxis.

3.0. Rheumatic fever and Rheumatic Heart Disease: What every health worker should know.

3.1 Background

In India, for every 1000 children, 6 are affected with Rheumatic Heart Disease. This disease can be compared to polio & T.B., which has National programmes. Because of this, under Prime Minister, under Jai Vigyan Mission Mode Project,Indian Council Medical Research Project, Directorate Health & Family Welfare and PGI have decided to control Rheumatic Fever and Rheumatic Heart Disease.

3.2 How does Rheumatic fever start?

Childhood infection in the throat with a type of streptococcal bacteria called Group A beta hemolytic streptococcus is the starting point for the development of RF. During RF, the heart gets damaged and if not immediately treated, it leaves the heart with long lasting damage called Rheumatic Heart Disease (RHD).

Streptococcal Sore Throat

↓

Rheumatic Fever

↓

Rheumatic Heart Disease

3.3 How is streptococcal sore throat distinguished from other causes of sore throat?

Sore throats are caused by a variety of bacteria and viruses and commonly affect all age groups; however, the criteria given below are helpful only to suspect a streptococcal cause for the sore throat.

IMPORTANT SYMPTOMS AND SIGNS OF STREPTOCOCCUS SORE THROAT
High Temperature
Tender cervical lymph nodes
Redness of pharynx
Pus like exudates on pharynx & throat
Bleeding spots in the throat
Pain while swallowing

Signs of common cold, conjunctivitis, running nose, hoarseness of voice are NOT by themselves suggestive of this infection.

Special tests such as culture of the throat are needed for laboratory confirmation.

If group A Streptococcal pharyngitis is not treated then some children can get affected by Rheumatic fever.

3.4 How to find out RF patients?

Acute rheumatic fever typically occurs in children between 5 to 15 years. Adult attacks although rare, occur at the end of the second and beginning of the third decades of life. RF occurs where there are lower standards of living, especially in crowded situations. The disease has been more common among socially and economically disadvantaged populations.

In RF typically, the child complains of fever, accompanied by pain and swelling in more than one joint of the body, particularly the large joints, with the pain moving from one joint to another. In addition, some could have involuntary movements of the limbs called ‘Chorea’. Picture given on the next page.

IMPORTANT SIGNS AND SYMPTOMS TO LOOK FOR IN RF
Fever
Pain and swelling of joints
Pain moves from joint to joint
Involuntary purposeless jerky movements of limbs (Chorea)

RF can be diagnosed by laboratory tests also.

3.5 How to identify RHD patients?

The diagnosis of RHD requires in addition to a detailed history from the patient, an examination of the heart for heart sounds.

Patients with RHD typically complain of breathlessness on exertion, chest pain, palpitations and the more severe cases will have breathlessness at rest and swelling of the feet.

IMPORTANT SYMPTOMS TO LOOK FOR IN RHD
Breathlessness on exertion
Palpitation
Swelling of feet (severe cases)
Breathlessness even at rest (severe cases)

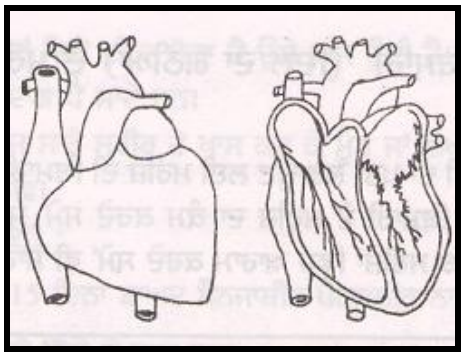
Confirmation of diagnosis is by different tests such as ECG and X-ray, and special test-ECHO.

If a patient is identified with RF/RHD sign and symptoms than he/she should be referred to a doctor. RHD patients should be administered InjectionBenzathine Penicillin every month. Due to this injection, a patient will not be affected with streptococcal sore throat. It will lessen the spread of disease.

