Tobacco Monograph

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Foreword

I am pleased to write this foreword of Tobacco Monograph. Tobacco use is a serious public health issue in India which is contributing to high disease burden. According to International Agency for Research on Cancer, tobacco use represents the largest preventable cause of cancer worldwide. The aim of bringing out this monograph is to bring together the various scientific evidences, as well as opinion, with information on legislations. Regulation of tobacco products is a complex problem and there needs to be an interaction between science and policy, with the caveat that it takes time to consider developments in science and adapt laws accordingly. Tobacco control is a global public health priority. We need to think globally and act locally. The tobacco industry has exploited the vulnerabilities of markets in developing countries as it faced with increasing health regulations in developed countries. India's tobacco problem is more complex due to the fact that tobacco is used in myriad forms in different parts of the country and it is a source of income to many. ICMR's experts in areas of public health, tobacco control, cancer research, health economics and other related fields were assembled to review the available literature, collect, collate and analyze data. This monograph has provided the platform where Indian initiatives in this regard could be compiled and documented.

I appreciate the efforts put in by all writers, reviewers, compilers and editors that led to the successful fruition of the monograph and hope that it will be disseminated to a wider target audience. It will be of interest to policymakers as well as to researchers, lawmakers, media and other health professionals who need to be aware of statistics and policies in tobacco. I am sure this will stimulate further stringent laws and policies on tobacco control and help curtail the tobacco epidemic in our country without leaving any room for complacency.

Balram Bhargava

(Dr. Balram Bhargava)

Preface

India is the second largest producer and consumer of tobacco after China and unfortunately also among top 4 countries having highest number of deaths due to tobacco use. Tobacco is used in various forms by a significant proportion of Indian population, the most common forms being bidis, cigarettes and khaini. The consumption of tobacco is a causal factor of at least 25 diseases of which cancer, coronary artery disease and chronic obstructive lung disease are the major ones. No single risk factor is expected to make such a giant claim on health as this one. Every single death from tobacco is a preventable tragedy.Thus it is evident that tobacco use is a serious public health concern that requires government intervention.

This monograph was conceptualized when the Indian Council of Medical Research, as the apex body, recognized the need for a compendium of cancer research in India and it was felt that tobacco being the single largest preventable cause of cancer should be documented separately. In this monograph the various initiatives taken by the Government of India and ICMR till 2019 to curb the tobacco menace have been compiled. The 1st chapter frames the issues addressed in the monograph and highlights the process followed by ICMR. Information on the prevalence of tobacco use in India before 1980s was gathered through sporadic community surveys. This information was not sufficient to assess the magnitude of the tobacco problem or understanding the trends of tobacco use. This necessitated the need for large community based surveys on tobacco use prevalence. In the 2nd chapter the efforts of the ICMR for inclusion of tobacco related questionnaire in the Nationwide surveys of the Government of India such as NSSO and NFHS have been described which provided a mechanism of assessing the total number of tobacco users in India both in smoking as well as smokeless form. To overcome shortcomings of the centralized surveys; other localized surveys conducted by ICMR in collaboration with WHO/ World Bank have also been discussed. Given the gravity of tobacco problem it was realized in 1986 that the Cigarette act of 1975 was alone not effective in controlling tobacco misuse by the community; so various other legislations and regulations such as including statutory warning on tobacco products, ban on tobacco advertising, prohibition of tobacco smoking in public spaces, partial ban on smokeless forms of tobacco, promotion of alternative cash crops to replace tobacco and anti-tobacco community education were enforced. All these have been summarized in chapter 4. In chapter 5 the efforts of ICMR to spread awareness against tobacco using radio an instrument of social change through programs such as RADIO DATE have been highlighted. Chapter 6 describes the role of tobacco in causing cancers of various anatomical sites; the major being oral cancer. The monograph ends with the last chapter describing the research activities conducted by various ICMR institutes on tobacco related cancers. The North East region reports comparatively higher cancer incidence rates compared to rest of the India; the main reason being higher tobacco consumption habits among the inhabitants and ICMR institutes are continuously working to decipher the role of tobacco in causing cancer. The ICMR has established Global Knowledge Hub on Smokeless Tobacco at NICPR that aims to generate and disseminate information on smokeless tobacco. In addition ICMR has also published White Paper on ENDS, that led to ban of e-cigarettes in India, and Smokeless Tobacco and Women's Health in India which have been summarized in Chapter 7.

In a nutshell this monograph describes efforts of ICMR towards effects of tobacco use in India that can be a blueprint for further public health interventions. I hope that this monograph will help inform the implementation of tobacco control efforts of the future in India.

(Dr. R.S. Dhaliwal)
Head, NCD

Acknowledgement

This monograph has been developed by the Indian Council of Medical Research under the scientific direction of Dr Balram Bhargava, Secretary, Department of Health Research and Director General, ICMR. It is the culmination of efforts from many authors and went through an extensive peer review process. I take this opportunity to thank the scientists who contributed to this monograph.

The origin of this monograph stems from the encouragement provided by Dr VM Katoch and Dr Soumya Swaminathan, Former Secretary, Department of Health Research and Director General, Indian Council of Medical Research. I am grateful to Dr RS Dhaliwal,Head, Division of Non Communicable Diseases, for his motivation and support in finalizing the document.The suggestions and inputs provided by all the expert group members from time to time are deeply appreciated. It is my pleasure to acknowledge the dedication and determination of each author who worked tirelessly for completion of this document. My sincere thanks to research staff Ms Jyoti Sharma and Mr Rahul Sharma for their efforts in compiling the information and editing the document. Data from National Cancer Registry Program is acknowledged.

The purpose of this document is to provide a consolidated ready reference of the work supported by ICMR in Tobacco research. All efforts have been made to compile available information. It is hoped that that this monograph will provide vital material and supporting evidence for planning future research areas and policies concerned with tobacco control.

(Dr. Tanvir Kaur)
Scientist 'F'
Programme Officer and Coordinator

Contents

1 Tobacco: A Public Health Problem

Tobacco

An estimated 250 million persons in India use tobacco in one form or the other. Most common form of tobacco smoking is bidis followed by cigarettes. Smokeless tobacco is used in the form of khaini, gutka, mawa, etc. The morbidity and mortality caused by tobacco is extremely high, which necessitates strict measures to control its use. India is one of the earliest signatory of the Framework Convention on Tobacco Control (FCTC) of World Health Organization. The ICMR helped the Government in identifying and consolidating its stance during various stages of negotiations, especially during the initial stage of identification of strategies by the Working Group on FCTC.

Indian Council of Medical Research (ICMR) considers tobacco use as an important public health issue. Tobacco is known to be an important risk factor in causation of 25 disease entities, including cancer of several body organs and tissues. The role of tobacco in cancers in India had been reported as early as 1902. But the need for legislative and public health action was considered important only during the second half of 20th century, especially after the publication of first report of the US Surgeon General in 1954. Several Indian studies, especially from Mumbai and Uttar Pradesh, during 1950s and 1960s highlighted the important aetiological role of tobacco use (both in smokeless and smoking form) in causation of various cancers, like oral cavity, pharynx, lung, oesophagus, etc.

The Cigarette Act of 1975 was the first legislative attempt by the Government of India aimed at tobacco control in India, which mandated cigarette packets to very clearly carry a specified warning. The limitations of this warning were recognized by Indian scientists very soon after its implementation. ICMR was proactive in advocacy for stronger tobacco control measures. However, the economic and social aspects of tobacco were considered compelling and delayed major action against tobacco. Under such a scenario, ICMR identified in 1970s, that generation of scientific evidence on tobacco related diseases may be an important direction for research. Such research was initially started on cancer; subsequently important projects were also carried out on role of tobacco in cardiovascular diseases, chronic obstructive lung diseases, stroke, etc. Important studies which changed the perspective included: assessment of magnitude of tobacco use, magnitude of tobacco related diseases, feasibility of reduction of tobacco use through existing infrastructures, role of pan masala (with or without tobacco) in oral cancers, cost of major tobacco related diseases to the country, feasibility of quickly carrying out large community based surveys on tobacco use patterns, etc. An important role performed by the ICMR was to provide impartial analysis of the existing situation to the Government along with possible control measures. This support on scientific data analysis, undertaking research studies and identifying control measures helped the Government to initiate action on tobacco control, including promulgation of comprehensive tobacco control legislation, anti-tobacco education activities, tobacco cessation measures, etc.

The following portion provides an account of various research studies by ICMR and how it changed the scientific knowledge and control activities in India.

Based on the scientific literature on tobacco, ICMR noted in 1970s that the tobacco being a major public health problem had not been projected adequately. Thus, it was decided to collect and analyze scientific data on the subject and assess the need for public health action, as well as decide on the research priorities. The research findings from Mainpuri (Uttar Pradesh) and Mumbai on oral cancers highlighted the importance of smokeless tobacco use which was peculiar to Indian sub-continent. Tobacco was considered as an important revenue as well as foreign exchange earner. The problem of population control and control of communicable diseases was taken as the paramount priority. On the other hand, the magnitude of non-communicable diseases had not been adequately documented.

Therefore, the first logical step seemed to be to prepare a document on tobacco, providing both its role in disease causation as well as a contributor to Indian economy. The document printed in 1984, provided the data on prevalence rates of tobacco use in India, diseases caused by tobacco, tobacco crop production figures and exports, revenue & employment by tobacco, legislation for tobacco control, need for tobacco control, etc. This document attracted a lot of attention including the need to review the then existing cigarette act 1975 which mandated writing a warning on all cigarette packages. ICMR advocacy in this direction succeeded, when a decision to develop a new legislation for all tobacco products was taken in a meeting of Ministry of Health & Family Welfare in 1986.

Prevalence of Tobacco Use in India

Information on prevalence of tobacco use in India before 1980s was through sporadic community surveys, carried out as a part of specific research projects. It may not have been sufficient to assess the overall magnitude of the tobacco problem, leave alone understand the finer nuances and trends of tobacco use pattern. Surveys conducted prior to 1970 showed that the prevalence of tobacco usage varied from 61% to 86% among males and from 15% to 67% among females. Prior to 1960, the major tobacco habit among males was chewing. However, the trend seemed to have reversed perhaps between 1960 and 1970. Population based surveys conducted in seven rural areas in 1960s indicated that more men smoked rather than chewed tobacco, the exception being Pune and Dharbhanga. A substantial proportion had mixed habit. Among the females, the major habit was tobacco chewing, except in Srikakulam and Dharbhanga where smoking was more popular. It would be logical to conclude that the changeover occurred at different time periods in different areas.

Under an ICMR collaborative study on the effect of intervention programme on nonmedical use of drugs in the community, baseline surveys on the prevalence of drug usage, including tobacco, were conducted. The intervention was carried out in Delhi only. The prevalence of tobacco usage in the baseline survey varied from 46 to 74% among males and 2 to 50% among females. Smoking was the commonest habit among males in Bangalore (urban and rural both) and Delhi. Chewing was the predominant habit among males in Dibrugarh & Ranchi and among females in all areas.

In surveys conducted in 1980s in three rural areas, under an ICMR project on anti-tobacco community education, the main habit among males was smoking and among females was chewing. However, in Uttar Pradesh, nearly all the users (males or females) chewed tobacco. The overall prevalence of tobacco usage among the males over the age of 5 years was 34% (range 31.9 to 36.7%) in Uttar Pradesh (Mainpuri

and Shekohabad) and 32% (range 33 to 36%) in Karnataka. The prevalence among females above the age of 5 years was 26% (range 20.1% to 29.1%) in Uttar Pradesh and 36% (32 to 43%) in Karnataka. In Goa, the survey on tobacco usage was conducted on population over the age of 15 years and showed an overall prevalence of 33% (range 23.4% to 40.8%) among males and 20% (range 15.3% to 26.4%) among females.

Overall, various studies in India in the 1980s showed that the prevalence of tobacco use among men over 15 years of age varied between 46% and 63% in urban areas and between 32% and 74% in rural areas. Among women, it varied between 2% and 16% in urban areas and between 20% and 50% in rural areas.

Thus, the wide variations in tobacco use prevalence did not permit a valid conclusion on prevalence of tobacco use. The use of tobacco crop pattern seemed to be the only assessment method for study of trends, which may have its inherent limitations. The data also suggested that prevalence of tobacco habit among males in 1980s was lower than those found in earlier surveys. There was no explanation for such a decrease, as no tobacco control measures were available and the surveys also did not substantiate population of quitters. Therefore, the possible reasons for this change were differences in methodologies, definitions, analysis, and possible geographic variations. The situation necessitated large community based surveys on tobacco use prevalence.

2 National Surveys on Tobacco Consumption

National Sample Survey Organization (NSSO) of India

The ICMR noted the possibility of undertaking large surveys on tobacco use as a component of the ongoing surveys conducted by the National Sample Survey Organization (NSSO) of India, which is an institution under Government of India. NSSO surveys are on consumer expenditure and are carried on yearly basis from July to June of next year. At the request of Indian Council of Medical Research, the tobacco use data was first included in the fourth quinquennial NSS survey (1987-88). The NSSO informed that the detailed questionnaire suggested by ICMR may not be possible but a small number of questions on regular or casual use for major habits were included. The questions were repeated during the fifth quinquennial survey (1993-94). Under these surveys, household were selected on a random basis, in about 12,000 to 14,000 villages and blocks in the central sample (covered by NSSO) and an independent sample of about 14,000 to 16,000 villages and blocks in the state sample (covered by the Governments of various states and union territories). The entire area of the country – rural and urban – was covered, with the exception of some interior areas of certain states. The surveys adopted a stratified two-stage sampling design with census villages/urban frame survey blocks at first stage and households at the second stage units. Consumption data was collected with a reference period of "last 30 days". Being a continuous survey, the reference period was a moving one, varying from household to household.

Availability of the nationwide surveys through NSSO provided a mechanism of assessing the total number of tobacco users in India both in smoking as well as smokeless forms. Application of age wise prevalence rates of 1987-88 data of NSSO to the 1991 census data indicated the number of tobacco users in India to be approximately 214 million. Based on the data from the 1993-94 survey data, the number of tobacco users in India was approximately 239 million in 1996. The details of tobacco habit prevalence from the 1993-94 survey data is given in Table 2.1

Table 2.1 Percentage of Persons aged 10 Years and above Reporting Habit of Consumption of Tobacco in Various Forms per 1000 Persons by Sex and age Group. National Sample Survey, 50th Round (1993-94).

All India Urban													
Form of Tobacco Consumption	Regularity	Age (in years)											
		10-14		15-24		25-44		45-59		60 & Above		All Ages	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Smoking	Regularly	0.1	0	5.5	0.2	30.5	0.5	38.1	1.8	26.6	1.8	20.2	0.7
	Casually	0.1	0.1	0.9	0	2.8	0.1	2.5	0.2	1.9	0.2	1.8	0.1
Chewing, Zarda, Dokta, etc.	Regularly	0.1	0	3.1	0.4	11.4	2.6	14.1	6.6	13.3	7.2	8.0	2.6
	Casually	0	0.1	0.6	0.1	1.7	0.4	1.7	0.6	1.3	0.6	1.2	0.3
Snuff	Regularly	0	0	0.1	0.1	0.3	0.3	0.9	0.8	1.4	1.9	0.4	0.4
	Casually	0	0.1	0.1	0	0.1	0.1	0.1	0.1	0.2	0	0.1	0.1
Burnt Tobacco/ Powder/ Paste	Regularly	0.2	0.1	0.6	0.6	1.9	1.4	2.8	2.9	2.5	2.8	1.5	1.5
	Casually	0	0.1	0.1	0	0.2	0.1	0.2	0.2	0.1	0.1	0.1	0.1
Consumption of Tobacco in Any Form	Regularly	0.4	0.2	8.7	1.2	40.7	4.5	50.9	11.4	39.5	13.0	27.7	4.7
	Casually	0.1	0.1	1.3	0.2	3.2	0.5	2.7	0.8	2.7	0.7	2.1	0.4

All India Rural													
Form of Tobacco Consumption	Regularity	Age (in years)											
		10-14		15-24		25-44		45-59		60 & Above		All Ages	
		Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
Smoking	Regularly	0.5	0.1	12.0	0.7	43.4	2.5	49.8	4.6	39.8	4.8	29.3	2.3
	Casually	0.1	0.1	1.3	0.1	3.1	0.4	3.0	0.5	2.8	0.5	2.1	0.3
Chewing, Zarda, Dokta, etc.	Regularly	0.4	0.3	6.6	1.9	20.5	5.9	25.9	10.3	26.4	10.7	15.1	5.3
	Casually	0.2	0.1	1.3	0.4	2.6	0.8	2.9	1.1	2.2	0.9	1.9	0.7
Snuff	Regularly	0	0	0.4	0.3	0.7	0.7	1.2	1.6	1.3	1.9	0.7	0.7
	Casually	0	0.1	0	0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Burnt Tobacco/ Powder/ Paste	Regularly	0.4	0.5	1.8	2.0	4.4	3.9	6.0	5.5	6.8	5.2	3.5	3.3
	Casually	0.1	0.1	0.2	0.1	0.5	0.2	0.5	0.3	0.4	0.3	0.3	0.2
Consumption of Tobacco in Any Form	Regularly	1.3	0.9	19.1	4.6	61.3	12.2	72.3	20.4	65.0	21.2	43.0	10.9
	Casually	0.3	0.2	1.9	0.5	3.0	1.1	2.8	1.5	2.9	1.3	2.2	0.9

Source: Sarvekshana, January-March 1998; p76.

National Family Health Survey

The National Family Health Survey (NFHS) is a large-scale, multi-round survey conducted in representative sample of households throughout India. The survey is organized by the Ministry of Health and Family Welfare of India. Three rounds of the survey have been conducted since the first survey in 1992-93. The survey provides state and national information for India on fertility, infant and child mortality, the practice of family planning, maternal and child health, reproductive health, nutrition, anemia, utilization and quality of health and family planning services. The survey provides important data for policy purposes. Data on tobacco use (in smoking or smokeless form) was collected during second (1998-99) and third round (2005-06) (Table 2.2) of the survey. While data on tobacco use during second round (like the NSSO survey data) was collected from the household respondent, the data for tobacco use during the third round was collected from individuals who were interviewed with individual questionnaire by asking four specific questions on current use of tobacco (smoke and non-smoke variants). The data was obtained by asking about use of tobacco during past 24 hours.

Table 2.2: Tobacco Use By Women and Men

Percentage of women and men aged 15-49 and men aged 15-54 by their use of tobacco, and percent distribution of those who smoke cigarettes or bidis, by number of cigarettes/bidis smoked in the 24 hours preceding the survey, India, 2005-06

Tobacco Use	Women			Men			
	Urban	Rural	Total 15-49	Urban	Rural	Total 15-49	Total 15-54
Use of Tobacco							
Smokes cigarettes or bidis	0.5	1.8	1.4	28.7	35.0	32.7	33.4
Smokes cigar or pipe	0.0	0.2	0.2	0.4	0.8	0.6	0.7
chews paan masala, gutkha or other tobacco	5.5	9.8	8.4	31.1	39.6	36.5	36.3
Uses Snuff	0.5	0.9	0.8	0.3	0.9	0.7	0.7
other	0.3	0.9	0.7	0.3	1.3	0.9	1.0
Does not use tobacco	93.3	87.1	89.1	50.1	38.9	43.0	42.4
Number of respondents	40,817	83,568	124,385	25,504	44,247	69,751	74,369
Number of cigarettes/ bidis smoked in the past 24 hours							
0	5.0	1.4	1.9	8.2	9.6	9.1	8.8
1-4	40.6	46.5	45.8	35.2	29.2	31.2	30.1
5-9	26.4	23.5	23.9	18.3	16.1	16.8	16.9
10 or more	24.0	25.8	25.6	38.1	45.0	42.8	44.0
Missing	3.9	2.7	2.8	0.2	0.1	0.2	0.2
Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0
Number of cigarette/ bidi smokers	196	1,510	1,707	7,322	15,478	22,800	24,875

Source: All India Report of 3rd NFHS (2005-06) of India.