Fever, Joint pain & Swelling

Tiredness and Breathlessness

Chorea



Damaged Valves

Heart Disease

Timely identification of disease

Timely medical intervention

4.0 STEPS IN ADMINISTRATION OF INJECTION BENZATHINE PENICILLIN

4.1 How to prepare Injection Solution?

This is your important task and if improperly done can harm your patients. Proceed carefully as follows. ("SEE DIAGRAM ON NEXT PAGE")

1. Removes the tin foil covering the penicillin vials. Don't touch or remove the rubber stopper.
2. Unwrap the syringes.
3. Fit the needle to the syringes without touching the needle with your fingers.
4. Draw 3 ml of distilled water into the syringes.
5. Inject the distilled water into the Penicillin vial through rubber stopper.
6. Shake the bottle vigorously to dilute the penicillin. Make sure it is well diluted and no solid particles remain undissolved before administering it.

4.2 Skin testing for penicillin sensitivity

1. Draw out 0.1 ml of this solution diluting this further with 1 ml distilled water.
2. In the left forearm introduce 0.1 ml injection subcutaneously (to be demonstrated in the training) as to raise a wheal.
3. Circle this area and put the time on the forearm.
4. Wait for 10 to 15 minutes and if there is no feeling of fainting, itching at site of the test, sweating, feeling of apprehension or any other unusual symptoms, the person is not sensitive to penicillin and can be given the injection.
5. In case of doubt repeat on the other arm with double strength test dose.

Remember before administration of Penicillin sensitivity test is a must.

4.3 How injection penicillin is administered?

1. Draw the diluted Penicillin into the syringe and withdraw the syringe from the vial
2. Point the syringe upwards and expel any air bubbles that may be present over the drug column.
3. Clean the gluteal region (upper outer quadrant) with spirit swab.
4. Introduce the needle into this clean area by stab technique (holding the syringe like a pen and introducing the needle with one quick movement/jab)
5. Draw the piston of the syringe slightly to ensure that the needle has not entered any blood vessel.
6. If no blood has been drawn, gently inject the drug over half a minute.
7. Withdraw the needle and clean the area again with a spirit swab.

4.4 Reactions due to penicillin

Reactions following administration of injection Benzathine Penicillin are very rare- particularly in the children in the age group of 5-15 years. However to be on the safer side it should be routinely done.

Reactions as already stated are very rare though some children may present with certain symptom arising due to the fear of injection or very rarely due to a true reaction.

4.4. (a) Reactions arising out of fright or nervousness:

This is not a true reaction but a nervous reaction arising out of fright. It is characterized by feeling of fainting, face turning pale, sweating and weak or rapid pulse.

Management of such patients:

Ask the patient to lie down, loosen the cloths and reassure him/her. Talk to the patients and allay his/her fears, by explaining that the condition is transient and he/she would be alright in 10-15 minutes. In case the condition does not improve, seek help.

4.4. (b) True Reactions:

True reactions are two types: immediate or delayed
Immediate Reactions
Occur within 30 seconds to two hours after the administration of inj. Penicillin. Characterized by:

1. Feeling of fainting
2. Itching all over body or at site of injection.
3. Rashes all over body.
4. Sudden pain or swelling on any part of the body particularly on face or below the eyes.
5. Difficulty in breathing.

Delayed or late Reactions:
Occur 5-15 days after the administration of injection Benzathine Penicillin. The features are:

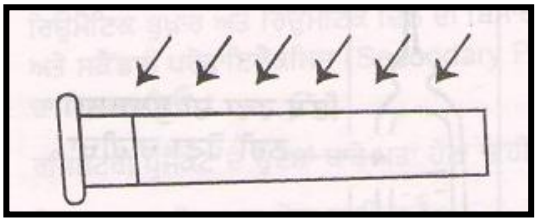
1. Generalized or localized rushed on body
2. Fever
3. Pain or joints
4. Difficulty in breathing

4.5. Management of Penicillin Reaction:

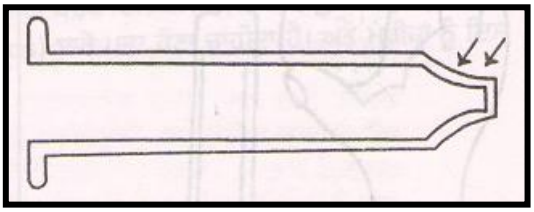
1. Give your total attention to every case of suspected or frank reaction arising due to injection Benzathine Penicillin and seek help immediately.
2. Reassure the patient, ask him/her to lie down and loosen the cloths.
3. Administer 2 ml of injection Hydrocortisone intra muscularly (I.M.)
4. Feel the pulse of the patient. If the volume is low, raise the foot end.
5. If itching, rash, or difficulty in breathing, are dominant features, give 2 ml of injection Avil I.M. (1 ml in children 5-10 years).
6. Injection adrenaline should be given only if the Health Worker thinks the patient's conditions are deteriorating. The dose is 0.5 ml given subcutaneously. In case of sudden stoppage of breathing or beating of heart, resort to external cardio thoracic resuscitation (thumping on chest with mouth to mouth respiration).

HOW TO ADMISTER BENZATHINE PENICILLIN

Opening of Syringe

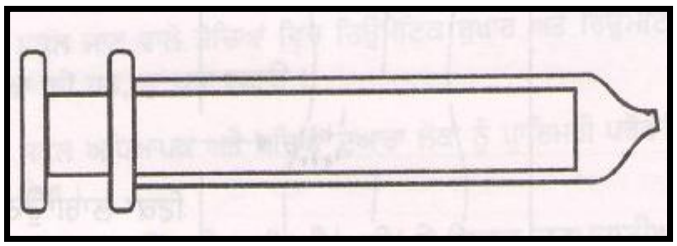


Syringe should be opened
Before administering injection,
One syringe and needle for one patient