ICMR- WHO Survey in Uttar Pradesh and Karnataka

Tobacco use prevalence from the NSSO or NFHS surveys is available for smoking and smokeless forms of tobacco for specified age groups. However, several details about tobacco use patterns according to different tobacco types and use characteristics including intentions to use and quit, etc., are not available. Such data is also not available to develop region or area specific intervention strategies. The data also does not provide information on changes in specific habit types at different time periods. Therefore ICMR undertook tobacco use prevalence surveys in Uttar Pradesh and Karnataka, with financial support & undertook discussions with WHO SEARO in 2001. The surveys also demonstrated the feasibility of quick survey on large population using cluster sampling approach. The study on about 60,000 population in 2 states was completed in 7 months. The study also provided detailed data on tobacco consumption patterns, dynamics of tobacco use during life time of respondents, quantum and duration of each habit, quitting patterns and opinion of community on tobacco control.

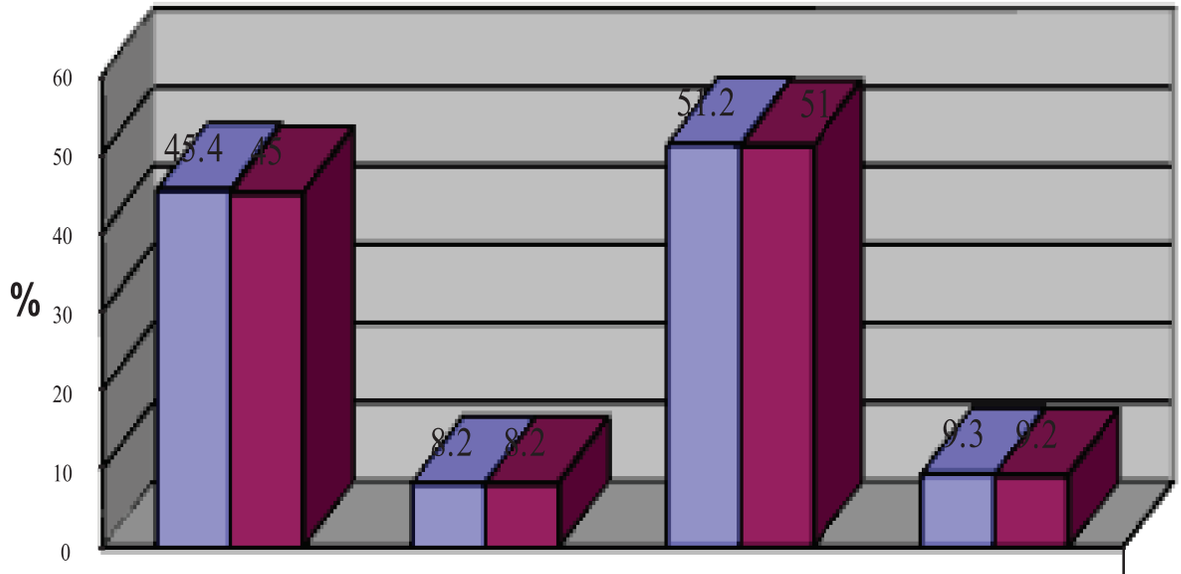
Prevalence of Tobacco Use in Uttar Pradesh and Karnataka in India (2001)

The study was a part of the three-nation project by the World Health Organization - South East Asian Regional Office (WHO SEARO), conducted in India, Indonesia and Bangladesh using a standard survey tool. The standard survey tool was to use cluster sampling approach to undertake a fast survey on tobacco use patterns. The timeframe for the entire survey was 6 months. Through this survey, WHO intended to help member countries to provide a baseline data on tobacco use which when repeated at periodic intervals may provide trends in tobacco use. ICMR was requested to carry out the Indian component of the survey. The overall survey was to assess the prevalence of use among different sexes, age groups and social classes. A small sample was proposed for the survey to collect data on presence or absence of tobacco use. However, during the discussions, the need for a higher sample size was realized in India due to presence of multiple tobacco habits and known differences in several demographic and social classes. Therefore, each survey in India was on a sample of approximately 30,000 population. The initial objective was to cover the entire country, but due to limited fund allocation, the survey was limited to two Indian states (Karnataka and Uttar Pradesh).

The survey was carried out with the objectives of building a database on prevalence of tobacco use in the total population and among specific population subgroups, for the purposes of advocacy for tobacco control and planning tobacco control interventions and evaluation.

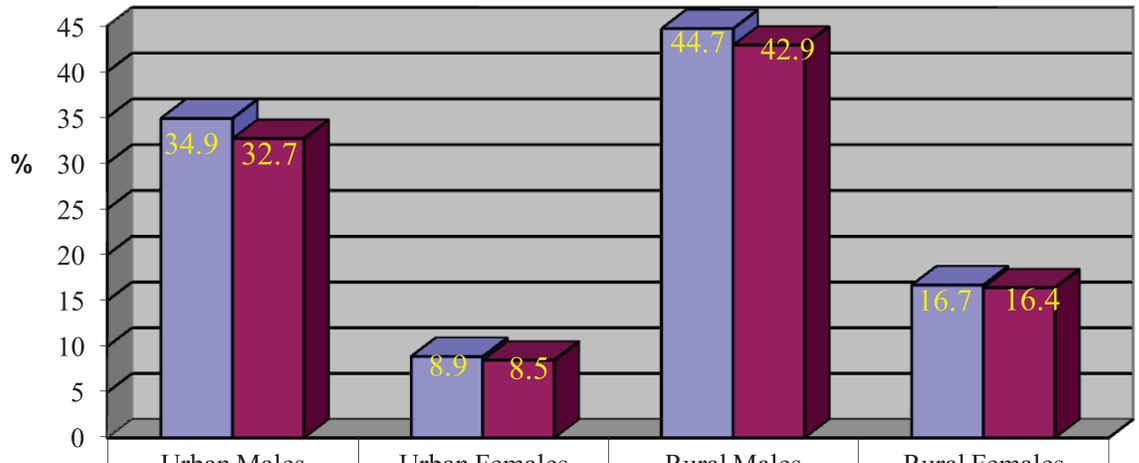
Three districts from each state were selected through simple random sampling method. To cover a population of about 30,000 above 10 years of age, 600 clusters in each of the state were selected by simple random method from the list of villages or urban wards, obtained from the Registrar General of India. The proportion of urban & rural population as observed from the census data from the specific district, was used for allocation of clusters to urban and rural population. Within a cluster, approximately 17 houses were visited by trained workers according to a pre-defined movement plan to provide approximately 50 persons above 10 years of age. The cluster size was decided based on the fact that each interviewer would be able to cover approximately 50 persons during each round. The data collection took about 5 months and the entire study encompassing 60,000+ persons was completed in 7 months after receipt of funds, indicating that fast survey on a large community is feasible. The survey activity started early in the morning. The low refusal rate was achieved by revisiting the missing persons later on during the same day. The proportion of persons missed or refusal for interview was small, being 3.1% in Karnataka and 0.2% in Uttar Pradesh.

The overall prevalence of ever-use of any kind of tobacco products among the population above 10 years of age was observed to be 29.6% in Karnataka and 34.6% in Uttar Pradesh. The overall prevalence of current use of tobacco in the same population group was observed to be 28.4% in Karnataka and 34.4% in Uttar Pradesh. The difference in ever-usage and current usage prevalence was observed to be very small, suggesting that tobacco quitters are very few in numbers (being 1.2% in Karnataka and 0.2% in Uttar Pradesh). Fig 2.1 and Fig 2.2 provide the prevalence of ever-use and current-use of tobacco according to sex and urban/rural residence status



	Urban Males	Urban Females	Rural Males	Rural Females
Ever Users	45.4	8.2	51.2	9.3
Current Users	45	8.2	51	9.2

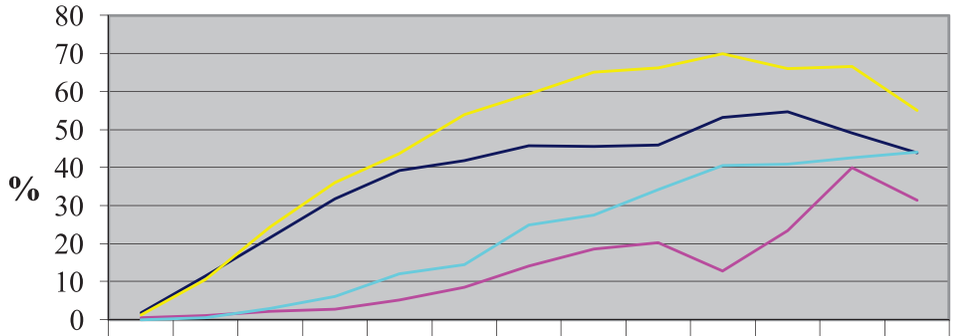
Fig. 2.1: Prevalence of Tobacco Use Uttar Pradesh (2001).



	Urban Males	Urban Females	Rural Males	Rural Females
Ever Users	34.9	8.9	44.7	16.7
Current Users	32.7	8.5	42.9	16.4

Fig. 2.2: Prevalence of Tobacco Use Karnataka (2001).

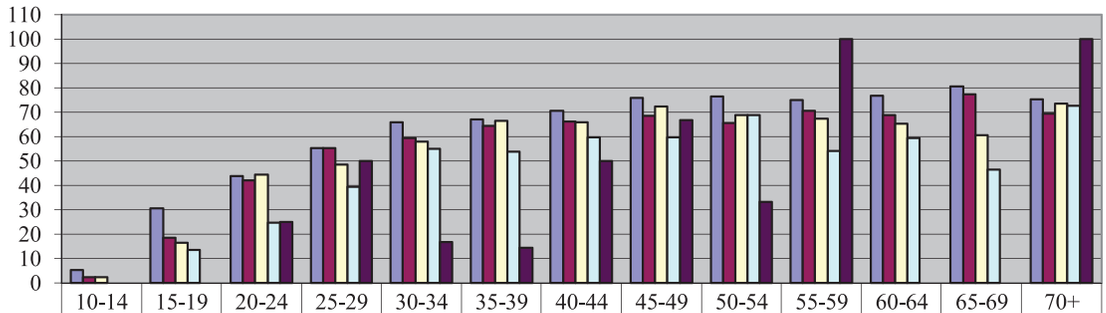
The prevalence of tobacco use increased with increasing age. The peak values were observed after 55 years of age or even continued to rise till the 70+ year age group in certain categories. The prevalence rates of tobacco use were higher in rural areas as compared to urban areas in most age-groups, the exception being the teenagers, where prevalence was comparable or higher in urban areas (Figures 2.3).



	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70+
Urban Males	1.8	11.5	21.5	31.7	39.2	41.9	45.8	45.6	45.9	53.1	54.6	49.1	43.9
Urban Females	0.4	1	2.2	2.7	5.1	8.4	14	18.5	20.2	12.7	23.3	40	31.3
Rural Males	1.2	10.6	24.3	36	43.7	54	59.3	65	66.2	69.9	66	66.6	55
Rural Females	0	0.4	2.9	6	12	14.4	24.8	27.4	34.1	40.5	40.9	42.5	44.1

Fig. 2.3: Agewise Prevalence (%) of Tobacco Use in Karnataka according to Sex and Rural/Urban Status.

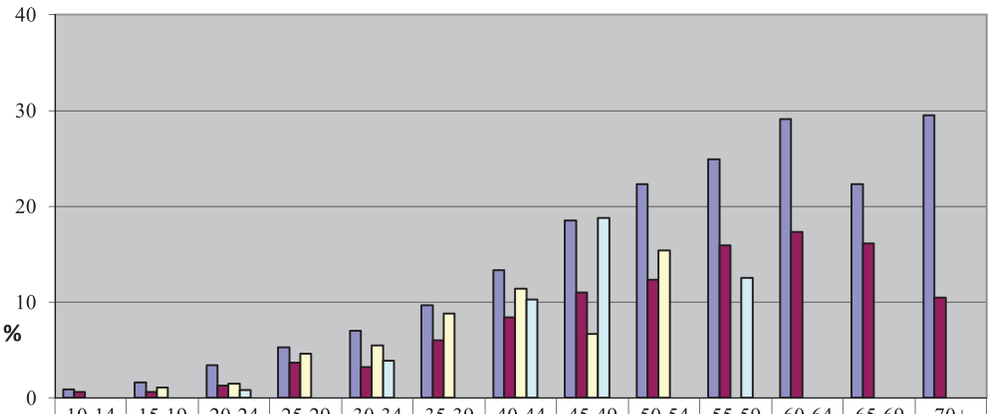
Negative association between education and prevalence of tobacco use was observed overall and in most of the age-groups in both the states (Fig 2.4 to 2.6). Similarly, higher family income levels were associated with a lesser prevalence of current tobacco use, although no difference in prevalence rates was observed between monthly family income categories below Rs. 2,000 per month. Religion did not seem to have any association with prevalence of current use of tobacco.



	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70+
Illiterate/ Just Literate	5.4	30.5	43.9	55.2	65.8	67.1	70.5	76	76.5	74.9	76.8	80.5	75.4
Primary/Middle	2.2	18.5	42.1	55.2	59.5	64.5	66.3	68.4	65.5	70.6	68.9	77.3	69.4
High/ Secondary School	2.4	16.5	44.5	48.4	57.8	66.4	65.9	72.2	68.7	67.2	65.3	60.6	73.5
College		13.5	24.8	39.5	54.9	53.8	59.7	59.8	68.7	54.1	59.5	46.4	72.7
Master & Above			25	50	16.7	14.3	50	66.7	33.3	100		0	100

Age Group

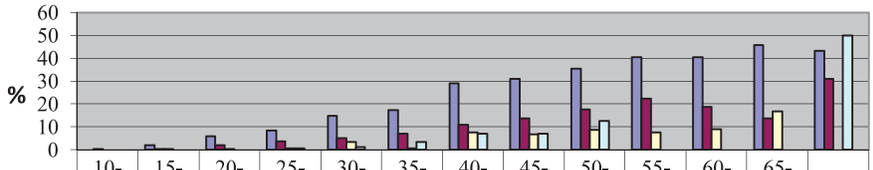
Fig. 2.4: Agewise Prevalence (%) of Tobacco Use in Uttar Pradesh Males according to Education.



	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70+
Illiterate/ Just Literate	0.9	1.6	3.4	5.3	7	9.7	13.3	18.5	22.3	24.9	29.1	22.3	29.5
Primary/Middle	0.6	0.6	1.3	3.7	3.2	6	8.4	11	12.3	15.9	17.3	16.1	10.5
High/ Secondary School	0	1.1	1.5	4.6	5.5	8.8	11.4	6.7	15.4	0	0	0	0
College		0	0.8	0	3.9	0	10.3	18.8	0	12.5	0	0	0
Master & Above			0	0	0	0							

Age Group

Fig. 2.5 Agewise Prevalence (%) of Tobacco Use in Uttar Pradesh Females according to Education.



	10-14	15-19	20-24	25-29	30-34	35-39	40-44	45-49	50-54	55-59	60-64	65-69	70+
Illiterate/ Just Literate	0	2.1	5.8	8.5	14.9	17.4	29	30.9	35.5	40.4	40.4	45.7	43.4
Primary/Middle	0.1	0.3	2	3.7	5.1	7	11	13.7	17.7	22.4	18.8	13.8	31
High/ Secondary School	0	0.1	0.2	0.6	3.4	0.7	7.6	6.8	8.8	7.7	9.1	16.7	0
College		0	0	0.7	1.3	3.4	6.9	7.1	12.5	0	0		50
Master & Above			0	0	0	0	0	0	0	0	0		

Age Group

Fig. 2.6: Agewise Prevalence (%) of Tobacco Use in Karnataka Females according to Education.

Tobacco use in smokeless form was predominant among women and among men below 30 years of age, both in urban and rural areas. However, smoking was the predominant form of tobacco use among men above 30 years of age. The overall prevalence of current smoking was 15.5% (29.3% among men & 0.6% among women) in Karnataka and 18.0% (27.5% among men & 2.6% among women) in Uttar Pradesh with gradual increase with age. The overall prevalence of current use of smokeless tobacco was observed to be 13.9% in Karnataka (13.4% among men and 14.4% among women) and 17.5% in Uttar Pradesh (24.3% among men and 6.6% among women).

Bidi was observed to be the most popular modality of tobacco smoking accounting for 91.7% and 84.5% of smoking habit (with or without other tobacco habits) in Karnataka and Uttar Pradesh, respectively. Cigarette smoking was practiced by 5.7% and 4.1% current tobacco users (with or without other tobacco products) in Karnataka and Uttar Pradesh, respectively. Cigarette smoking was more popular in urban areas as compared to villages.

Only a limited number of persons started their tobacco habit before 10 years of age. among those starting tobacco use before 10 years of age, 66.7% men (12 out of 18) in Karnataka and 98.4% men (62 out of 63) in Uttar Pradesh had also started using tobacco on a regular basis before the age of 10 years.

The mean daily frequency of tobacco use was 13.0 ± 9.7 in Karnataka (14.9 times/ day among men & 7.5 times/ day among women) and 9.1 ± 6.5 in Uttar Pradesh (10.0 times/ day among men & 7.9 times/ day among women). Cigarette smoking was mainly limited to men with 36.6% and 55.2% of them using it 6 or more times a day in Karnataka and Uttar Pradesh, respectively. About 89% persons in Karnataka and 87.2% men & 74.8% women in Uttar Pradesh smoked bidis 6 or more times a day.

Duration of use of tobacco products increased with increasing age. In Karnataka, 18.4% of men and 9.3% of women had ever considered tobacco cessation, but only 4.0% men and 2.2% of women could quit the habit. In Uttar Pradesh, 3.5% of men and 1.4% of women ever contemplated cessation, but only 5 men and 1 women (<0.1%) could quit the habit. The data also suggested that several of the persons reporting quitting may actually have switched to other forms of tobacco use (say from smoking to smokeless tobacco). Among those ever considering cessation, 59.4% in Karnataka and 63.0% in Uttar Pradesh were currently interested in quitting. Common reasons for quitting the habit included long-term health effects, economic impact, & moral/ religious reasons. Self-determination was the chosen method in most of the cases.

In Karnataka, at-least one of the parents was reported to be a tobacco user among 68.3% men and 74.3% women tobacco users. Tobacco use by a parent was reported by 49.8% men and 45.2% women never-users of tobacco. In Uttar Pradesh, parental tobacco use was reported by 73.8% men and 60.3% women tobacco users, in contrast with 66.4% men and 59.9% women never-users of tobacco.

In Karnataka, 61.7% of tobacco users and 78.0% of never-users reported knowledge of at least one harmful effect of tobacco. In Uttar Pradesh, 90.8% of tobacco users and 88.7% of never-users reported knowledge of harmful effect of tobacco. Cancer was the commonest response in all age groups in both the states, both amongst users as well as non-users of tobacco, followed by respiratory diseases, heart diseases and stroke. Second-hand smoke was considered to be harmful for adults by 57.1% men tobacco users and 26.6% women tobacco users in Karnataka, while in Uttar Pradesh, 95.2% men and 92.7% women tobacco users considered it harmful. Second hand smoke was considered to be harmful for children by 56.4% men & 26.4% women tobacco users in Karnataka and 95.3% men & 93.7% women tobacco users in Uttar Pradesh.