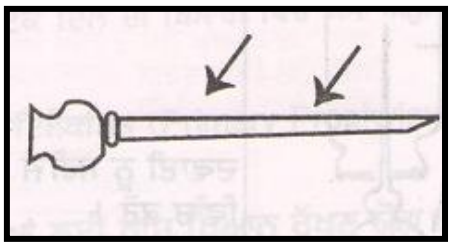


Do not touch the area
shown by arrow

HOW TO MOUNT NEEDLE ON SYRINGE

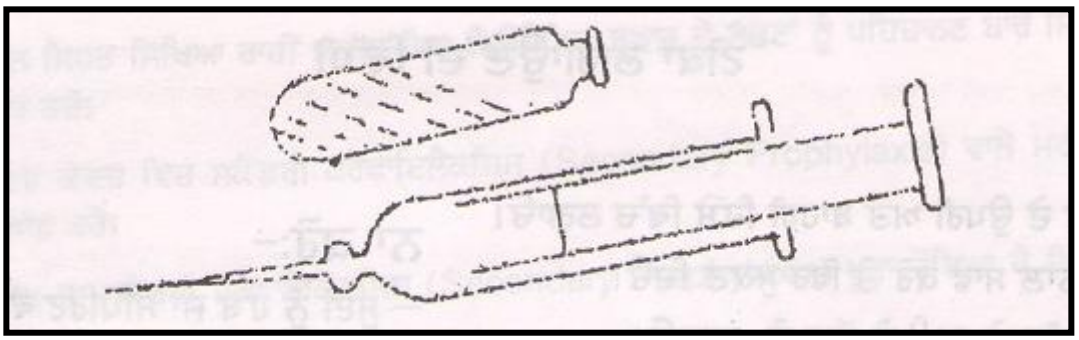


Mount Needle on Syringe



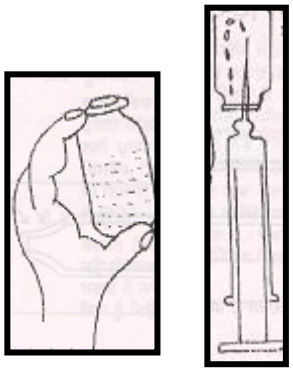
Do not touch the area shown by arrow

MIXING THE MEDICINE



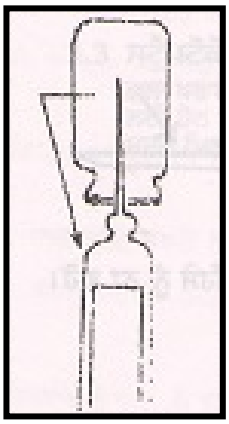
Prepare Solution

(9)

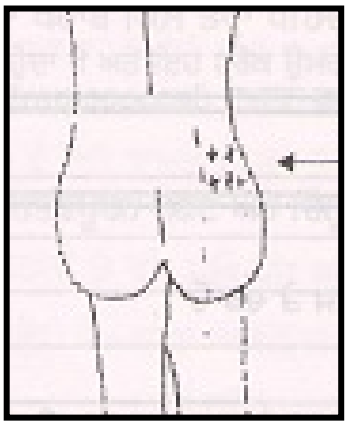


Take 3CC of Distilled water

There should not be air bubble here



Fill the medicine in syringe



Site for injection (upper, outer quadrant of Gluteal region)

5.0 Health Education:

Health worker and school teacher are educators. Health education is an important part of your service. By health education your work becomes easy and will be easily acceptable to community. Whenever you give Health Education your coverage will spread.

Where to give Health Education:

1. Amongst relatives of patients.
2. Amongst Community (especially small group like Mahila Mandals) and schools.

5.1Important Health Education message:

Specific Health Education Message/Communication

You transpire the following messages:

- Recurrent sore throat in children is not a trivial disease particularly when cause is streptococcus.
- If untreated, streptococcus sore throat can lead to RF/RHD, which will make the child disabled for the whole life. Surgery as a cure is costly.
- Sore throat thus treated will not lead to complication like RF/RHD.
- The disease should be diagnosed by PHC doctor.
- Some patients required injection Benzathine Penicillin once every month for several years and may be throughout life.
- Make your neighbour aware of what you know.

5.2Selection of suitable methods and media:

You can communicate these messages by

- Informal personal contact with community members.
- Talking in a group.
- By organizing village meetings through local leaders and with help of your supervisors.
- By demonstrating the fate of affected patients of RF/RHD and patients cured through your efforts.
- Media that can be utilized for disseminating this message will be made available to you in the shape of posters, folder, models and flip chart.
- Posters to be fixed in school or at other public places including your centre.

6.0. What you can contribute in this programme.

1. Early referral of sore throat Rheumatic Fever and Rheumatic Heart Disease patients to doctors.
2. Those patients who require secondary prophylaxis must be advised
3. Educate through School Health programme how to identify Rheumatic Fever sign and symptoms in schools.
4. Compile a list of patient on secondary prophylaxis in health institution.
5. To follow up patients for compliance of secondary prophylaxis.
6. To involve community, involve officials, Mahila Mandals, Village Heads in giving health education regarding RF and RHD.

Annexure V

Annexure 1

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD
Directorate of Health & Family Welfare, Punjab
Depts. of Community Medicine, Cardiology, Exp. Medicine & Biotechnology, PGI, Chandigarh
Indian Council of Medical Research, New Delhi

Registration and Follow-up Record

Registry at (Name of Hospital/ Health Center)

Date of Registration
dd mm yy

Registration No.
Sub. Reg Code | Sub Reg.No. | Main Reg.No.

Name of the Patient: _____

Sex: Male/ Female Marital status: Married/ unmarried

Date of birth: _____ Age: _____

Son/daughter/wife of: _____

Grandchild of: _____

Address: House No. _____ Mohalla /Street_____

Nearby landmark_____

Village _____ Post Office_____

Block_____ District_____

Tel. No (if any) _____

School: _____

For registration referred by: _____

For follow up referred to: _____

Registered by: Name _____ Signature_____
(MO)

Registration No.

Symptoms and signs (tick whatever is present) **Date of Examination:**

Acute Rheumatic Fever	**Rheumatic Heart Disease**	**Laboratory Tests**
JONES CRITERIA	**On Auscultation Or by Echo**	**(as per the diagnostic or prognostic need)**
MAJOR	1. Mitral Stenosis	Date Result
1.Carditis	2. Mitral Regurgitation	TLC
2. Arthritis	3. Aortic Stenosis	ESR
3. Chorea	4. Aortic Regurgitation	CRP
4. Subcutaneous nodules	5. Tricuspid Stenosis	ASO
5. Erythema Marginatum	6. Tricuspid Regurgitation	Chest X-Ray
MINOR		ECG
a. Clinical	**Complications of RF/RHD**	ECHO
1. Fever	1 Congestive cardiac failure NYHA Grade:	Any other (specify)
2. Arthralgia		
3. Previous H/o RF/RHD	2.Infective Endocarditis	
b. Laboratory		
1. Acute phase reactants		
▪ Leucocytosis>10,000 mm^3		
▪ Raised ESR		
▪ Elevated CRP		
2. Increased PR interval		
ESSENTIAL		
▪ Positive throat culture for group A streptococcus.		
▪ Raised ASO titre		

DIAGNOSIS (circle whichever is present)

1A. ARF with Carditis
1B. ARF without Carditis
2A. RHD with rheumatic activity
2B. RHD without rheumatic activity
3A. Documented past RF without RHD
3B. Not documented

SECONDARY PROPHYLAXIS RECORD

Inj. Benzathine Penicillin: Oral Penicillin: Any other (specify):

Write the date of injection / number of tablets taken in a month

Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Date										
January										
February										
March										
April										
May										
June										
July										
August										
September										
October										
November										
December										

Remarks if any about prophylaxis:

Registration No.

Follow up Record

Date	Physicians Notes	Treatment

Annexure VI

Annexure 3

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD

Directorate of Health & Family Welfare, Punjab
Depts. of Community Medicine, Cardiology, Exp. Medicine & Biotechnology, PGI, Chandigarh
Indian Council of Medical Research, New Delhi

Referral Card

Name of the Patient: _____

Age : _____ Sex: Male/ Female

Son/daughter/wife of: _____

Grandchild of : _____

Address: House No. _____ Mohalla/Street_____

Village _____ Post Office_____

Block _____District_____

School Name :_____ Class _____

Referred to

_____

_____

_____

_____

Symptoms/Signs/

Diagnosis _____

Referred by :

Name:_____ Signature_____Date:_____

Annexure VII

SECONDARY PROPHYLAXIS RECORD

Inj. Benzathine Penicillin: Oral Penicillin: Any other (specify):

Write the date of injection / number of tablets taken in a month

Year	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Date										
January										
February										
March										
April										
May										
June										
July										
August										
September										
October										
November										
December										

Remarks if any about prophylaxis:

Registration No.

Follow up Record

Date	Physicians Notes	Treatment

Annexure VIII

Annexure 2

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD

Directorate of Health & Family Welfare, Punjab
Depts. of Community Medicine, Cardiology,
Exp. Medicine & Biotechnology, PGI, Chandigarh
Indian Council of Medical Research, New Delhi

PATIENTS' CARD

Date of Registration

dd mm yy

Registration No.

Sub Reg. Code | Sub Reg. No. | Main Reg. No.