Overall, 61.3% men & 38.0% women tobacco users and 75.0% men & 69.6% never-users of tobacco in Karnataka felt that spending money on tobacco products makes people poorer. In Uttar Pradesh, 80.2% men & 74.3% women tobacco users and 79.3% men & 80.1% women tobacco users felt that expenditure on tobacco makes people poorer. Reasons for tobacco use included relaxation, sophistication, or fun. Some users also found tobacco to be repulsive or immoral.

The common responses in decreasing order about perception about tobacco industry included revenue generation, harm to economy, provision of jobs and killing citizens in both the states. Among tobacco using respondents in Karnataka, 77.9% supported discontinuation of advertising and sponsorship by tobacco industry; 75.8% supported increase in prices of tobacco products; 79.9% supported banning of smoking in public places; and 80.5% supported banning of sale to minors. About one-fifth (between 19.0% and 21.5% for different questions) of respondents had no opinion on various control measures.

About 3% of tobacco users opposed increase in prices of tobacco products, while opposition for other measures was less than 1%. Support for control measures by tobacco users of Uttar Pradesh was 91.8% for discontinuation of advertising; 74.5% for increase in prices; 90.9% for banning smoking in public places; and 90.5% for banning sale to minors. Opposition for above measures was voiced by 5.0%, 11.2%, 3.8% and 3.6% of tobacco users respectively.

The study demonstrated the feasibility of undertaking large community based survey to collect detailed data on tobacco use. The earlier large studies on the subject were carried out over a long time, sometimes over 2 to 3 years, which may have difficulty in relating to a particular time period. The current study was completed in 7 months after the funds were available.

The earliest attempt by ICMR on collection of nationwide data on tobacco use prevalence was to motivate National Sample Survey Organization (NSSO) to include information on tobacco survey in their surveys on quinquennial basis in early 1980s. The NSSO had agreed to only a small number of questions due to the length of their existing questionnaire. While the NSSO data was able to provide indication of the overall prevalence of tobacco use data both in smokeless and smoking forms, it was not optimal to provide information on specific forms of tobacco use, trends in change of specific habits, knowledge of harmful effects of different tobacco types, perceptions about tobacco use, reasons for initiation and quitting of tobacco habit, community view on control measures, etc. Such information would be useful not only about designing intervention programmes and materials, but would also help in assessing the effect of intervention strategies and plan legislative and administrative actions.

The study also demonstrated the feasibility of detailed data collection about different types of tobacco habits in a short period of time. The analysis also suggested the need for continuing such methodology, due to the suggestion that several persons who earlier could have been categorized as tobacco quitter, may actually have been persons who changed from one type of tobacco habit to another, say cigarettes to bidis or from smoking to smokeless form of tobacco. The questionnaire was able to find out the tobacco habits of a person at any time, thus, providing the opportunity of knowing when the person changed tobacco habit. This may explain the small number of quitters observed under the study. The finding would be important for expansion of tobacco cessation activities in India.

The study showed the limited knowledge on tobacco hazards in the community and the fact that level of this knowledge may be different in different areas. This highlights the need for developing specific intervention programmes suited to particular region, besides intervention programmes common to the country or a larger area. The data also demonstrates that a large number of people are willing to quit, but they do not have the will power and the social support to quit. Most of the people including tobacco users also do support legislative and administrative measures for tobacco control, including even ban on tobacco.

The questionnaire was specifically designed to obtain detailed information on different forms of tobacco use, based on the experience from earlier ICMR projects on the subject. Some of the limitations of the questionnaire observed during the study were corrected during the conduct of another study needing tobacco usage information of 70,000+ persons in a community survey in New Delhi.

This study indeed showed that there were several people who as per the earlier studies could have been identified as tobacco quitter, actually might have changed their form of tobacco use. The questionnaire is

being utilized for a survey in Lucknow on about 400,000 people, and seems to be optimal. After analysis of this data expected shortly, the questionnaire would be available to the scientific community.

Age at Initiation and Prevalence of Tobacco Use Among School Children

Tobacco use among school children is becoming a serious problem in developing countries. The early age at initiation highlights the imperative need to intervene and protect this group.

At ICMR's National Institute of Cancer Prevention (erstwhile Institute of Cytology and Preventive Oncology) at Noida; the study was undertaken with an aim to assess the prevalence of tobacco use among school children and to determine the age at initiation of this habit. The study included 4786 students of class 7-12 (age range 11-19 years) studying in various schools in Noida, U.P, India. Cluster and random sampling methods were used for selecting the students and a self-administered questionnaire was prepared. Any kind of tobacco use was seen in 537 (11.2%) of the students. Of these, 419 (8.8% of total) were 'ever smokers' (including current smokers) and 219 (4.6%) were 'ever tobacco chewers'. Tobacco use exclusively by smoking was elicited in 179 students (3.7%) while 118 (2.5%) were 'exclusive chewers'. The mean age at initiation of tobacco use was 12.4 years. Nearly 70% boys and 80% girls 15 year of age initiated the habit before the age of 11 years. Private school students reported a significantly early uptake of tobacco chewing as a habit. More than 50% of tobacco chewers reported use of khaini at least once prior to the study. This study highlighted the emerging threat of tobacco use among children. In addition, a downward shift in the age at initiation of tobacco uptake and rising prevalence among girls was also noted.

Risk Factors Associated with Tobacco Use Among Adolescents: A Cross-Sectional Study

Subsequent to elucidation of the prevalence of tobacco use among school children, at NICPR, Noida; a study was undertaken to determine the factors associated with tobacco use in this group. Knowledge of the factors leading to tobacco use at this young age might be helpful in devising ways to curb this problem. The same study group utilized in prevalence study was administered questionnaire regarding factors associated with their tobacco habit. The various factors associated with tobacco use in the study group included: father in blue collar jobs, less educated mothers and tobacco use by father/ mother/ siblings/ friends. The habit was manifold higher if the students bought tobacco for teachers (10.6-fold), brother (6.4- fold) or father/ relatives (3.1-fold). The reasons for tobacco habit included: refreshing themselves (31.5%) and influence of actors smoking in films (61%). about half of the students preferred smoking outside their home. Socio-economic status of the family, education level of the parents and influence of family and peer habits are some of the most important factors in tobacco habits in children. Hence, the methods of information, education and communication (IEC) should be directed at these to have a major impact on curbing this habit in children and adolescents.

Non-communicable Disease Risk Factor Survey, 2007-08, Phase-I states of India

The Government of India through the Ministry of Health & Family Welfare (MoHFW) initiated a decentralized, state based Integrated Disease Surveillance Project (IDSP) in the country with the assistance of the World Bank in the year 2004. The component of non-communicable disease surveillance planned periodic community based surveys of population aged 15-64 years to provide data on the risk factors. It is in line to help the state health administrators to plan strategies for the control of non-communicable

diseases by modifying the risk factors. All Indian states were proposed to be surveyed in a phased manner under the project. The first phase of the survey included seven states namely Andhra Pradesh, Kerala, Madhya Pradesh, Maharashtra, Mizoram, Tamil Nadu and Uttarakhand. The overall objective of the NCD risk factors survey was to improve the information available to the Government health services and care providers on a set of high-priority risk factors, with a view to improve the quality health care and services. The survey also aimed to establish the baseline database of NCD risk factors needed to monitor trends in population health behavior and risk factors for chronic diseases over time. This would provide evidence for evolving strategies and interventions for identified risk factors in the community to reduce the burden of non-communicable diseases.

A National Technical Advisory Committee was constituted to provide the technical guidance to the survey and a National Monitoring Committee was formed for monitoring the overall progress of the project. Indian Council of Medical Research was the implementing agency while the National Institute of Medical Statistics (NIMS) was appointed as the National Nodal Agency (NNA) for coordinating the survey. Five medical institutes/ colleges were selected as a Regional Resource Centre (RRC) for monitoring the quality of data collection and technical support to State Survey agency (SSA) of seven states selected in the first phase for conducting the survey. WHO STEPS methodology for NCD Risk Factor Surveillance has been adopted for the survey after carrying out suitable modifications, based on a multi-site ICMR- WHO collaborative initiative for NCD risk factor surveillance. The survey was designed to provide prevalence estimates of risk factors for each 10 years age group (15-24 through 55-64) by sex (male/ female) and place of residence (urban/rural). The survey used uniform sample design, bilingual schedules (English and the regional language of the state concerned), field protocol for data collection and physical measurements to facilitate comparability across states and also to ensure high quality data. For the present survey, appropriate sampling weights for households were used for urban and rural areas of the state. From each selected household one member aged 15-54 was selected using the KISH method and all members aged 55-64 were selected. Such post stratification was used for improvement of efficiency of the estimators. For each state, post stratification weights for individuals were constructed using the age distributions by sex. Two types of questionnaires - one at household level and another for individual level were used for the survey. At household level, information was elicited on religion, household facilities, ownership of agricultural land and livestock, and possession of durable goods for each selected household. The individual questionnaire collected information from the selected individuals regarding demographic, behavioral and physical measurements. The individual questionnaire was divided into two segments based on WHO STEP methodology. The first section (step-1) collected the demographic information of individuals including age, sex, marital status, education, and occupation. In the behavioural information section, information about tobacco use, alcohol consumption, diet, physical activity, history of raised blood pressure and history of diabetes were collected. In the second section (step-2), physical measurements of individual such as height, weight, waist circumference (not measured for pregnant women), blood pressure and pulse rate.

Behavioural Risk Factors for NCD

Tobacco Smoking: As per the WHO STEPS guidelines, the smokers are presented into the categories of current smokers, current daily smokers, past daily smokers and those who have never smoked in lifetime are classified as non smokers. The percentage of current daily smokers varied between a low 9% in Maharashtra and high 42% in Mizoram (Fig 2.7). The mean number of smoking beedis ranged from a low of 3 in Maharashtra to a high of 14 in Uttarakhand.

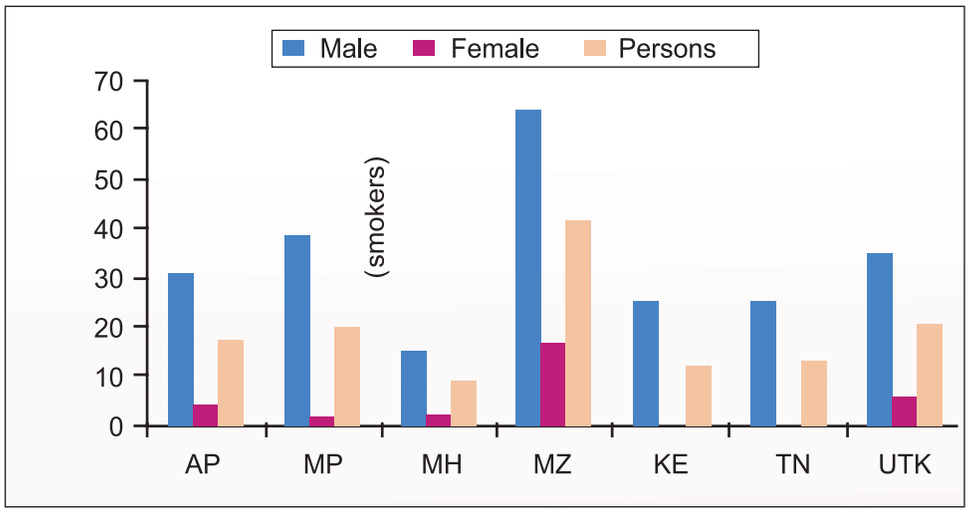


Fig. 2.7: Current daily smokers (%) by sex and phase-I states.

The mean number of smoking manufactured cigarette in a day was low in Madhya Pradesh (<1) and a high of 11 in Mizoram. The average age of onset of smoking ranged from 17 years in Mizoram to 20 years in Maharashtra, Kerala and Tamil Nadu and in rest of states it was 19 years. In Andhra Pradesh, Kerala, Tamil Nadu and Uttarakhand, 4-12% respondents were current daily users of smokeless tobacco. In rest of the states, it ranged from 32-48% (Fig 2.8). The mean frequency of chewing tobacco in a day ranged from less than 1 in Kerala and Andhra Pradesh to 10 in Mizoram. The mean frequency of chewing pan with tobacco ranged from a low <1 in Madhya Pradesh and Maharashtra to a high 9 in Mizoram. The mean age of initiation of smokeless tobacco use was 18 years in Mizoram and 20 years in rest of states among young respondents (15-34 years).

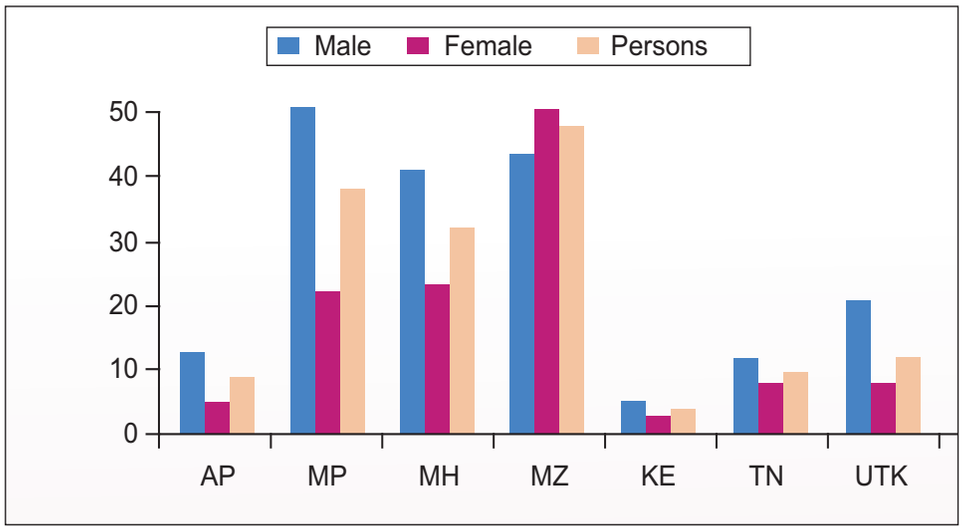


Fig. 2.8: Current smokeless tobacco users (%) by sex and phase-I States.

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3 Economics of Tobacco

Economics of Tobacco Use in India

Computation of economics of tobacco was one of the identified research area for ICMR. In order to achieve this goal, it was identified that cost of management of tobacco related diseases is an important missing link. ICMR initiated studies on this aspect in 1989. However, by mid 1990s, the importance of information on tobacco economics was a matter of concern for the Government of India. The Ministry of Health & Family Welfare constituted an Expert committee on Economics of Tobacco in India vide a notification issued on 26th July 1995. The ICMR acted as the secretariat for this committee.

The Expert committee was set up by the Department of Health, Ministry of Health and Family Welfare, Government of India, to undertake a comprehensive study on economics of tobacco use inter alia examining the tax revenue and foreign exchange earnings, employment and consumer expenditure on the one hand, and the cost of tertiary level medical care facilities for treatment of tobacco related diseases, losses due to fire hazard, ecological damage due to deforestation and disposal of tobacco related waste on the other hand, with a view to making an economic study of the impact of tobacco consumption.

The Expert committee initially had 12 members. Subsequently by means of further notifications (the last being dated 13th September 1996), the committee was expanded to include 21 members. Most of the additions to the committee were from tobacco industry. The committee held a number of meetings. During the first meeting of the committee, the components for computing the economics of tobacco as developed by ICMR representative were discussed and agreed to. Several members of the committee were requested to prepare specific chapters. The final report of the committee was submitted to the government on 13th February 2001. The long time taken in submitting the report was attributed to lack of literature, fairly difficult and delayed access to lots of data, particularly regarding the cost of treatment of tobacco related diseases, no more than nominal research and other facilities available to the committee, the gaps in literature and data. Besides review of the scientific literature, the Committee collected data from major institutions like Department of Oncology and Cardiology, Ministries of Finance, Agriculture, Commerce, Labour, Industry Environment and Forests.

The committee report had noted that there were hardly any benefits, which accrue either at the individual or social level to the consumers of tobacco products, the demand for which is, by and large, supplier-induced and determined. The indirect, incidental, short-run presumed benefits in terms of employment, output, foreign exchange earnings, tax revenue, etc., are there because the consumers are in various ways induced and addicted to spend a part of their incomes on this commodity. The report highlighted

the losses to the society due to tobacco use as well as economic gains accrued through its commercial trade. The benefits of its use are for different people/ groups whereas the losses are for different set of people, thereby the two components are not directly comparable. The report concluded that tobacco is a demerit product.The costs of medical treatment and other external costs incurred by the patients and society, even in their underestimated form, were considered to be so staggering as to dwarf the putative indirect financial benefits. The cost to the society due to three major disease entities in India during the year 1999 was Rs. 27,761 crores (details in Table 3.1). The value of all the tobacco products in India had been assessed at Rs. 24,000 crores. The report had tremendous implications on the till then perceived economic contribution to the economy.

Table 3.1: Cost of Tobacco to India (1999)

No. due to Tobacco	Tobacco Related Disease		
	Cancers	Coronary Artery Disease	Chronic Obstructive Lung Disease
1996	1,54,300	4,200,000	3,700,000
1999	163,500	4,450,000	3,920,000
average cost (1999)	350,000	29,000	23,300
Total cost India (1999) in billion Rupees	57.225	129.05	91.336
Total cost (1999) = Rupees 277.611 billion or US$ 6.5 billion			

The issues addressed here are mainly the impressions provided by the chairman and the member-secretary as given in the report and the preface written by them. The report was not scrutinized by ICMR and thus may not provide the official stance of ICMR.

The literature on tobacco economics at that time brought it out clearly that there is a good deal of work which has been in various ways inspired by the tobacco interests, more particularly by the organized cigarette manufacturing industry. There seemed to be a great need for and large scope for many studies in this largely unexplored area.

Cost of Management of Tobacco Related Diseases

During early 1980s, need for tobacco control was increasingly being recognized by the scientific community of India. However, the suggestions were not being translated into control measures. One of the major stumbling block was the economic contribution of tobacco in the form of revenue and employment generated by tobacco industry. Some studies elsewhere had suggested that the revenue provided by tobacco industry to the Government was less than the costs posed by diseases caused by tobacco. However, no such data was available from India. An ICMR advisory committee on cancer research suggested that ICMR should carry out a study on the subject.

The preliminary work at ICMR was in the form of an inventory for comparing the benefits and costs of tobacco for India. Tobacco industry had generated a lot of data on advantages and contribution of tobacco to Indian economy, but the data on costs was only in the form of estimates. The available estimates were on costs of treatment of some tobacco related cancers through adding the cost of drugs during the treatment period. However, in reality, the cost of any disease includes direct as well as indirect

medical costs for treatment incurred by the patients, their families and their friends. It was also important to consider the costs borne by the Government institutions as well as out of pocket expenditure by the patients/ families/ friends. The societal cost of any disease also included secondary & tertiary costs due to absenteeism, premature death, indirect economic costs as a result of tobacco production, occupational diseases, etc. assessment of the diseases burden caused by tobacco use (not the magnitude of tobacco related diseases) was also important. A look at the inventory suggested that it may be possible from the scientific literature to make a fair assessment of the disease burden of cancers, coronary artery disease and chronic obstructive lung diseases, caused by tobacco. Stroke was considered to be an important tobacco related disease category for India, but the literature was not sufficient at that time to assess the diseases burden caused by tobacco. However, no data existed on comprehensive cost of any tobacco related diseases. The western studies had calculated the data based on the hospital costs for treating patients. But, Indian hospital had never calculated such costs and there was absolutely no information on the money spent or lost by the patients, which was likely to be more than the money spent by hospitals. Thus, it was decided to undertake a study on cost of management of tobacco related diseases as a first step.