Name of the Patient: _____

Sex: Male/ Female Marital status: Married/ unmarried

Date of birth: _____ Age: _____

Son/daughter/wife of: _____

Grandchild of : _____

Address: House No. _____ Mohalla/Street _____

Nearby landmark: _____

Village _____ Post Office _____

Block _____ District _____

School: _____

DIAGNOSIS (circle whichever is present)

1A. ARF with Carditis

1B. ARF without Carditis

2A. RHD with rheumatic activity

2B. RHD without rheumatic activity

3A. Documented past RF without RHD

3B. Not documented

Name of Hospital/ Health Centre for Follow up _____

Annexure IX

RF/RHD Register

JAI VIGYAN MISSION MODE

Directorate of Health &
Departments of Community Medicine, Cardiology, Exp.
Indian Council of

S.No.	Date of Regn.	Regn. No.	Name of patient	Son/of Daughter/of Wife/of	Date of Birth	Age	Sex M/F	Address with Telephone No. (if any)	Diagnosis 1A. ARF with Carditis 1B. ARF without Carditis 2A. RHD with rheumatic activity 2B. RHD without rheumatic activity 3A. Documented past RF without RHD 3B Not documented past RF without RHD	Confirmed by 1. Auscultation 2. Echo

Note : Use codes wherever given

Annexure 6

PROJECT ON CONTROL OF RF/RHD

Family Welfare, Punjab
Medicine & Biotechnology, PGI, Chandigarh
Medical Research, New Delhi

Secondary Prophylaxis 1. IM Penicillin 2. Oral Penicillin 3. Erythromycin 4. Others	Date of starting	Adherence status each year									Date of recurrences after registration	Status of patient	Outcome with date	Remarks
		2002	2003	2004	2005	2006	2007	2008	2009	2010		1. Stable 2. Heart Failure 3. NYHA grade 4. Waiting for Valve Surgery 5. Valve surgery done	1. Died 2. Migrated 3. Prophylaxis stopped: 3a. by doctor 3b. by patient	

Annexure X

SUPERVISORY CHECK LIST

Date of Visit	**Sub-registry Visited**	**Status of clinical forms** *Complete/ Incomplete*	**Inj. Penicillin Adequate/ Inadequate**	**Monthly Report** *Sent/ Not sent*	**No of cases registered (Total)**		**Issues discussed with authority**
					Old	**Current**	

Name of the supervisor:

Annexure XI

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF-RHD

Directorate of Health & Family Welfare, Punjab
Deptts. of Community Medicine, Cardiology, Exp. Medicine & Biotech, PGIMER, Chandigarh
Indian Council of Medicine Research, New Delhi.

SCHOOL SURVEY FORM

ID No.: Date:

Name _____ Father's Name _____

Age _____ Sex _____ Class _____

School _____ Height _____ cm, Weight _____ Kg

- Past H/o ARF - Yes/No
  (If yes fill School Health Form)
- Cardiac murmur - Yes/No
  (If yes fill School Health Form)

- BP (1) _____
- BP (2) _____
- BP (3) _____

- Throat Swab II:
- Cough: Yes/No Coryza: Yes/No
- Pain in throat: Yes/No Duration (1-14 days) _____
- Fever >38°C: Yes/No
- Lymphadenopathy: _____
  (No = 0, Non tender = 1, Tender = 2)
- Tonsil size _____
  (No = 0, Mild/Moderate = 1, Large = 2)
- Tonsillar erythema: _____
  (No = 0, Mild = 1, Sever = 2)
- Tonsillar exudates: _____
  (No = 0, Yes = 1)
- Pharyngeal erythema: _____
  (No = 0, Mild = 1, Severe = 2)
- Pharyngeal exudates: _____
  (No = 0, Yes = 1)

Signature of Medical Officer

Annexure 7

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD

Directorate of Health & Family Welfare, Punjab
Depts. of Community Medicine, Cardiology, Exp. Medicine & Biotechnology, PGI, Chandigarh
Indian Council of Medical Research, New Delhi

Survey of Primary School Children

SNo. _____

Name _____ Father's Name _____

Date of Birth _____ Age _____ Sex: Male/Female

School _____ Class & Section _____

Village/ Town _____

Chief complaints, If any:

Past History of ARF: Yes / No. If yes, documented diagnosis: Available/ Not available
Encircle the symptoms and signs: Joint Pain with swelling, Joint pain without swelling, Fever, Breathlessness, Easy Fatigability, Palpitation, Abnormal purposeless movements

Cardiac Evaluation: Murmur Yes / No
If yes, tick the area where murmur is heard and tick the timing of the murmur; for two murmurs heard in the same area tick both

	Location	Timing of Murmur	
		Systolic	Diastolic
1.	Mitral		
2.	Tricuspid		
3.	Pulmonary		
4.	Aortic 2		
5.	Aortic 1		

Additional Findings of General Physical Examination, If any:

Previous Echo done: Yes/ No
If yes, findings

Already on Penicillin Prophylaxis: Yes/ No
If yes, describe the type of prophylaxis

Diagnosis: (Circle only one of following)

1A. ARF with Carditis
1B. ARF without Carditis
2A. RHD with rheumatic activity
2B. RHD without rheumatic activity
3A. Documented past RF without RHD
3B. Not documented

Referred to:_____ for confirmation of diagnosis and or management

Name of doctor_____ signature_____ Date_____

Annexure XII

ICMR Jai Vigyan Mission Mode project on

Community Control of RF-RHD

Laboratory Reporting Form

Date & Time of Sample Collection (field)	
Date & Time of Receiving Samples (lab)	
ID No.	
Name	
Fathers name	
Age	
Sex	
Class	
School/Hospital/ Other centre	

Pharyngitis **:** Yes/No

ARF : Yes/No

BHS : Positive/ Negative

No. of colonies : ……

Morphology : Glossy/ Matt/ Mucoid/ Intermediate

Grouping : A/C/G/nil

……

Signs (Date & Time)

Annexure XIII

Annexure 4

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD

Directorate of Health & Family Welfare, Punjab

Depts. of Community Medicine, Cardiology, Exp. Medicine & Biotechnology, PGI, Chandigarh

Indian Council of Medical Research, New Delhi

MONTHLY PROGRESS REPORT

Name of Sub/Main registry_____

Block _____District_____

Month_____ Year _____

	During the month	Cumulative since 1 April
No. of suspected RF/RHD cases referred to centre		
No. of cases of - RF with carditis		
- RF without carditis		
- RHD with Rheumatic activity		
- RHD without Rheumatic activity		
- documented past RF without RHD		
- not documented past RF without RHD		
No. of ECHO done in RF/RHD cases		
No. of ASO done		
No. of RF/RHD cases received secondary prophylaxis		
Benzathine penicillin		
Oral Penicillin		
Erythromycin		
No. of adverse reactions		
No. attended training session		
No. attended health education sessions		
Remarks, if any		

Reporting by:

Name_____ Signatures_____ Date _____

Annexure XIV

Annexure 5

JAI VIGYAN MISSION MODE PROJECT ON CONTROL OF RF/RHD

Directorate of Health & Family Welfare, Punjab

Depts. of Community Medicine, Cardiology, Exp. Medicine & Biotechnology, PGI, Chandigarh

Indian Council of Medical Research, New Delhi

Annual Report of Secondary Prophylaxis

Name of the Sub/Main registry:_____ **Date of Report**_____

PROPHYLAXIS		MONTH													
		1	2	3	4	5	6	7	8	9	10	11	12	TOTAL	Remarks if any
Inj. Benzathine Penicilin	No. of patients registered														
	No. of patients compliance														
Oral penicillin	No. of patients registered														
	No. of patients compliance														
Erythromycin	No. of patients registered														
	No. of patients compliance														
Total	No. of patients registered														
	No. of patients compliance														
Rheumatic Fever recurrences in Registered Cases															

Centre compliance (No. of Compliant Registered patients/ No. of Registered patients*100) ____ %

Penicillin adverse reactions: number_____ type_____ death_____

Name of Reporting Officer_____ Signatures_____