As the magnitude of the disease, and studies on attributable risks of disease due to tobacco was likely to be available for three disease entities (cancers, coronary artery disease and chronic obstructive lung disease), the ICMR study was also restricted to costs of management of these diseases. No distinction on disease caused by tobacco was necessary for this study, as the management principle was (and is) the same for all cases regardless of aetiology. However, the study design was to be adjusted as per the availability of data on magnitude of these disease entities. Thus, a longitudinal study design was finalized for study on tobacco related cancers (as the data was available on incidence rates of cancer); and a cross-sectional design was considered adequate for coronary artery disease and chronic obstructive diseases (as the data on magnitude was available through prevalence studies). The study was aimed:

1. To estimate the average cost of diagnosis and treatment of tobacco related diseases by the patients and their relatives/friends.
2. To determine variables which influence the expenditure by patients on treatment of their diseases.
3. To estimate the average cost of diagnosis and treatment of tobacco related diseases by the institution.
4. To estimate the loss of productivity due to absenteeism as a result of the illness, for the patients and their relatives/ friends.
5. To estimate the loss of productivity due to death and disability due to tobacco related cancers.

The study collected data from patients of the identified diseases and their relatives/ friends on the expenditure on diagnosis & treatment of their disease; travel for treatment/ diagnosis; additional expenses for lodging & food during the treatment period; and loss of wages because of the disease. The expenditure incurred by the treating institution on management of these patients was also collected. In case of premature death, the cost imposed upon the society (due to premature death) was also calculated.

A cohort approach was adopted for assessment of the cost involved in management of tobacco related cancers. The cohort included cases of cancers of the oral cavity (including gums), pharynx (excluding nasopharynx), larynx, and lungs. The patients were followed up for three years after registration at the hospital or till death, whichever occurred earlier. At the time of first contact, the patients were enquired about demographic details, the duration of the illness, the health agencies contacted by them for diagnosis and treatment of their illness (specific or non-specific). The item wise expenditure made by the patients, their relatives/ friends, was recorded, under various headings, namely, consultation, investigations, treatment with different modalities travel for the purpose, and any additional cost incurred for lodging and boarding. The information was also collected on any loss of wages for treatment of the disease, or if the disease resulted in loss of job. Specially trained medico-social workers collected the information on a pre-tested questionnaire. Intangible costs caused by the disease, and tertiary costs of tobacco use, were not attempted in this study. The follow up information was attempted every 3 months either during the scheduled visit of the patients to the hospital or by visiting the homes of the patients. All the expenses or losses by the patients incurred during the study duration were combined to provide the total expenses by the patients and their relatives/ friends. The procedure of discounting was adopted for the expenditure incurred by the patients (or their relatives/ friends) during different years, the rate of discounting being 10%. The expenditure given in the report pertained to the year 1990, the first year of the study. The information sought from the patients was on recall basis. The medico-social workers engaged in the study were trained to know the prevalent charges for various services by the private hospital in the city, approximate transport charges by various modalities of travel, charges of food in various facilities around the hospital, etc., for the purpose of further probing, to assess the reasons for variations. The costs on coronary artery diseases and chronic obstructive diseases were collected on similar lines and items (as for cancers), but on a cross-sectional basis. The reference period for collection of data was past one year.

Expenditure by various departments of the hospital was determined by the investigations rather than the diagnosis of the patients. Thus, the data collection included, identification of various investigations and service activities undergone by the patients; the determination of unit cost of various investigations and other services needed by patients of tobacco related cancers; the charges paid by the patients for undertaking the investigations, etc.; and calculation of the excess expenses incurred by the institution in treating these patients (Fig 3.1). The details of investigations & other hospital services, and charges paid by them, were collected from the patients during interview. Data was collected from various concerned departments of hospital, on the staff and the equipment available with them to perform the functions needed for treatment and investigations of tobacco related cancer cases. The hospital costs pertaining to tobacco were calculated through analysis on optimum number of investigations per day per concerned personnel, number of personnel engaged on work, salaries of the staff, the proportion of time spent for carrying out that investigation/ service, the purchase value & annual maintenance of equipment, and cost of reagents/ consumables used for undertaking the investigation/ services, and per patient costs of general maintenance of the hospital. The cost of the equipment was also obtained. The data collected from patients was on recall basis and it was accepted that the costs thus collected would be lower than actual due to expected recall bias. In case of any estimation, the lower expected value was used for

calculation, thus, sticking to the principle of underestimation (in case of doubt) followed throughout the study.

The difference between the actual age at death and expectation of life at that age (as available from the Registrar General of India) was used to compute the salary loss, savings of pension to the government or the organization (in case the patient was entitled to pension), loss of family pension. The retirement age in India at that time was 58 years, which was considered as the productive age for those in job, whereas for those engaged in business the remaining life expectancy was considered as the productive age. As the age of the spouse of the deceased person was not collected, the age of the deceased was used for calculation of the family pension (which again was considered to be an under-estimate).

The average cost due to a case of tobacco related cancer was observed to be Rupees 1,34,449 (discounted to 1990 level) (Fig 3.2). The patients in the cohort, spent an average of Rupees 17,965 (including loss of income due to absenteeism), with another Rupees 4,009 being contributed by the institution in the form of various services. The loss due to premature deaths of patients of tobacco related cancers amounted to Rupees 1,12,475. annual per capita direct expenditure by patients of CHD and COPD was Rs. 8,520.3 and Rs. 2,257.6, respectively. The annual indirect losses by the patients & state/ employer for patients of CHD and COPD amounted to Rs. 6,388.4 & Rs. 9,694.1 respectively. Thus the total average annual expenditure for a patient of coronary artery disease was Rs. 14,909 and for a patient of chronic obstructive lung disease was Rs. 11, 952 (Fig 3.3).

Expenditure by Patients of Tobacco Related Cancers (1990 Prices)

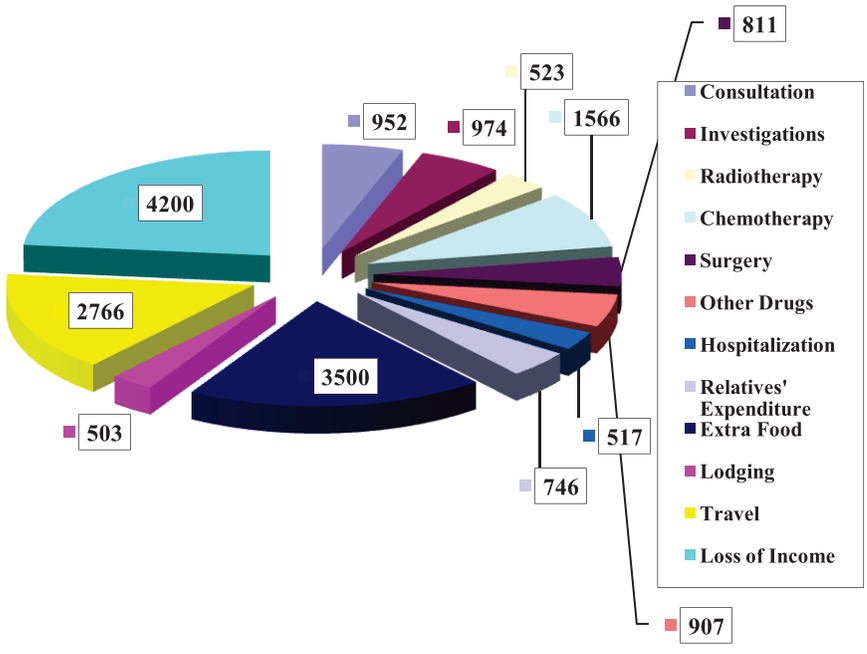

Fig. 3.1: Total Average Expenditure by a Patient of Tobacco Related Cancer = Rs. 17,965.

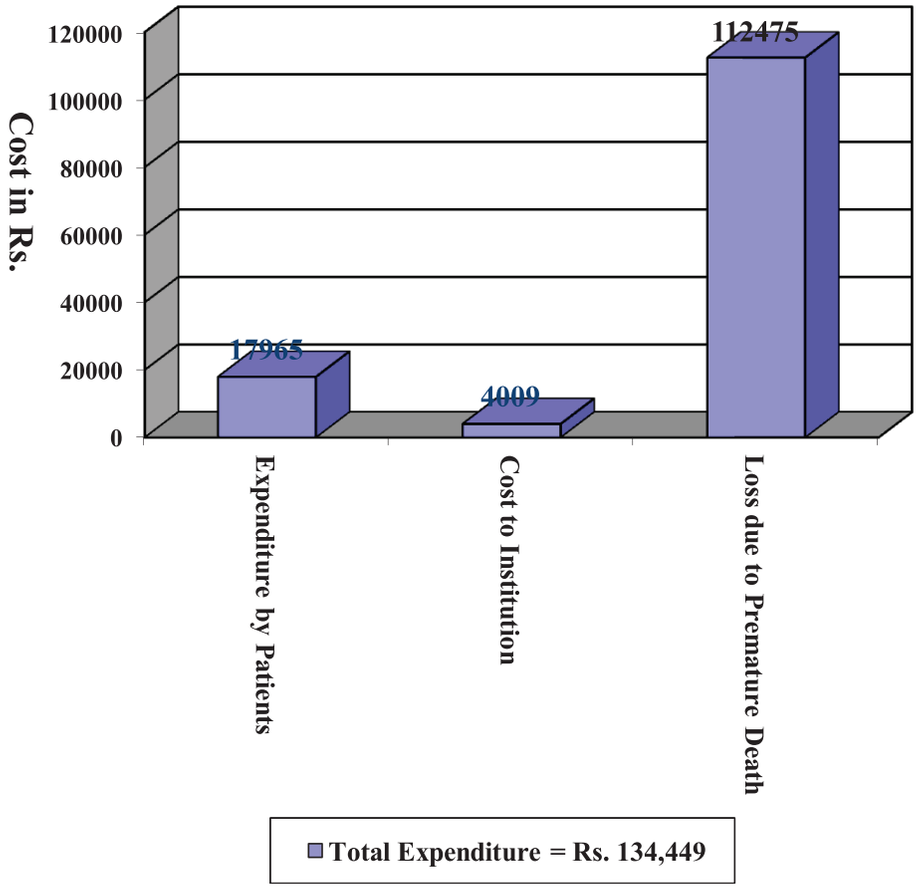

Fig. 3.2: Average per Patient Cost of Tobacco Related Cancers (1990 Prices).

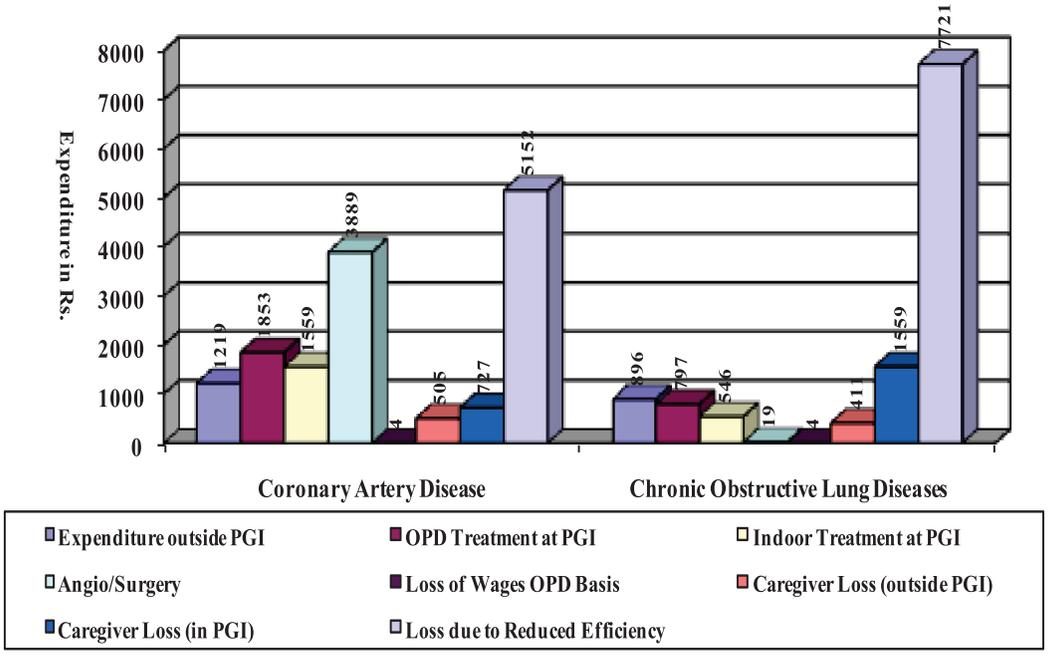

Fig. 3.3: Average Expenditure by Patients of Coronary Artery Disease and Chronic Obstructive Lung Disease (1992 Prices).

Total average Expenditure by Patients of coronary artery Disease = Rs.14,909

Total average Expenditure by Patients of chronic obstructive Lung Disease=Rs. 11,952

There was very little difference in expenditure by the patients on items related to direct medical treatment, according to different demographic attributes of the patients. The few exceptions where such differences were noted included a lower expenditure on chemotherapy among old patients; a higher expenditure by residents of Delhi on consultation and surgery; and higher expenses on radiotherapy on patients where the intent of treatment was curative. The direct non-medical expenditure (on travel, lodging, etc.) on treatment was influenced by personal characteristics of the patients', suggesting a variation in expenditure due to their paying capacities. Better occupation, greater distance of the hospital from their place of residence, younger age of the patient, and curative intent of treatment (probably influenced by longevity and higher degree of follow up), was associated with higher expenditure.

The study provided important inputs for computing the overall cost of three major disease entities to the country. The earlier estimates on the subject related only incomplete estimates on direct medical costs of these diseases. Thus, the study was a turning point for country's policy.

The study did require meticulous planning in terms of identification of components which may be required while analyzing the data. It was clear that if some component is missed at the time of planning, the study may need to be conducted all over again to get information on that aspect. Therefore, the phase of pre-testing of the questionnaire was extremely critical. The questionnaire for this study was finalized after three rounds of pre-testing. This also provided an opportunity to identify the diagnostic tests and therapies the patients preferred from outside the base hospital and thus prepare the interviewers on probable involved issues.

The study also required very close day-to-day monitoring, especially in the beginning when the interviewers required very frequent guidance. Although not anticipated during planning, it became clear very soon that there would be no option but to adopt the principle of underestimation of costs in case of doubt. The study very clearly shows an important role of socio-economic factors in determining the overall costs of the diseases. The investigations and management practices have also changed since that time. There has been major increase in availability of cancer treatment facilities in private sector in India. The GDP and economic status of Indian population has also increased since the conduct of the study. Data on magnitude of more tobacco related diseases like stroke may also be available. The above highlights that if a similar study is carried out today, the cost of tobacco related diseases is likely to be higher than those observed by the study.

The above data was converted into the total cost for the country due to three major tobacco related disease entities. The data based on the final data on cancer related study and preliminary results from the coronary artery disease and chronic obstructive lung diseases was presented during a WHO- Government of India conference in January 2000. The cost to the country due to three major disease entities for the year 1999 was estimated at Rs. 27,761 crores. The data changed the strategy of advocacy by the tobacco promotion groups in the country, who used to harp on the economic advantage of tobacco at any indication of government taking a major step on tobacco control. Obviously, the study helped in making a paradigm shift in the policy related decision-making of the government.

Support for Tobacco Control

The rich experience in research related to tobacco was utilized in helping and guiding decision makers in matters related to tobacco control. Some of the specific areas where major inputs were provided, included, economics of tobacco in India (through an expert committee constituted by the Ministry of Health & Family Welfare), health hazards of pan masala containing tobacco (through expert committee constituted by the Director General of Health Services), preparation of health education messages to be broadcast through television (at request of Ministry of Health & Family Welfare), provision of facts and information to the Parliament's Committee on Sub-ordinate Legislation on the Cigarette Act, organization of International Conference on Global Tobacco Law: Towards a WHO Framework Convention on Tobacco Control, and organization of an inter-ministerial committee meeting to discuss issue related to frame work convention on tobacco control. ICMR was also represented in the meeting of the WHO's Working Group on Framework Convention on Tobacco Control.

4 Legislations

Development of a Comprehensive Tobacco Control Legislation

The need for a comprehensive legislation on tobacco control was accepted in 1986 itself, wherein the gravity of tobacco problem was noted along with the fact that the existing cigarette act was ineffective. It has to be realized that any legislation is enacted after consultation and agreement with all ministries and departments of the Government. While the Ministry of Health & Family Welfare was convinced, it took sometime before other ministries could be sensitized about the need for major action on tobacco control. The Ministry of Health and Welfare started consultations in early 1990s with other ministries, which suggested that an expert group on study of tobacco economics in India be constituted. A national workshop on tobacco control held in 1991 identified major tobacco control activities (both for smoking and smokeless tobacco use) in the country. In the meantime, a Parliament Committee on Cigarette Act of 1975 was constituted in 1995. It was prudent that the recommendations of this Committee are considered by the Government. In fact, the report of this Parliament Committee helped a lot in not only proposing a strong legislation for tobacco control, but also take initiative in requesting various departments to initiate activities in their sphere for tobacco control. The observations of the Committee were based on the consultations carried out with various concerned departments, parties, companies, NGOs, etc. In fact, several inter-ministerial meetings were held during the next few years to suggest and monitor actions taken on the recommendations of the committee. ICMR played a very active role during these consultations. The details of the observations and recommendations of the Parliamentary committee are briefly given below.

Observations in the 22nd Report of the Committee on Sub-ordinate Legislation:

The Committee observed that the statutory warning on cigarette packs laid down by the Cigarette Act 1975 has not proved effective. Limitations of the warning identified by the Committee included: its language, being only English; the monotony of the message; small lettering and its presence on only one side of the pack; its size, being smaller than the brand name; the absence from the purview of the act of *bidis*, the most prevalent form of tobacco smoked in India; the absence of a maximum permissible limit for tar and nicotine content and the absence of tar and nicotine concentrations on the packs. The Committee observed that the existing provisions on tobacco advertising were ineffective & insufficient; glamorous tobacco advertisements create illusion about smoking being pleasurable, sophisticated and helpful for achieving success; sponsorship of sports and cultural events gives the tobacco industry high visibility; tobacco industry's claim that advertising is for brand switching and does not increase tobacco

consumption was wrong and grossly misleading; risk for disease also exists for those who passively inhale tobacco smoke; and ban on smoking in public places in other countries has resulted in widespread change in attitudes, leading to smoking cessation. The Committee also noted that parental practices at home and peer habits at school affect initiation of tobacco habit, which makes it essential that a coordinated, rational educational strategy is carried out at both these levels. The Committee also observed the success of a nationwide radio programme, 'Radio DATE', carried out jointly by AIR and ICMR, as well as the anti-tobacco community education projects of ICMR. The Committee also felt that increasing the production of tobacco on the one hand and framing comprehensive legislation to curb its use cannot be justified, and the need for taking action on substitution of tobacco crop by some other crop and addressing the issues of livelihood of millions of workers engaged in the manufacture of bidis and cigarettes.

Recommendations in the 22nd Report of the Committee on Sub-ordinate Legislation

The Committee provided detailed recommendations on various facets related to tobacco control which related to all concerned sectors, like health, agriculture, commerce, sports, etc. Salient aspects for various actions are given below.

Statutory warning on tobacco products: The Committee recommended that the health warning(s) should appear on all tobacco products; it should be worded strongly, be rotated periodically and be supplemented by symbols or pictures; should be in English and regional language(s); lettering of the warning should be as large as that of the brand name, and be displayed on both sides of the pack; concentrations of tar and nicotine should be printed on packs and cartons of all tobacco products and maximum permissible limits be fixed; individual cigarettes should also bear the health warning; health warnings should also be displayed prominently at every shop where tobacco products are sold; and imported cigarettes and other tobacco products must meet the statutory warning requirements of India.

Tobacco advertising: Government should make provision in the proposed legislation for a total ban on all forms of advertisement for tobacco, with stringent penal provisions for violation of the law. There should be a total ban on the sponsorship of major sports events by cigarette companies.

Prohibition of tobacco smoking in public places: The Committee recommended a complete ban on smoking at least in all public places where large numbers of people are expected to be present for long periods, such as hospitals, dispensaries, other health-care establishments, educational institutions, conference halls, cinemas, theatres, offices, all workplaces and railway waiting rooms. There should also be a complete ban on smoking in public transport systems, domestic flights and Government vehicles.

Social awareness about tobacco: People should be educated about the effects of smoking and passive smoking; non-smokers who object to smoking and other forms of tobacco use should have legal backing; anti-tobacco education should be compulsory in schools and colleges; teachers should not smoke within school premises; sale of tobacco and tobacco products should be banned in the vicinity of schools and colleges, with provision for punishment of vendors for violation; persons below a minimum age (say, 18 years) should not be sold cigarettes; social awareness should be created through electronic and print media; as far as possible, scenes in which characters smoke in an obtrusive manner should not be included in programmes shown on television; and the Government should allocate adequate resources and personnel to carry out effective anti-smoking education.

Alternative cash crops to replace tobacco: Initiative should be taken by the Ministry of Agriculture to persuade farmers to switch over to alternative crops, first on an experimental basis, and the results then widely publicized to convince farmers of its viability; farmers be given anti-tobacco education; Government might consider giving monetary assistance to farmers to help them change to alternative crops; Indian Council of Agricultural Research develop new techniques for high-yield varieties and for fertilizers for alternative cash crops; research be continued to explore alternative uses for tobacco; Tobacco board should not promote internal consumption of tobacco, although the Committee had no objection to production of tobacco for export; a gradual approach be adopted wherein efforts were made to phase out cultivation of tobacco for human consumption over time; and conduct a study of the resources required for rehabilitating workers in tobacco production and the areas in which they could be absorbed, to formulate a concrete proposal in this regard.

The Committee report provided a lot of support for tobacco control activities and helped in further expanding and widening the scope of the comprehensive tobacco control legislation. Various ministries did in fact start experiments to achieve the recommendations of the Committee. ICMR strongly recommended the initiation of the Framework Convention on Tobacco Control (FCTC), during the initial consultation of WHO with various countries. The ICMR very actively participated in developing a country stance for FCTC, and represented India in the two meetings of the Working Group of FCTC which laid down the provisions of FCTC based on scientific knowledge. ICMR also took very active part in suggesting unbiased approach for tobacco control, developing stance on various provisions, likelihood of considering FCTC provisions under the country's legislation, organizing meetings to discuss various issues, preparing background notes for various Ministry meetings including inter-ministerial meetings on FCTC, tobacco control legislation, consideration of some legislations like ban on smokeless tobacco use, warnings on smokeless tobacco products, tobacco cessation clinics, educational strategy, alternatives for tobacco farmers, work related to health hazards of pan masala, economics of tobacco use in India, etc. a paper on multi-sectoral approach for tobacco control was also prepared.

Carcinogenicity of Pan Masala Containing Tobacco and Consideration of Ban on Use of Tobacco in Smokeless Form in India

A major change in modality of use of smokeless tobacco occurred in early 1970s, when pan masala was introduced in Indian market. Pan masala contains the ingredients of traditional betel quid, except the betel leaf. Pan masala removed the inconvenience of frequent preparation of pan due to its ready to use nature and longer shelf life. The increasing popularity of pan masala resulted in introduction of pan masala–containing tobacco and gutka. Gutka has been defined by manufactures as tobacco with ingredients of pan masala, and thus essentially would be similar to pan masala-containing tobacco but with higher proportion of tobacco. Availability of this product in small sachets further increased its popularity. In fact, the ICMR survey on tobacco use in 2001 showed that pan masala containing tobacco was the commonest tobacco modality among population below 40 years of age.

The Indian scientists in 1980s pointed out that certain toothpastes and toothpowders being sold in India contained tobacco. This product produces dependence among its users forcing them to brush their teeth several times a day with this preparation. Therefore, the Directorate General of Health Services and Ministry of Health and Family Welfare decided to ban this formulation, which was contested by the

manufacturers in High Court and later in Supreme Court. In 1994, while upholding the validity of the Government of India notification for banning the addition of tobacco to toothpaste and tooth powder, the Hon'ble High Court of Rajasthan directed the Central Government to appoint a committee of experts to assess the public health impact of use of tobacco in pan masala, gutka, and to prohibit the manufacture of these products if found to be injurious to health. The Directorate General of Health Services constituted an expert committee on use of tobacco in pan masala, gutka, etc., in August 1994.

The commonest modality of tobacco use in smokeless form in India till mid 1980s had been the betel quid containing tobacco, whose causative role in oral cancer had been reviewed and accepted by International Agency for Research on Cancer, in its monograph on smokeless tobacco use. The expert committee of the Directorate General of Health Services on pan masala-containing tobacco and gutka discussed the available literature on the subject during its first two meetings. Based on the published literature most scientists believed that tobacco use in any form was harmful to health. However, some scientists pointed out that this assumption may hold good for programmes on awareness on tobacco, but in the court of law specific evidence would be necessary if there was a move to ban these products. These scientists believed that sufficient evidence was not available to prove the association of pan masala-containing tobacco with oral cancers and it would not be appropriate to suggest a ban on these products. The ICMR was requested to prepare a review paper for consideration of the expert committee. The background paper was published after the committee had provided its recommendations. The paper considered all the studies on pan masala-containing tobacco, related mixtures, and its individual components. The interpretation on carcinogenicity of pan masala containing tobacco was made, based on (i) studies on pan masala containing tobacco; (ii) studies on similar mixtures; and (iii) studies on effect of individual ingredients of the mixture and the likely effect of their combination. The literature showed a limited evidence of pan masala containing tobacco being carcinogenic to animals. Proportion of areca nut and tobacco in pan masala containing tobacco is between the proportion of these substances in two known tobacco-areca nut mixtures of India (Mainpuri tobacco and Mawa). Studies on Mainpuri tobacco indicate it to be carcinogenic, while literature suggests an association between mawa use and oral sub-mucous fibrosis. The review concluded that based on human evidence on similar mixtures and limited studies on pan masala containing tobacco, pan masala containing tobacco is expected to be carcinogenic. Direct evidence of its carcinogenicity in human beings is not likely to be available at present, even with well designed studies. This is due to the fact that the incubation period of oral cancer is 15 to 20 years, and the habit of chewing of pan masala containing tobacco is less than the incubation period.

The conclusions of the background paper were accepted unanimously by the committee during its third meeting in 1996. The committee however, debated if indirect evidence would be enough in the court of law. The chairman of the committee felt that direct epidemiological evidence was must if a drastic action like banning the product was to be taken. Therefore, preparation of epidemiological research projects to assess the association of the product with pre-cancerous conditions was suggested. The issue was debated again during the fourth meeting of the expert committee in September 1997 under the chairmanship of the Director General of Health Services. By this time there were many reports from ENT and dental specialists about increase in number of cases of sub-mucous fibrosis. It was pointed out that even an epidemiological study on pre-cancerous conditions may not tremendously change the scenario. The review had tried to assess the health hazards of the product in many ways and a direct question

was posed to the committee if they could think of any possible reason to conclude that the product may not be carcinogenic. It was also argued that it would be against the principles of preventive medicine if a decision was not taken and people are allowed to fall prey to diseases for the next 15 to 20 years, which was expected to be the minimum period for availability of direct evidence. The argument was accepted and the expert committee unanimously concluded that pan masala-containing tobacco and gutka, are hazardous to health, and the hazards are likely to be similar to those of conventionally chewed tobacco, mainly sub-mucous fibrosis and oral cancers. As suggested by the paper, the committee also felt that the incubation period of the disease caused by pan masala containing tobacco is likely to be shorter than after the use of conventionally used betel quid with tobacco. The committee felt that the background paper has used the principles of preventive medicine in pre-empting the health hazards of newer mixtures. It was felt that at present, modified tobacco mixtures can be introduced in the market without any license, and it would not be appropriate to wait for the next 20 years to carry out human studies on its carcinogenicity and then recommend its ban.

The opinion of the expert committee was considered by the Central Committee on Food Standards (CCFS), which is a statutory committee under the provisions of Prevention of Food Adulteration Act 1954, to advise the Government on matters relating to food safety and quality. The CCFS examined the report in November 1997, along with the known literature on health hazards of smokeless tobacco use. The committee noted that Section 23 of Prevention of Food Adulteration Act 1954, already empowers the central Government to prohibit the sale of any substance which may be injurious to health when used as food or as an ingredient of food. Taking into consideration all aspects of health hazards of tobacco chewing, the committee recommended a total ban on use of tobacco in pan masala/ gutka or as an ingredient in food item or as such. Based on the recommendations of the CCFS, the Directorate General of Health Services proposed a notification for consideration of the Ministry of Health & Family Welfare, aimed at banning the manufacture, production, sale or trade of smokeless tobacco.

A sudden ban on smokeless tobacco could be considered as a drastic recommendation for a country where it is practiced by about half of tobacco users. As a first step, the Ministry of Health & Family Welfare held discussions with some experts in the field, to reassess the technical confidence in the findings and also the likely implications of such a ban. The change in tobacco use habits because of non-availability of smokeless tobacco was also discussed. It was felt that majority of people may not consider cigarette smoking as an alternative due to the comparative differences in cost of smokeless tobacco products and cigarettes. However, shift to bidi smoking was a distinct possibility. In view of the multisectoral implications of this step, it was decided to discuss the issue in an inter-ministerial meeting. ICMR prepared a background paper for the meeting. It was felt that if a ban on smokeless products was agreed by all sectors concerned with tobacco, the Ministry of Health & Family Welfare would need to establish a large number of tobacco cessation clinics, so that people tend to quit their habit of smokeless tobacco use rather than shift to smoking. It was agreed by all sectors of the Government that both tobacco smoking and tobacco use in smokeless form are injurious to human health. It was felt that suitable campaigns need to be initiated to reduce the prevalence of tobacco smoking in the first phase. It was also indicated that the tobacco habit being as addictive as cocaine or heroin, tobacco users would require help in cessation of their habit.

Further deliberations on the issue were received from various ministries providing operational issues connected with sudden ban on smokeless tobacco. In view of this, sudden ban of all tobacco habits was not agreed. Some states banned sale of gutkha as a short term measure, in view of the recommendation of CCFS. As the legislative provisions enable such a state action only for a short period, the Supreme Court of India asked the states to repeal the legislation after a few years.

Anti-Tobacco Community Education

The study was to assess if anti-tobacco education can effectively be imparted to community, through use of existing Government infrastructure. Such a possibility was expected to be cost-effective, long-lasting, and more acceptable to the community. The study was started in 1985, at a time when quitting tobacco was considered to be extremely difficult (which still remains to be the prevailing opinion among tobacco users) and the health services had not perceived the need for an active role in this direction. No tobacco cessation guidelines or services existed, neither in the Government nor in private sector. At the time of initiation of the project health services and schools were considered to be two existing infrastructure for the purpose of testing their response to carry out an organized anti-tobacco education activity.

The multicentre task force project of ICMR was to study the feasibility of involving existing infrastructures in anti-tobacco community education. The outcome measures were to find any change (reduction as a positive outcome) in tobacco use prevalence brought about by (i) reduction in tobacco use among tobacco habituees; and (ii) reduction in uptake of tobacco by non-users.

The intervention by health services was directly on the community by para-medical health personnel. The direct intervention by school network was on the children attending schools but the indirect and secondary effect was expected on the community and the change in tobacco use was measured in the overall community.

The study was carried out in Karnataka (near Bangalore), Kerala (Trivandrum district), Uttar Pradesh (Mainpuri district) and Goa (entire Goa state). At the time of initiation, health services were proposed to be involved in all the four areas. In Goa one section was to carry out intervention through schools alone, the second through health services and schools, with the third to act as control. The willingness to carry out the intervention by health services was high in Karnataka, whereas it was low in Kerala and minimal in Goa and Uttar Pradesh. The workers considered it as an additional burden and did not carry out intervention. The study in Kerala was truncated to see the work of some para-medical workers who had opted to participate. The study in Uttar Pradesh at the advice of expert group was modified to raise a group of community volunteers to carry out intervention for a short period. The Goa study compared two areas with school based intervention with one area acting as control. During the preparatory phase, the first control area in Karnataka was considered to be too close to the city (which may make analysis difficult due to possible overall education through other sources) and thus a second control area was added.

The study involved one year of preparatory phase, wherein the concerned workers were trained, requisite educational material was prepared and a baseline survey on knowledge, attitude and practice (KAP) was carried out on a representative sample of the community. The intervention was for a period of 3 years in Karnataka & Goa, and for a period of 1 year in Kerala and Uttar Pradesh. The KAP survey was repeated

after intervention. The data analysis was also carried out during the fifth year of the study. The trained primary health workers in Karnataka and community health volunteers in Uttar Pradesh also examined the oral cavity to identify and classify lesions as normal and abnormal. All the abnormal lesions identified by the workers were advised to attend a clinic specially arranged by the investigators for this purpose.

Pre-tested health education material was prepared by the project staff and used by the existing infrastructure personnel. The main health education aid available with the health workers in Karnataka was a photograph of oral cancer patient, which helped in initiating the discussion with individuals. The educational sessions were carried out individually or in groups by the health workers, during their routine visits to the community which happened approximately once in 15 days. This educational procedure was aided by organization of mobile exhibitions of posters in the community. Similar procedure was followed by the community volunteers in Uttar Pradesh. The health education material in Goa was more extensive and included pamphlets, posters, booklets, models, exhibitions and dramas. The school children were provided educational material for taking to their homes and read them out for their parents and neighbors in case they were illiterate.

The overall reduction in the prevalence of tobacco usage in Goa was 11.8% among men and 9.1% among women in intervention zone 1; 13.4% among men and 13.3% among women in intervention zone 2; and 2.0% for men and 10.2% for women in control zone. The proportional reduction in the rate of tobacco habit was 33.5% in men and 45.5% in women of intervention zone 1; 32.6% in men and 50.4% in women of intervention zone 2; and 8.5% in men and 33.3% in women of control zone (Figure 4.1). Thus, the school based intervention was considered to be effective and feasible for the community. Based on the experience of this project, Ministry of Education, state of Goa, included an 8 hour academic course on tobacco as a part of co-curricular activities for standard five and above.

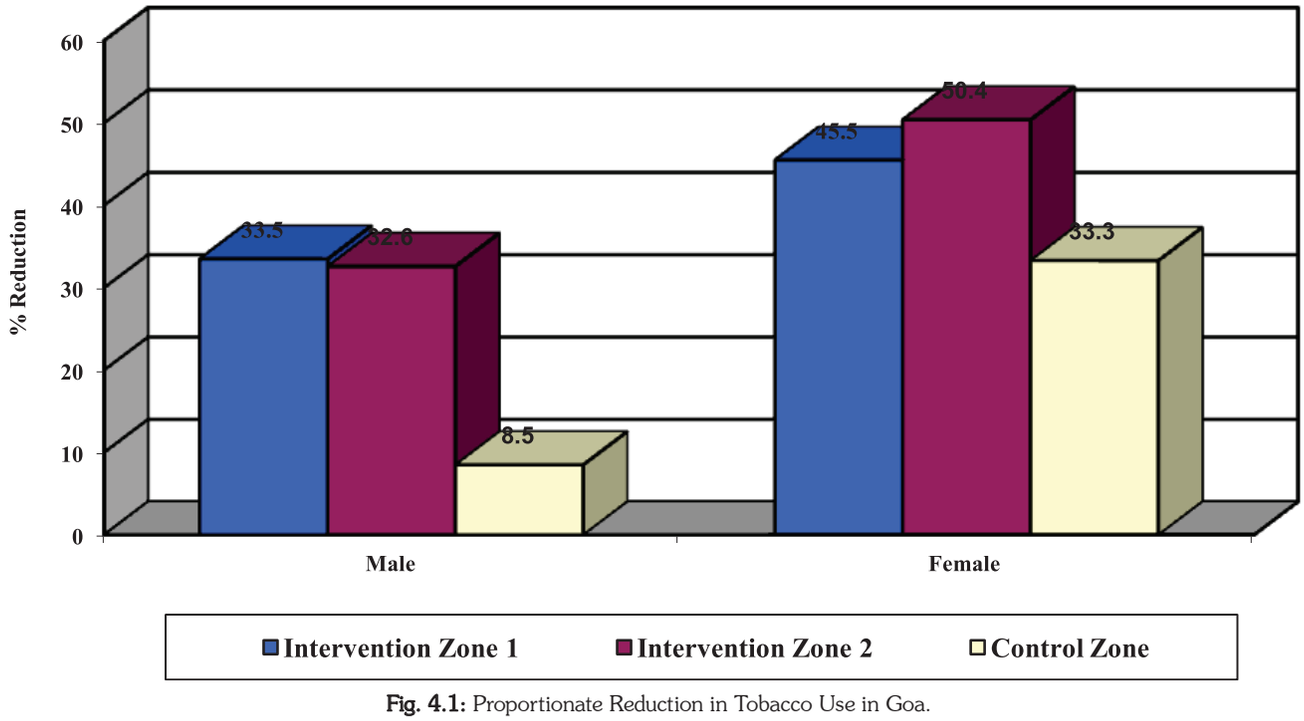

Fig. 4.1: Proportionate Reduction in Tobacco Use in Goa.

Intervention at Bangalore centre achieved a reduction of tobacco habit in experimental area, amounting to 5.7% in the males and 6.9% in the females. The control area I showed an increase of 3.8% among male and 7.8% among female, while in control area II, among men there was a 2.9% increase in habit and 4.6% decrease among females (Figure 4.2).

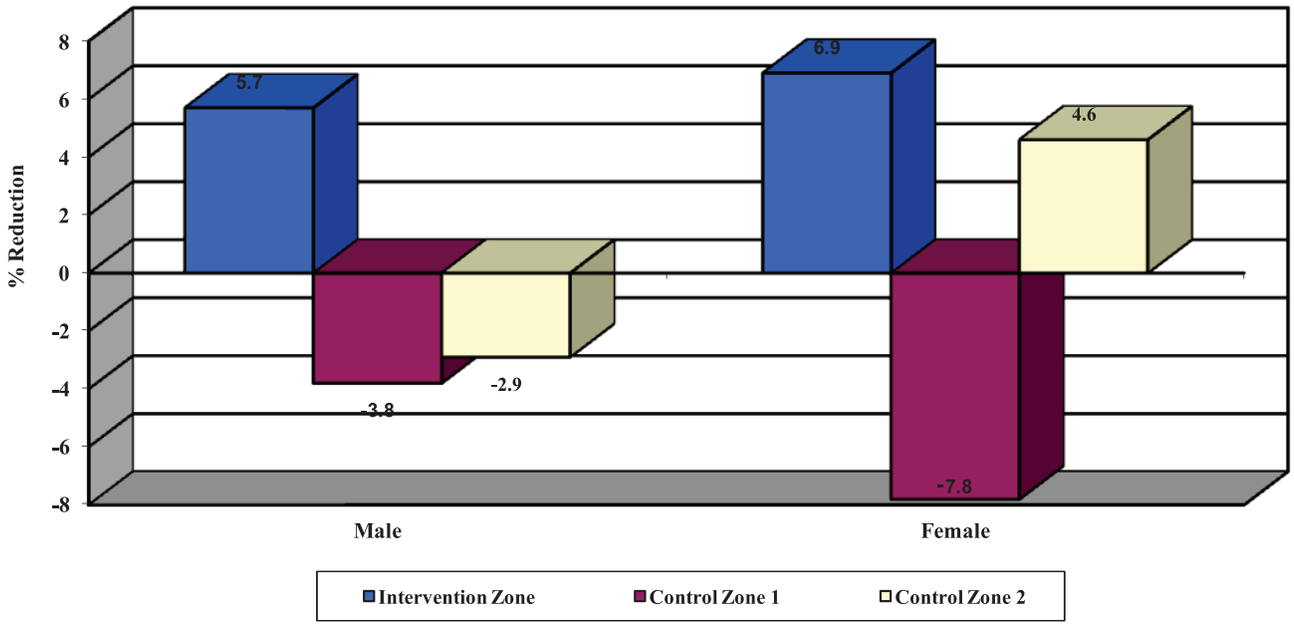

Fig. 4.2: Proportionate Reduction in Tobacco Use in Karnataka.

The intervention through community volunteers at Agra centre showed that 26.3% males and 10.5% females left tobacco and another 10.1% males and 4.3% females as likely quitters (6 months have not passed after leaving tobacco), after an intervention of about one year. The project at Trivandrum centre could not achieve optimum participation of health care workers. The nine workers, who worked on the project, referred 408 patients out of which 258 reported, giving a compliance of 63.2%. About 59% of these were found to have cancers (10) or pre-cancers. Of the 10 cancer cases five were in stage I & II. 29 old cases were also examined, out of which four recurrences were detected.

The study demonstrated the feasibility of undertaking anti-tobacco education by health services, if receptive. A major lesson learnt from the study was that local health services should be approached through the administrators at the central/regional levels. The Karnataka centre started the project by contacting the state health administrators at Bangalore, who in turn issued a circular for the concerned area to carry out the intervention as per the instructions by the investigators. The limited data from Kerala also suggested that if all the workers were receptive, the gains could have been expected. The Uttar Pradesh centre showed that community was willing to work for this purpose, if guided adequately.

The Goa centre results were unique showing that children could be powerful tool to bring about a social change in the community. This happened through careful planning for an organized plan supported under their curriculum. The schools did require some health education aids (like video players and screens/ TVs), which were provided to them. The cooperation provided by the health infrastructure was also extraordinary.

While the study showed the efficacy of simple as well as multiple health education aids, the study did not plan efficacy of individual health education strategies or packages. The study reiterated that well conducted educational activities add to the learning of individuals at any age, which actually changed the impression of the subject as an interventional activity and not under the research domain. The study also helped in learning and hypothesizing that health education aids should be aimed at desired change for the target community and the intervention should be considered as a package of activities relevant to the local area.

5 Information, Education & Communication

Radio DATE (Drug, Alcohol & Tobacco Education)

Background

The project Radio DATE was a collaborative effort of Indian Council of Medical Research (ICMR) and All India Radio (AIR). The acronym DATE stood for Drugs, Alcohol and Tobacco Education. The project was conceived and agreed when a team of high officials from AIR visited ICMR with the request for help for a small educational activity. At that time India had only Government controlled radio system. Since the officials belonged to the central set up, ICMR suggested conduct of a nationwide programme on education on tobacco, alcohol and drugs. The discussions also finalized that the first episode was aired from World Health Day of 1990 (7th April 1990), which was about 3 months away. ICMR agreed to provide the subject areas for different episodes along with the scientific contents for that purpose. AIR agreed to develop the episodes with the help of provided scientific contents and translate them to local languages. The suggestions of experts to feature in the programme were also provided by ICMR, who were contacted directly by AIR. The coordination for the broadcast of episodes was done by AIR, whereas ICMR helped in pre-testing and analysis of the data. The surveys to assess the reach and efficacy of the programme were carried out by ICMR.

Overall Objectives

To assess the effect of Radio as an instrument of social change in regard to drugs, alcohol and tobacco consumption in the community.

Specific Objectives

Developmental objectives

1. To design and develop a series of radio programmes aimed at generating awareness in the community on the holistic approach to health hazards of drugs, alcohol and tobacco and their management.
2. To inform and educate the community in promoting healthy life styles, which are impaired with the consumption of drugs, alcohol and tobacco.

Evaluation objectives

1. To assess the immediate effect of such radio programmes in a defined group of radio listeners (registered audience).
2. To assess the reach of the programme in general population.

Methodology

The radio programme was in the form of 30 weekly episodes of 20 minutes each. Ten episodes focused on tobacco, eight each on alcohol and drugs, and two episodes on legal aspects. The introductory and concluding episodes touched all the three themes. The episodes were broadcasted from 84 stations of all India Radio (out of 104 existing at that time) at prime time, simultaneously in sixteen languages.

The major content areas for different episodes were finalized by ICMR with the help of an expert panel, members of which also provided background scientific material to be provided to the team of AIR producers. The AIR developed the storyline combining the scientific contents and also featured experts. The prototype was developed in hindi and was sent to selected radio stations of all India Radio for translation in the concerned regional language, as per the specified guidelines. While developing regional language episodes, experts from the local area with ability to communicate in the regional language were invited. Thus, the contents and delivery modality was closely controlled by AIR, although each episode was finally translated in local language. The translated episodes were sent to all the radio stations requiring the concerned language episode. The broadcast was during a specified time with the exact time to be decided by the radio station but definitely between 8.00 A.M. and 9.00 A.M. on sundays, with a repeat broadcast during the week, generally in the evening. The name Radio DATE was used by all over the country, but some radio stations also coined and used names in local languages.

Evaluation of the reach and effect of the tobacco component of the programme was carried out through two community based surveys carried out after the broadcast of tobacco episodes (which was the first topic to be covered). These surveys were among randomly selected persons above 15 years of age in selected rural Goa and Karnataka, where no organized anti-tobacco programmes were being conducted. The control areas of an ICMR project on anti-tobacco community education were used for this survey. The intervention phase on the earlier project had just finished in that area and the only intervention that had happened in these area was through the project Radio DATE.

A call for sending posters was given to audience by AIR, during the last episode of the programme. These posters were screened by an expert group to select three best posters for each subject. The number of entries also helped AIR in assessing the reach of programme.

Observations

The ICMR surveys carried out immediately after the broadcast of tobacco episodes, showed that the potential listeners of radio comprised 80.4% of the population in Goa and 59.1% of the population in Karnataka. In Karnataka 31.6% of the potential listeners and in Goa 26.7% of the potential listeners, had heard at least one of the first eleven episodes (on tobacco). Education level was observed to be the determinant of reach in Goa; while education and occupation influenced the reach in Karnataka.

The mean number of episodes heard by the listeners was 2.6±1.46 in Goa and 2.57±1.13 in Karnataka. The factors associated with listening higher number of episodes included higher education, male sex, non-usage of tobacco and radio ownership in Goa; and, higher education, radio ownership and caste in Karnataka. Most of the listeners considered the programme to be very good or good, and felt that it would have effect on the tobacco users to quit their habit as well as on children to prevent the initiation of habit. About 4% tobacco users in Goa and about 6% users in Karnataka quit their habit after hearing

the programme (Figures 5.1 to 5.4). About 98% to 99% of the listeners expressed that such programmes should continue.

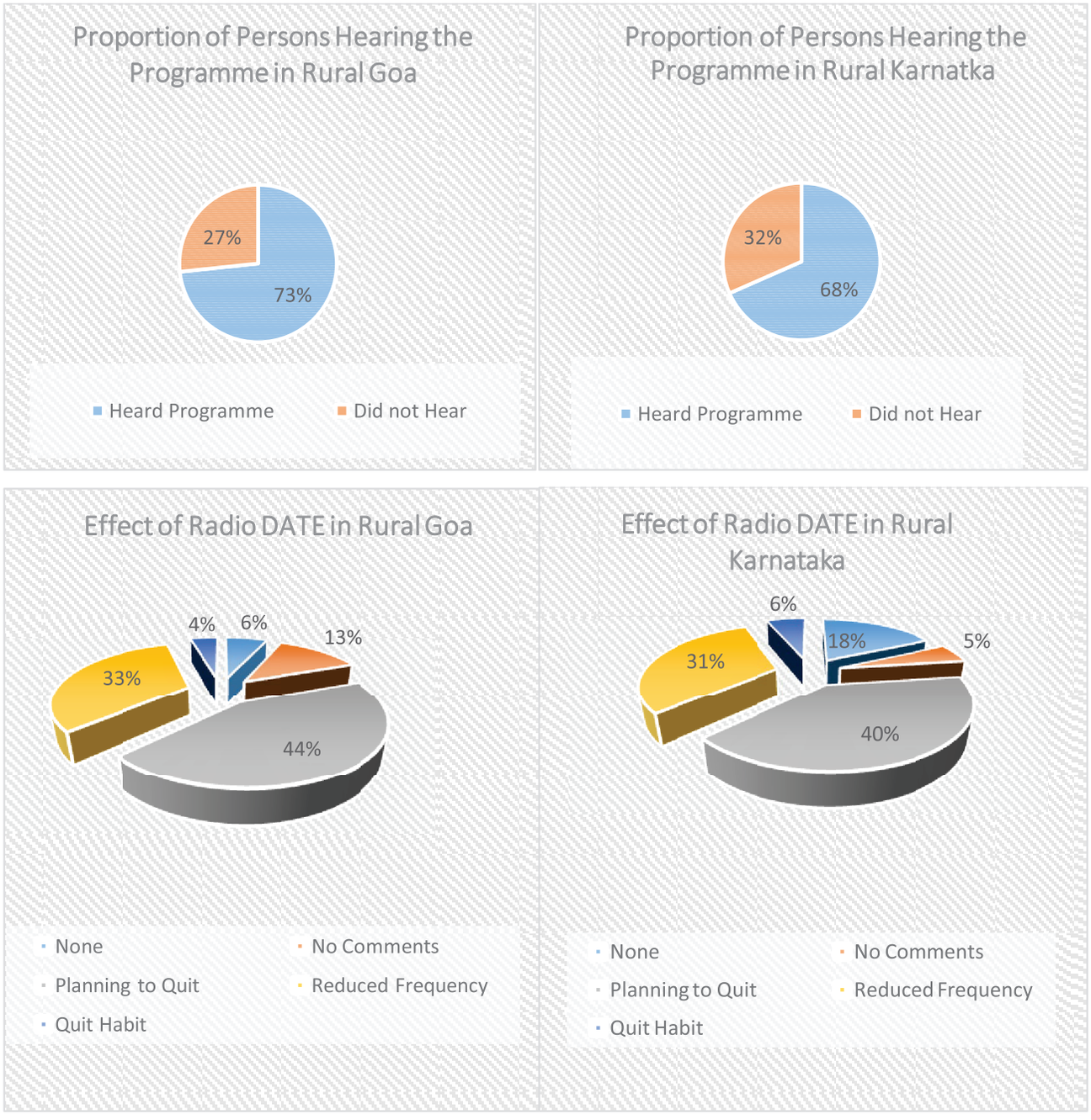

Fig. 5.1 to 5.4

Summary

All major tobacco control programmes have tended to use mass media, either as a major plank or as a mechanism to inform people about the intervention. Scientists generally favoured television over radio, believing that it can provide behavioural skills by actors or by programme participants. The radio at the time of carrying out the study, was considered to have a bigger reach in the Indian community (97% vs 15%) than television. The Indian radio network had capability of translating the programmes in all

17 official languages of India and the interest shown by the radio managers for the programme was exemplary. Thus, the study group considered that radio in India was expected to have the same advantages as reported for television. At the time of planning this project, there was only one scientific study in a small area of USA, which reported useful role of radio in reducing tobacco use in the community. This ICMR project was the largest project of its kind wherein the entire India was covered.

Quick planning and development of the episodes was the hallmark of the study. The broadcast started about 14 weeks after this mega project was conceived. The episodes had been prepared in about 4 months after conception of the project.

While the programme was on AIR, print media extensively reviewed it. These comments were encouraging and at times also provided suggestions on the contents for future episodes. Most of these suggestions had been incorporated and thus required no change in the episodes which had already been prepared. However, two additional episodes on legal aspects were prepared based on suggestions of mass media and internal discussions.

The project helped in generating interest on developing stories on the three chosen subjects (tobacco, alcohol & drugs) on their own. After the programme, the sole existing television channel at that time in India (Doordarshan), made a 20 minute film on the making of "Radio DATE", and televised it at prime time. One year after the project, ICMR made one and a half minute spot on tobacco and provided it to Doordarshan, which used it as a time filler, between the main programmes (at prime times as well as at other times). The film was run for more than 500 times (about 300 times during the first year itself) but ICMR did not have to pay for it. After Radio DATE, requests from print media for background material on tobacco also increased. The radio stations also prepared and aired programmes on their own. An evaluation of number of programmes and duration accorded to the subject of tobacco on Delhi station of All India Radio, showed that both the annual number of programmes and time to the subject increased after the programme Radio DATE, sustaining for the next two years and decreased slightly thereafter. All this publicity was achieved without any expenditure.

The programme also received appreciation from scientific community as well as politicians. The biggest political accolade was the appreciation from the Union Health Minister of India and the request that more such programmes should be developed. Audio cassettes prepared and distributed to all ICMR institutions for further duplication and distribution, as well as for use during their educational activities.

The cost of such a mega programme would have been massive or even prohibitive. The project was possible only because of the active participation of the radio with the scientific group of ICMR, highlighting the importance of both media and scientific managers. The broadcast was during the regular broadcast hours of AIR and was considered as an opportunity availed. Thus, the cost of broadcasting was not considered by AIR or ICMR. The additional expenditure for preparation of the programme was towards arranging the participation of experts, for travel funds for the team, and for consumables. The additional expenditure for the programme was Rs. 6,35,000 in 1990, which amounted to Rs. 0.58 per 100 listeners (US $ 0.03 per 100 listeners, at 1990 conversion rate). The cost per 100 population was Rs. 0.07 (or US $ 0.004).

The project also provided a rich experience on collaborating with media (both electronic and print media). Most media personnel would not have time and/or aptitude for extensive research or collection of information. While anti-tobacco groups wish for wide dissemination of information, the media also looks for material, which should be new (to them), non-repetitive, crisp & simple language, to be used by them as a base to the total story. Both scientists and media personnel are looking for gains from such stories, but the type of credits to be gained by the two groups are different. Thus, preparation of such stories is a mutually beneficial exercise. The interaction also highlighted the need for considering the aptitude of target group rather than considering mainly the sensitized group of audience. Thus, the active role of both media managers and scientific managers can result in execution of projects which in isolation may be an extremely difficult proposition.

6 Tobacco Related Cancers

Oral Cancer

Oral cancer accounts for around 30% of all cancers in India and is the most common cancer among Indian men. India has one third of oral cancer cases in the world . As per the Globocan, 2012 data, there have been 77,003 new cases and 52,067 deaths due to oral cancer in India. In general, more men suffer and die from oral cancer than women.

Risk Factors for Oral Cancer

- **Tobacco consumption**

All forms of tobacco, including cigarettes, beedi, pipes, cigars, and chewing (smokeless) tobacco, can cause oral cancer. Keeping tobacco quid inside mouth may lead to cancer of cheek, gums and inner cavity of mouth. Paan and betel nut are also causal agents.

- **Alcohol consumption**

Alcohol increases the risk of oral cancer. The risk is about twice as high in people who have 3 to 4 alcoholic drinks per day compared to those who don't drink alcohol. The risk of oral cancer is even higher in people who use both alcohol and tobacco.

- **Sharp teeth or ill fitting dentures**

Diet: Lack of proper nutrition and diet low in fruits and vegetables: linked with an increased risk of cancers of the oral cavity and oropharynx.

- **Human Papillomavirus (HPV)**

Infection with certain high risk HPV types increases the risk of oral cancer, especially in younger people.

- **Weak immune system**

People with weakened immunity are more prone to suffer from oral cancers. Certain immune deficiency diseases at birth, radiotherapy and chemotherapy, medicines given to organ transplant recipients and the acquired immunodeficiency syndrome (AIDS) may be responsible for weakened immune system.

- **Exposure to sun's ultra violet rays may cause lip cancer.**

Oral Pre-Cancers: Use of Pan-Masala

Study on Association of Oral Pre-cancers with Use of Plain Pan Masala (Extramural)

In addition to tobacco use (both smoking as well as smokeless forms), plain pan masala use is of public health importance to India. While studies are available on effect of smokeless tobacco on oral cavity, the effect of plain pan masala and areca nut are not well proven. It is also known that oral cancer is often preceded by pre-cancerous conditions of the oral cavity. Some precancerous conditions like oral submucous fibrosis have increased in recent times, which coincide with the increase in the habit of use of gutka or pan masala (with or without tobacco). Areca nut is used in India as a component of betel quid (with or without tobacco), pan masala (with or without tobacco), or gutka. Areca nut is also used as such (plain or scented supari). Any confidence of pan masala being carcinogenic is derived mainly from IARC's recommendation about betel quid being carcinogenic. These studies have not tried to differentiate the different forms of areca nut usage. Moreover, epidemiological studies on carcinogenicity of pan masala mixture are not available. The substance has however, been shown to be mutagenic. Thus, an epidemiologic study is needed to fill the gap in knowledge on carcinogenicity of plain pan masala.

The study objectives were to conduct a survey to obtain the (i) prevalence of use of plain pan masala; (ii) prevalence of various oral precancerous lesions among users of plain pan masala, as well as among and non-users of pan masala / tobacco/ areca nut; and (iii) to calculate the odds ratio of development of oral pre-cancerous lesions due to use of plain pan masala chewing.

Major limitation for a case control study on the subject was the non-availability of sufficient number of oral cancer or pre-cancer cases with history of use of plain pan masala alone. Therefore, the study is in the form of a survey to be carried out among 425,000 persons above 15 years of age to provide about 1,700 persons using plain pan masala. The study is being carried out in population residing within the area encircled by the ring road of Lucknow city, and is expected to provide the desired sample. The data on use of plain pan masala, tobacco and areca nut is being collected through personal interviews of all persons by trained social workers after a house-to-house visit. The examination of the oral cavity was carried out simultaneously by trained doctors/ dental surgeons. Regular supervisory visits were made to address any field level problem. The persons with oral pre-cancerous conditions were advised appropriate treatment.

The study pre-tested and finalized a questionnaire, and procured the necessary material for survey and examination of the oral cavity.

In summary, the study tested the feasibility of using the ICMR questionnaire on collecting detailed information on tobacco habits.

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7 Extramural Research

North East India- Understanding the Role of Tobacco

North eastern states of the country have reported high incidence of cancer of many anatomical sites and most of them are associated with use of tobacco. The RMRC Dibrugarh carried out this study in the six population based cancer registry areas of the NE region with a case control epidemiologic design in collaboration with 6 (six) PBCRs of northeast; NCRP Bangalore; NIOP Delhi, ICPO Delhi and NIOH Ahmedabad. A total of 2027 newly histologically confirmed 4(four) tobacco related cancer (TRC) sites i.e oral cavity, oesophagus, lung and stomach, were recruited in the study alongwith equal number of controls with age, sex and place of residence matched from 6 (six) population based cancer registries viz. Dibrugarh, Guwahati, Silchar, Imphal, Aizawl and, Gangtok. Of these total cases,735 were oral cavity (36.3%), 529 were oesophageal (26.1%), 333 were stomach (16.4%) and 430 were lung (21.2%) cancer cases.The summaries of findings are as follows:

(i) Oral Cavity Cancer:

Most cases occur in the age group of 31 to 80 years with male preponderance. Illiterate people were more among oral cancer patients. Smokeless tobacco chewers were more at risk to develop oral cancer. particularly chewers of combined chewing item of betel nut and tobacco were at more risk. Early age chewers with a long duration of chewing habits are more prone to develop oral cancer. Retention of chewing quid for long duration and keeping during sleep in mouth was found to be more risky behavior for oral cancer. Smokers who also chew tobacco are at higher risk.

(ii) Oesophageal Cancer:

Cases with male preponderance occur in the age group of 31 to 80 years. Illiterate people are more among oesophageal cancer patients hailing from rural areas. Chewers of betel nut with tobacco had clear dose response effect with the development of oesophageal cancer. Consumption of locally prepared food item like “Kalakhar” (particularly in Assam) had shown significant risk of development of oesophageal cancer.

(iii) Stomach Cancer:

Most cases occur in the age group of 31 to 70 years with male preponderance. Uses of local smoking items like *meizial* or *zozial* etc are at higher risk to develop stomach cancer. The consumption of locally prepared alcohol like *rakzu*, *chang*, *sekmai* etc. are at more risk to develop stomach cancer. The frequent eater of *smoked salted fish* and *meat* are at higher risk for stomach cancer.

(iv) Lung Cancer:

The occurrence of lung cancer among bidi smokers was significantly higher than non-smokers. It was also indicated that smokers with drinking habit and drinker with chewing habit were at higher risk to develop lung cancer than persons with no habits. The risk to develop lung cancer among bio-mass fuel users were more than non-biomass fuel users. The use of fire wood and animal dung was found to be exterminating risk factors.

Cancer in North East India-Understanding the Role of Pesticides

This study was envisaged to investigate the link between pesticide use and the cancers of two anatomical sites in North East and genetic variation including polymorphism/mutations. The study was carried out in the six population based cancer registry areas of the north-east with a case control epidemiologic design in collaboration with 6 (six) PBCRs of northeast; NCRP, Bangalore; IOP, Delhi, ICPO, Delhi and NIOH Ahmedabad. A total of 842 newly diagnosed and histologically confirmed for 2 (two) pesticide related cancer sites breast and non-hodgkin lymphoma were recruited. Of the total cases, 585 were breast cancer and 257 were NHL cancer cases. The summaries of the epidemiological study are as:

Breast Cancer

Most of the female cases are in the age group 31 to 60 years of age and most of them are female farm workers exposed to pesticide showed association with breast cancer.

NHL Cancer

Most of the male cases are in the age group 51 to 60 years of age. Farm workers exposed to pesticides are at higher risk of developing NHL cancer.

Genetic Polymorphism in Drug Metabolizing Enzymes and Oral Cancer & Pre-Cancers

Squamous cell carcinoma of head and neck (HNSCC) is an important disease for India, contributing to significant morbidity and mortality. While the causal association is well known, the mechanism(s) of pathogenesis is still not very clear, more so with regard to the use of smokeless tobacco. Existing studies on CYP1A1 and GSTM1 adopted case-control approach and the results from these studies were equivocal and not able to produce confidence on the role of these genetic variations.

The study focused on determining the prevalence of usage of tobacco and chewing products and oral precancerous lesions in Delhi through a population based survey; to determine the frequency of polymorphism of CYP1A1 and GSTM1, in patients with precancerous lesions identified in the above survey and in healthy controls; follow up of patients with precancerous lesions and healthy controls identified in the survey in a prospective cohort study, to assess the relative risk of conversion to cancer or progression of oral lesions; and to determine the influence of at-risk genotypes on progression of precancerous lesions.

Data on tobacco usage and existence of oral lesions were collected from 71,022 individuals using cluster and selective sampling of low and middle income areas of southern Delhi. Any form of tobacco use (ever) was found in 15789 (22.2%) of the population being substantially higher in males (37%) than in females (6.6%). Tobacco smoking was observed more frequently in males (23%) than consumption of the smokeless form of tobacco (18.4%). However in females the frequency of usage of smoking (3.2%) and smokeless (3.5%) forms of tobacco was similar. Bidi was observed to be the most popular form of tobacco smoking accounting for 16.3% in males and 2.8% in females. Among the smokeless forms of tobacco, gutkha (8.7%) and khaini (8.1%) were observed to be more commonly used by males. among females,

pan with tobacco (1.3%) followed by khaini (1.1%) and gutkha (0.8%) were popular form of smokeless tobacco consumed. The proportion of tobacco users was small among persons under the age of 20 years (587/21001, 2.8%). There was a gradual increase in prevalence of tobacco use with age. Of the total population surveyed 2833 (4.0%) were alcohol consumers, of which 70.4% also used tobacco products. The habit of drinking alcohol increased with age predominantly among 30 to 69 years age group.

A total of 3.4% (2389/71022) prevalence of precancerous lesions was observed in the total surveyed population. There were considerable differences between tobacco consumption habits of cases and controls. Most of the cases (92.6%) consumed tobacco in one or another form as compared to 55.9% controls. Genotype analysis showed no significant differences in the allele frequency for GSTM1 null and distribution of CYP1A1 Ile/Val genotype among cases and controls suggesting no significant association with oral precancerous lesions or progression of these lesions.

The longitudinal follow up of patients with oral precancerous lesions and controls was a unique aspect of the study. Of the 1629 patients available for follow up, 227 patients showed progression of the lesions during the study period of 4 years. The progression in lesions was observed most commonly in subjects harboring erythroplakia (20.6%), followed by lichen planus (18.8%). Motivating people to quit tobacco by increasing general awareness about the harmful effects of tobacco by counselling showed significant effect on the progression of the lesions. GSTM1 and CYP1A1 Ile/Val genotype were not significantly associated with risk modification, or alteration alone or in the development and progression of oral lesions in this study cohort.

The study is a successful example of collaboration of principles of epidemiology and laboratory aspects on oral carcinogenesis, which is a priority area for India. Such multi-disciplinary projects can provide important information on the subject.

The study also helped in validating the tobacco use questionnaire developed by ICMR. This modified questionnaire is currently being used in another task force project, and would be available to the scientific world.

Molecular Cytogenetic Studies in Oral Cancers

Oral cancers are leading cancers in Indian men and are closely linked to the habit of chewing tobacco. Tobacco specific carcinogens are known to interact with DNA causing DNA damage, which, may eventually lead to the development of cancers. Genomic damage in target tissues may lead to chromosomal alterations, which have been found to be a driving force in several human malignancies. Oral cancers develop and progress through the accumulation of genetic and epigenetic changes, which ultimately results in gross genomic instability. The chromosomal alterations or genetic imbalances can serve as a marker of genomic instability and damage. comparative genomic hybridization (CGH) analysis is a direct method for comparing genetic imbalances in DNA from tumor and normal cells, which helps in rapid screening of tumor genomes. At the time of initiation of study (early 2000s) there was limited information about the presence of definite genetic alterations in oral cancers and their relationship with the biological behaviour.

The study aimed at identification of chromosomal markers that may be specific to oral cancers in India at primary tumour site and metastatic lymph node using comparative genomic hybridization and related molecular cytogenetic techniques.

Study identified the genetic alterations in 97 primary oral cancers and investigated their relation with different clinicopathological parameters such as site, size, stage, nodal status and differentiation. All oral

cancer samples were first assessed for proportion of malignant cell in the biopsy tissue/ surgically resected samples. Only those samples with malignant cell proportion of 60% or more were considered for CGH.

The average gains were higher in moderately and poorly as compared to the well-differentiated oral tumors. A nonrandom pattern of chromosomal alterations was observed with frequent gains (25%) on 8q, 9q, 11q11-13, 7p, 20q, 3q and 20p and frequent losses (25%) on 3p, 8p and 18q chromosomes. Gain of 8q was detected as the most frequent alteration and was considered to play an important role in the development of diseases. Chromosomal alterations showed statistically significant associations with both, differentiation and nodal status. Gains of 11q11-13 and 20p chromosomes correlated with moderately and poorly differentiated tumors. Gains of 7p and 19p chromosomes and, loss of 8p and 18q chromosomes were associated with the lymph node positive tumors. Multivariate analysis suggested that specific interactions of 7p, 8p, and 19p chromosomes might be required for nodal metastasis. Thus, CGH analysis revealed chromosomal alterations associated with differentiation and nodal status, which are important prognostic evaluators of oral cancer. These alterations may serve as potential biomarkers to complement histopathological analysis.

Analysis of the T cell Receptor Repertoire (Vβ, Vγ and V) and Immune Dysfunction in Patients with Oral Cancer

Immunosuppresion appears to be more frequent and more profound in patients with Head and neck cancer than in patients with malignancies involving other sites. Decreased or lost expression of signal transducing molecules could be another mechanism underlying functional defects in patient's T cells. Indian studies in early 2000s had shown that these patients exhibit low lymphocyte proliferative responses, decreased intracellular calcium release and altered cytokine (Th1/Th2) profiles when stimulated with Phytohaemoagglutinin (PHA), Phorbol myristyl acetate (PMA) +Ionomycin and anti CD3 MAb. As the stage of the disease progressed further from stage I to stage IV, a marked decrease in the lymphocyte responses was observed.

The project focused on analyzing T cell receptor repertoire (TCR, Vβ, Vγ and V as well as immunophenotypes αβ and γ) and clonality in lymphocytes (by heteroduplex analysis) present in peripheral blood, tumor compartment and in lymph nodes of patients with cancer of buccal mucosa. other parameters studied in the same materials included, determination of TCR diversity in junctional regions of TCR genes; expression of TCR signaling molecules CD3-ζ chain, lck and ZAP-70 in T cell subsets (αβ and γ) using dual color flow cytometry.

The TCR Vβ, Vγ and V repertoire was analyzed in peripheral blood (PBL), tumor (TIL) and lymph node (LNL) compartment of oral cancer (OC) patients. A heterogenous and skewed TCR repertoire was observed in PBL, TIL and LIL of oral cancer patients. The CD3 ζ chain defect was narrowed down to specific clonal Vβ subsets in OC PBL. CD3 ζ chain was restored back in subsets of T cells by stimulating lymphocytes of OC patients by anti TCR Vβ subset specific Mab and anti CD28 MAb.

Studies further demonstrated that a decreased CD3 ζ chain expression translates into inefficient T cell signaling resulting in a partial or complete loss of T cell function. The expression of CD3 ζ chain mRNA in peripheral blood lymphocytes (PBL) remained unaltered indicating a posttranslational alteration. A decrease in the expression of phosphorylated form of CD3 ζ chain was observed which correlated with the tumor stage. Increased ubiquitination of CD3 ζ chain was also observed in patients with oral cancer.

In order to characterize the factor released by oral tumor cells that cause CD3 ζ chain degradation, the

tumor supernatant was analyzed in a sandwich ELISA for the presence of TNF (Tumour necrosis factor alpha). Results indicated that TNF might play a role in the degradation of CD3 ζ chain.

In order to establish CD3 ζ chain as prognostic marker, a retrospective analysis of CD3 ζ chain expression at diagnosis was correlated with patients having recurrence of the disease. It was noted that those patients who had a recurrence of the disease showed low expression of CD3 ζ chain at the time of diagnosis. It was also observed that the expression of CD3 ζ chain was restored in patients after surgery followed by radiotherapy as compared to surgery alone.

The study suggested the importance of CD3 ζ chain as a biomarker for prognosis in oral cancer patients. The results indicated that this biomarker should be further studied for specific circumstances like use of specific tobacco products, other polymorphisms, presence and persistence of pre-cancerous lesions, etc.

Oral Cancer in North East India

India has the highest rate of oral cancer in the world. It comprises 30-40% of total malignancies in India and ranks as the leading cancer site in males and the third leading site in females. A retrospective study (from 1993 to 2004) on the prevalence of head and neck cancers in NE India showed significantly high prevalence 54.48%, affecting males more than females in the age group of 40-69 years. Moreover a very high AAR of carcinoma of the tonsil has been reported from at least five districts in Assam State with Kamrup district recording the second highest AAR in India. Approximately 30% of oral cancers are attributed to betel/tobacco chewing alone and an additional 50% to the combined habits of chewing and smoking. Ninety-two percent of oral squamous cell carcinoma (OSCC) in men and 61% of OSCC in women are attributable to tobacco usage. The combined use of peculiar betel/tobacco quid chewing habits, widely prevalent in this region, increases the relative risk of developing oral cancer. The pathogenesis and molecular mechanism implicated in smokeless tobacco consumption is unknown. Currently there are no genetic studies available to explain the alarmingly high prevalence of oral cancers from North east region of India.

The quantitative absorption, distribution, metabolism, and excretion of carcinogenic tobacco constituents depend on the activity and efficiency of metabolic and enzymatic detoxification pathways. The enzymatic detoxification process is mainly divided into three phases. Phase I enzymes involved in activation of toxic compounds predominantly by oxidation into more reactive intermediates that are neutralized and conjugated by phase II family of enzymes such as glutathione-S-transferase (GST), N-acetyltransferase (NAT). The resultant water-soluble and less-toxic conjugated product can easily be eliminated from the cell by phase III transport mechanisms for the elimination of glutathione conjugates. The detoxification efficiency of GST enzymes is determined by the presence and nature of the isoenzymes coded by GSTT1, GSTM1, and GSTP1 genes. The prevalence of tobacco and betel quid chewing habits as well as the occurrence of tobacco-associated cancers is high in the northeast (NE) region of India. However, the prevalence of polymorphism in GST genes in tobacco-associated cancer patients from this region is not well known.

Frequencies for GST enzyme genes (GSTT1, GSTM1, and GSTP1) polymorphism was analyzed in oral cancer cases and age and sex matched controls from the same ethnic group. The conditional logistic regression analysis revealed that the risk of developing oral cancer significantly increased in tobacco chewers (OR =2.44, 95% CI: 1.47–4.05, p=0.001), tobacco smokers (OR=1.72, 95% CI: 1.08–2.73, p=0.02), and betel quid chewers (OR=2.20, 95% CI: 1.29–3.76, p=0.004). When adjusted for other

variables under consideration, no significant association was found for GSTM1 and GSTT1 null genotype independently or in combination with oral cancer risk. although no significant independent association of oral cancer with null genotypes of GSTT1, GSTM1, and the variant alleles of GSTP1 was found, individuals with both GSTM1 null genotype and variant alleles of GSTP1 were found to have marginal increased risk for developing oral cancer (OR=1.84, 95% CI: 0.91–3.72, p=0.08). Study of polymorphisms in three genes [*CYP1A1* (*Msp1* and *Nco1*), *NAT2* and *NQO1*] in oral cancer cases and healthy controls from this region showed significantly higher frequency of both heterozygous Pro/Ser (AOR=1.64, 95% CI=1.04-2.58) as well as homozygous Ser/Ser (AOR=1.81, 95% CI=0.98-3.32) *NQO1* genotypes in cases than controls suggesting polymorphic variant genotypes of NQO1 are significant risk for oral cancer with homozygous variants genotypes showing a higher risk compared to heterozygous genotypes in univariate analysis. Gene-environment interaction analysis however showed that the variant genotypes of *NQO1* did not interact with tobacco consumption habits. Although variant genotypes of *NQO1* may play an important role in the genetic susceptibility to oral cancer, its pathway appears to be unrelated to the detoxification mechanism of tobacco constituents. No significant association was found between polymorphisms of *CYP1A1* (*Msp1 and Nco1*) and *NAT2* genes with oral cancer risk.

The human TP53 tumor suppressor gene plays a central role in many cellular processes, regulating cell growth, DNA maintenance and apoptosis. It is an important component of DNA repair machinery in response to DNA damage induced by radiation or adduct formation. This might explain the occurrence of the *P53* gene mutation and alteration in about 50% of all cancers, particularly tobacco related cancers.

Studies have shown a relationship between tobacco smoke exposures, carcinogen-DNA adduct formation, tumor specific mutation of TP53 gene and cancer risk.

Numerous polymorphism in the wild type *P53* have been reported both in coding and non-coding regions. Out of the five polymorphisms described in the coding region, polymorphisms in codon 47 and 72 in exon 4 are functionally well characterized. More common of the two, codon 72 polymorphism is a single base substitution of cytosine for guanine, leading to arginine (A72) being replaced by proline (P72) that has been reported to be associated with the risk of several cancers. Studies on codon 72 polymorphism have revealed striking ethnic differences in frequency of *P53* variant allele that varies with latitude, increasing in a linear trend as populations near the equator. Thus ethnicity might be related to allelic distribution of the gene and its determinacy in disease involvement; however some studies do refute the ethnicity-risk confounding relationship.

A case control study had been undertaken in oral cancer and normal age matched controls collected from Dr. B. Barooah cancer Institute, Guwahati, civil Hospital, Aizawl, and Sir T.N.M. Hospital, Gangtok in three north east states to investigate the role of p53 codon 72 polymorphism and its interaction with tobacco, betel quid and alcohol. Tobacco chewing was the strongest risk factor for oral cancer with a 3 fold increased risk (OR2= 3.05, 95% CI=1.79-5.20; p<0.001). Both tobacco smoking (OR2=1.68, 95% CI=1.00-2.81;p=0.04) and betel quid chewing (OR2=1.85, 95% CI=1.02-3.33;p=0.04) also increased risk for oral cancer. A strong association of risk of oral cancer was seen in patients carrying Arg/Arg and Arg/Pro genotypes (OR2= 8.62 95% CI=2.19-33.93; p=0.002 and OR2=5.22 95% CI=1.38-19.75; p=0.01 respectively) irrespective of smoking habit. Although tobacco and betel quid chewing emerged as a risk factor yet no interaction of *p53* genotypes with the habit showed statistical significance.

Curcumin Modulates Cellular AP-1, NF-kB and HPV 16 E6 Protein in Oral Cancer.

This study, performed on HPV 16-positive oral cancer cell line 93VU147T, demonstrated the beneficial effects of curcumin. curcumin was not only a potent inhibitor of the activity of transcription factors AP-1 and NF-kB but it also suppressed transcription of HPV16 E6 oncogene.

This study suggested a therapeutic potential of curcumin in high-risk HPV-infected oral cancers.

Differential Expression and Activation of NF-kB Family of Proteins during Oral Carcinogenesis: Role of High Risk HPV Infection

Human papilloma virus (HPV) has been shown to be associated with oral carcinogenesis in addition to other known risk factors. Reciprocally, cellular transcription factors such as NF-kB and AP-1 are known to modulate expression of viral and other genes. However, there was a lack of data on NF-kB expression in relation to HPV infection in oral cancer.

This study was aimed at evaluating the DNA binding activity and expression pattern of NF-kB family of proteins in different stages of oral cancer and its correlation with HPV infection. A total of 110 fresh tissue biopsies were included comprising of 10 controls, 34 precancer and 66 untreated oral cancer lesions. Diagnosis of HPV was done by both consensus and type-specific PCR. Electrophoretic mobility shift assays, western blots and immunohistochemical analysis were performed to assess the binding activity and expression pattern of NF-kappaB family of proteins (p50, p65, p52, c-Rel, RelB and Bcl-3) in oral tissue biopsies. Of the oral cancer biopsies, 27% showed the presence of exclusive high-risk HPV type 16. A high constitutive activation of NF-kappaB with concomitant upregulated expression of all the NF-kappaB members in oral cancer tissues was observed. Expression of NF-kappaB components gradually increased as the severity of lesion increased from precancer to invasive cancer. NF-kappaB p50 was found to be the major DNA binding component, which is indicative of homodimerization of p50 subunits. Interestingly, in HPV16 infected oral cancers although p50 showed high binding activity, p65 also showed a partial involvement as evidenced in supershift assay. Both by western blotting and immunohistochemistry, a differential overexpression and nuclear localization of p50, p65 and partially of Bcl-3 were observed in HPV16 positive oral cancer patients that also showed an over-expression of p21

This study demonstrated a constitutive activation and differential expression of NF-kappaB proteins, which change as a function of severity of oral lesions during development of oral cancer. It was hypothesized that the involvement of p65 in HPV infected oral cancer may be linked to improved differentiation and better prognosis of the disease when treated.

Comparative Study between HCII Test and PCR Based Assay for Detection of HPV DNA in Oral Submucous Fibrosis and Oral Squamous Cell Carcinoma

Oral malignancy is a major global health problem. Besides the main risk factors of tobacco, smoking and alcohol, infection by human papillomavirus (HPV) and genetic alterations are likely to play an important role in these lesions. The purpose of this study was to compare the efficacy of HC-II assay and PCR for the detection of specific HPV type (HPV 16 E6) in OSMF and OSCC cases as well as find out the prevalence of the high risk HPV (HR-HPV) in these lesions.

Four hundred and thirty patients of the potentially malignant and malignant oral lesions were taken, of which 208 cases were oral submucous fibrosis (OSMF) and 222 cases were oral squamous cell carcinoma (OSCC). The HC-II assay and PCR were used for the detection of HR-HPV DNA.

The overall prevalence of HR-HPV 16 E6 DNA positivity was nearly 26% by PCR and 27.4% by the HC-II assay in case of potentially malignant disorder of the oral lesions such as OSMF. However, in case of malignant oral lesions such as OSCC, 32.4% HPV 16 E6 positive by PCR and 31.4% by the HC-II assay. In case of OSMF, the two test gave concordant result for 42 positive samples and 154 negative samples, with an overall level of agreement of 85.4% (Cohen's kappa = 66.83%, 95% CI 0.553-0.783). The sensitivity and specificity of the test were 73.7% and 92.05% ($p < 0.00$). In case of OSCC, the two test gave concordant result for 61 positive samples and 152 negative samples, with an overall level of agreement of 88.3% (Cohen's kappa = 79.29, 95% CI 0.769-0.939) and the sensitivity and specificity of the test were 87.14% and 92.76% ($p < 0.00$).

This study concluded that slight difference was found between the positivity rate of HR-HPV infection detected by the HC-II and PCR assay in OSMF and OSCC cases and the HC- II assay seemed to have better sensitivity in case of OSCC.

Functional Polymorphism of MMP-1 Promoter in Potentially Malignant and Frankly Malignant Head and Neck Lesions

Matrix metalloproteinases (MMP) are a family of zinc-dependent proteases that degrade the entire component of the extracellular matrix. This study explored the association of the MMP1 gene promoter (-1607 1G/2G) polymorphisms in oral submucous fibrosis (OSMF) and head and neck squamous cell carcinoma (HNSCC) in an Indian population. The MMP1 single-nucleotide polymorphism (SNP) was genotyped by polymerase chain reaction-restriction fragment length polymorphism analysis in 412 patients with OSMF, 422 with HNSCC and 426 controls. Results showed that the frequency of 1G/2G or 2G/2G promoter genotypes having the 2G allele was associated with higher enzymatic activity and significantly increased in OSMF ($p<0.001$) and HNSCC cases ($p<0.00$). In this study, results concluded that SNPs in the MMP1 promoter region may be associated with susceptibility to OSMF as well as HNSCC in an Indian population and addiction habits such as areca nut chewing and alcohol abuse may enhance the expression of the 2G allele of MMP1 genes in OSMF and HNSCC cases.

Synergistic Effect of Stromelysin-1 (MMP-3) Promoter Polymorphism in Oral Submucous Fibrosis and Head and Neck Lesions

Matrix metalloproteinases (MMPs) are enzymes that degrade all the components of extra cellular matrix and collagen. Various types of MMPs are known to be expressed and activated in patients with oral submucous fibrosis (OSMF) as well as head and neck squamous cell carcinoma (HNSCC). The purpose of this study was to assess the association of the single nucleotide polymorphism (SNP) adenosine insertion/deletion polymorphism (-1171 5A->6A) in the MMP-3 promoter region in these lesions.

MMP-3 SNP was genotyped by polymerase chain reaction-restriction fragment polymorphism (PCR-RFLP) analysis in a case control study consisting of 362 participants; 101 cases of OSMF, 135 of HNSCC and 126 controls, compared for age, sex and habits. ROC distribution was plotted to assess the contributions of genetic variation in MMP-3 genotypes with relation to age.

Analysis of MMP 3 (-1171 5A->6A) polymorphism revealed the frequency of 5A allele in OSMF, HNSCC and controls to be 0.15, 0.13 and 0.07, respectively. A significant difference was found in 5A genotype frequency between OSMF (5A genotype frequency = 0.15, $p = 0.01$, OR = 2.26, 95% CI = 1.22-4.20) and in controls (5A genotype frequency 0.07) as well as HNSCC (5A genotype frequency 0.13, $p = 0.03$, 95%CI = 1.06-3.51) and controls (5A genotype frequency = 0.07) In this study, 5A genotype had greater than two fold risk for developing OSMF (OR = 2.26) and nearly the same in case of HNSCC (OR

= 1.94) as compared to controls. In patients with OSMF as well as HNSCC, the ROC analysis between the MMP-3 genotype and age, 6A/6A allele was found to be significant in patients both over and under 45 years of age; while the 5A/5A carrier alleles showed an association only in patients less than 45 years of age.

This study concluded that the expression of MMP-3 genotype associated with the 5A alleles may have an important role in the susceptibility of the patients to develop OSMF and HNSCC.

Study of Genetic and Molecular Epidemiology of Oral Cancer in 2 States (Assam & Meghalaya) of North Eastern Region of India

The study included a total of 343 study subjects (Case: 171, Control 172). Biopsy was the predominant (82%) mode of diagnosis of the cases. Major cancer sites were gum (39%) followed by buccal mucosa of cheek (31%). Major clinical presentation of the cases were ulceration in the mouth (39%) followed by swelling (19%). The cases from illiterate and lower income group from rural areas were found to be more prone to develop oral cancer. Betel nut chewer has synergistic effect on oral cancer. Among the genotypes studied GSTM1 null genotype and MSP1 mutant genotype of CYP1A1 gene are independent risk factors of oral cancer. Risk of oral cancer in subject with GSTM1 null genotype is enhanced by habit of tobacco chewing and smoking. Risk of oral cancer in subjects with MSP1 mutant genotype is increased by GSTT1 null genotype.

Risk Factors of Lung Cancer in Manipur and Mizoram, India: A Case-Control Study

The incidence of lung cancer is very high in the state of Manipur and Mizoram in comparison to the other parts of the country. Particularly, incidence among women superseded the counterpart in the state of Mizoram. A case-control study has been initiated to find out the epidemiological risk factors in the development of primary lung cancer in Manipur & Mizoram, India and estimation of lung cancer risk imposed by inheritance of polymorphic alleles of GSTM1 and CYP1A1 genes by comparing allele frequencies among lung cancer patients and appropriate control population. This study revealing significantly higher risk for environmental exposure like users of Meiziol, a locally made cigarette (OR=2.25; p=0.006) as compared to general cigarette users (OR=1.68; p=0.171) among women in Mizoram. Current users of Tuibur, a liquid tobacco (OR=1.59; p=0.039) was also significantly associated with increased risk for lung cancer among women in Mizoram. Traditional dietary practices in Mizoram such as consumption of smoked fish (OR=2.57; p=0.006), smoked meat (OR=3.03; p=0.001) and soda (OR=7.96; p<0.001) were more prone to develop lung cancer among women in Mizoram. Exposure of cooking oil fumes (OR=2.56; p<0.003), wood as heating source for cooking (OR=1.50; p=0.044), kitchen inside living room (OR=1.79; p=0.001), improper ventilated house (OR=2.10; p=0.003) were also significantly prone to develop lung cancer among women in Mizoram. GSTM1 null genotype and CYP1A1 homozygous mutant were significantly associated with the increase risk of lung cancer in both Manipur (GSTM1 OR=2.59; p<0.001 & CYP1A1 OR=4.12; p<0.001) and Mizoram (GSTM1 OR=2.95; p<0.001 & CYP1A1 OR=2.23; p=0.003). Gln/Gln alleles of both XRCC1 and XPD genes appear to amplify the effects of household exposure, smoking and betel quid chewing on lung cancer risk in the study population of both the states. Gln/Gln genotype was higher among cases than control groups in both XRCC1 (8.5% vs 6.3%) and XPD genes (12.9% vs 10.5%). Significant protective effect for lung cancer was observed for intake of bamboo shoots (OR=0.15; p=<0.001) and egg (OR=0.05; p<0.001) in both Manipur and Mizoram. In addition to these among the traditional dietary habits of Manipur

consumption of citrus fruits (OR=0.07; p<0.006) and garlic (OR=0.01; p<0.001) also plays an inverse association for lung cancer risk specifically in Manipur.

Study of Genetic and Molecular Epidemiology of Stomach Cancer in Mizoram of North Eastern Region of India

Tobacco smoking, especially meiziol (local cigarette) is the important risk factor for stomach cancer in Mizoram. GSTM1 and GSTT1 genes modify the effect of tobacco habits. This study revealed that p53 codon 72 polymorphism and dietary and tobacco habit interactions influence stomach cancer development in Mizoram, India. Although no direct association between CYP2E1RsaI polymorphism and stomach cancer was observed, relations between CYP2E1 RsaI polymorphisms and different tobacco and dietary risk habits in terms of developing stomach cancer exist in this high risk population of north-eastern part of India, however further elaborate study recruiting larger population is required to shed more light. This study is a first step in understanding the epidemiology of stomach cancer in Mizoram, India.

Study of Genetic and Molecular Epidemiology of Breast Cancer in 2 States (Assam & Meghalaya) of North Eastern Region of India

After establishing network with the different hospitals, recruitment of staffs, finalization of epidemiological questionnaire (Breast cancer) and procurement of different laboratory chemicals, the epidemiological information and biological samples has been collected as per protocol. During this period under report a total of 234 nos. of blood samples have been collected so far. Genetic polymorphism of tumor suppressor gene p53 and XRCC1_Arg399Gln were associated with increased risk of Breast Cancer in this study. Family history was also found to be associated with Breast Cancer. Ten cases had family history of Breast Cancer and out of 10 cases 1 has mutations in BRCA1

Comparative Study of Genetic, Clinical and Epidemiological Factors of Breast Cancer in Rural and Urban Area of India (Mizoram & Tripura)

Betel nut chewing with or without tobacco was found to be an important risk factor of breast cancer in Tripura but not in Mizoram. Smoking habit was found associated with breast cancer in both states. Genetic mutations in BRCA1 gene was found in 12% cases of Mizoram but only 2.44% of cases from Tripura. Carriers of mutations in XRCC1 and XRCC3 and TP53 genes significantly increased the risk of breast cancer subjects from Mizoram and Tripura. Next Generation Sequencing data along with TaqMan allelic discrimination facilitated in identification of a novel mutation in PKHD1 gene which predisposed carriers of the variant allele to increased risk of breast cancer (OR = 3.1; CI = 1.4 – 7.2; p = 0.007). As a proof of concept the present study based on Next Generation Sequencing technology has revealed that NGS have a significant utility for healthcare diagnostic especially by quickly screening mutomes which will be specific for different ethnic groups.

Genome-wide Analysis of Genetic Alternations in Patient's Oesophageal Cancer from North-East India using Single Nucleotide Polymorphism Arrays

Epidemiological Study :

The epidemiological part of the project was carried out at RMRC, Dibrugarh. 65.8% of the cases were males while 34.2% were females. Majority of male cases belong to the age group of 60 - 70 yrs. Male cases were mostly cultivators i.e. 44.3%; while among the female cases, majority of them were housewives i.e. 65.8%. Topography inclination indicated more towards C15.4 (middle-third of esophagus) among both the sexes. Squamous cell carcinoma was mostly predominant (90.7%). The pathological grade of most of

the cases was moderately differentiated (G2) showing 81% of the total cases irrespective of sex. Chewing of tobacco was significantly associated with increased risk of esophageal cancer among the study subject (OR=2.17; p=0.040). Significant risk association was also observed for those who consume betel nut leaf with lime katha and zarda (OR=7.30; p<0.001).Smoking of bidi (OR=2.18; p=0.018) and those who smoke both bidi and cigarette (OR=3.21; p=0.020) were also significantly prone to develop esophageal cancer. Significant risk was also observed for those who consumed alcohol (OR=2.23; p=0.001). While among the type of alcohol consumption significant risk was observed for those who consumed whisky (OR=3.41; p=0.002) and Rice beer (OR=2.75; p=0.011). From the dietary habits, significant risk association for esophageal cancer was observed for the intake of kalakhar (extract made from banana leaf used as food additives) (OR=2.77; p=0.029). The study showed protective effect for the intake of curd among the subjects (OR=0.40; p=0.018)

Epigenetic Studies in Oesophageal Cancer in High Risk Region of Northeast India

Epidemiological Study :

The epidemiological part of the project was carried out at RMRC, Dibrugarh. Among the cases 74.6% were males and out of which majority of them belonged to the age group of 51-60 years. On the other hand, female percentage was 25.3% and majority of the cases belonged to the age group of 51-60 yrs. Most of the cases had the family income in the range of Rs.1000-5000 and among controls majority had their income in the range of Rs.5000-10000. Male cases were mostly cultivators (42.85%) followed by business (19.64%), service (16.07%), unskilled (12.5%) and skilled (8.92%). Among the female cases, majority were housewives (78.9%) followed by cultivators (10.52%) and service (10.52%). Squamous cell carcinoma type which was mostly predominant (94.7%) followed by adenocarcinoma (5.3%). Most of the tumors were found to be moderately differentiated (66.7%) compared to well differentiated (20%) and poorly differentiated (13.3%). Tobacco smoking and tobacco and betel nut chewing was higher among the cases. 70.7% cases were smokers and 93.3% cases are chewers. Alcohol drinking habit was also more among the cases about 45.3%

Pattern of Survival and Quality of Life of Esophageal and Stomach Cancer Patient in North Eastern Region of India

Out of the total 100 cases of esophageal cancer, males were preponderance with an estimated rate of 68% and maximum of the cases belonged to the age group of 50-59 yrs, whereas in case of stomach cancer females were preponderance with the estimation rate of 53% out of total 55 cases belonging to the age group of 50-59 yrs. Regarding caste/ethnic group is concerned, the non tribe was the main victims of both esophageal and stomach cancer. Geographically, the esophageal cancer was more prominent in urban area with an estimation of 48% whereas stomach cancer was more prominent in rural area with 52.7% out of total cases. Maximum of the esophageal cases were found to be service holder with education upto middle level whereas in stomach cancer, house wife was the most victim and they were found to be generally illiterate. The nuclear families were the main sufferer of both esophageal and stomach cancer. It was found out that the maximum of the esophageal cases were from the middle class group and the maximum of the stomach patient were from the lower category. In case of anatomical stage, the cancer has spread towards stage IIIA and in both esophageal and stomach cancer. In esophageal cancer, radiotherapy was used for treatment by most and in stomach cancer chemotherapy was used by many for treatment. 60% of the esophagus cancer and 50.9% of the stomach cancer patient were given treatment prior to the Reporting Institution (RI). 90% of the esophagus cancer patient and 53% of the stomach cancer patient were continuing the prescribed treatment. Maximum of the esophagus and stomach cancer

patient chose to take treatment in their own state than go out of state for treatment. In context to clinical information most of the esophageal cases were squamous cell carcinoma with pathological grade G1: well differentiated and the topography inclination indicated more towards C15.5: lower-third of esophagus. In case of stomach cancer, adenocarcinoma was the most common type of cancer with pathological grade G1: Well differentiated and the topography inclination indicates more towards CI6.3: gastric antrum. The overall average survival probability of esophageal cancer patient was 10.81 month and stomach cancer patient was 8.96 months are found. Results showed that almost all the multi-item scales of the questionnaire registered high value of (> 0.70) signifying that the scales are internal consistent.

Risk Factors of Hepatocellular Carcinoma (HCC) in Sikkim and Arunachal Pradesh, India

Male cases were reportedly higher than the female cases in both Arunachal Pradesh (61.9% vs. 38.1%) as well as in Sikkim (60% vs. 40%). Majority of the cases in both the states (for both male and female) were in the age group of 51 – 70 years. Majority of the cases were illiterate and cultivators in both the states. In Arunachal Pradesh, 76.2 of the cases were cultivators, 14.3% were in service or business and the remaining 9.5% were housewives while in Sikkim 50% of the cases were cultivators, 40% of the cases were either in service or business, and housewives and unskilled persons occupy 20% of cases each. Regarding family income, it was seen that in both the states, 50% of the cases had family income in the range of Rs.500-1750 and among controls majority had their income more than Rs.4000. It was found that the most common type of Hepatocellular Carcinoma was " Hepatocellular Carcinoma, NOS(C22.0)" in both the states. Most of the tumors were found to be moderately differentiated (85.7%) followed by well differentiated (14.3%) in Arunachal Pradesh while in Sikkim most of the tumors were poorly differentiated (50%) followed by moderately differentiated (30%). Further majority of the cases had diagnosed HCC through FNAC while the remaining cases have done AFP in both the states . Cases were mostly suffering from abdominal pain (32%), inability to eat (30%) and weight loss (27%). Hepatitis B positive was found to be the common history of illness in both the states. Chemotherapy was given to majority of the cases at the time of treatment. Chewing of tobacco (Khaini) was significantly associated with increased risk of Hepatocellular Carcinoma among the study subject. Risk was also observed in case of smoking but it was not significant in either of the cases. Alcohol consumption was also significantly associated with increased risk of HCC among the study subject especially those who consume Government approved local drinks and *rice beer*. Diet mostly includes rice, pulses and green leafy vegetables along with non vegetarian foods which comprises of eggs, meat, and fish (fresh, dried and smoked). 89.5% of the people consume non-veg as well as leafy green vegetables. Consumption of fermented and non fermented bamboo shoot is widely preferred by the people of Arunachal Pradesh. Fruits are occasionally consumed which include citrus fruits, apples, jackfruit, etc.

Sites of Cancer Associated with use of Tobacco

There are cancers of several anatomical sites known to be associated with the use of tobacco. The NCRP has been using the classiication provided by the International Agency for Research on Cancer (IARC), World Health Organization monographs on overall evaluations of carcinogenicity (IARC, 1987). The recent Monographs of IARC have added more anatomical sites addressing their relationship between tobacco usage and cancer. However, In this report the earlier listing has been retained for comparison purposes. The list of anatomical sites of cancer (along with corresponding ICD-10 codes) considered known to be associated with the use of tobacco is given in Table 7.1.

Regional demarcation (North, South, East, West, Central and North East) of data from the 58 HBCRs indicate the pooled data of all HBCRs present in the region irrespective of the residential status of the patient.

Table 7.1 Sites of Cancer Associated with Use of Tobacco with ICD-codes

Anatomical Sites of Cancer	ICD-10 Codes
Lip	C00
Tongue	C01-C02
Mouth	C03-C06
Pharynx	C10 and C12-C14
Oesophagus	C15
Larynx	C32
Lung	C33-C34
Urinary Bladder	C67

East Khasi Hills district of Meghalaya had the highest relative proportion of cancers associated with the use of tobacco with 70.4% and 46.5% of males and females, respectively. Among males, the lowest proportion of sites of cancers associated with use of tobacco was in West Arunachal (24.5%) whereas in females the lowest proportion was observed in Thiruvananthapuram district (10.1%). Higher proportion of females had cancers associated with use of tobacco in the north eastern states, followed by registries in the central and western regions in India.

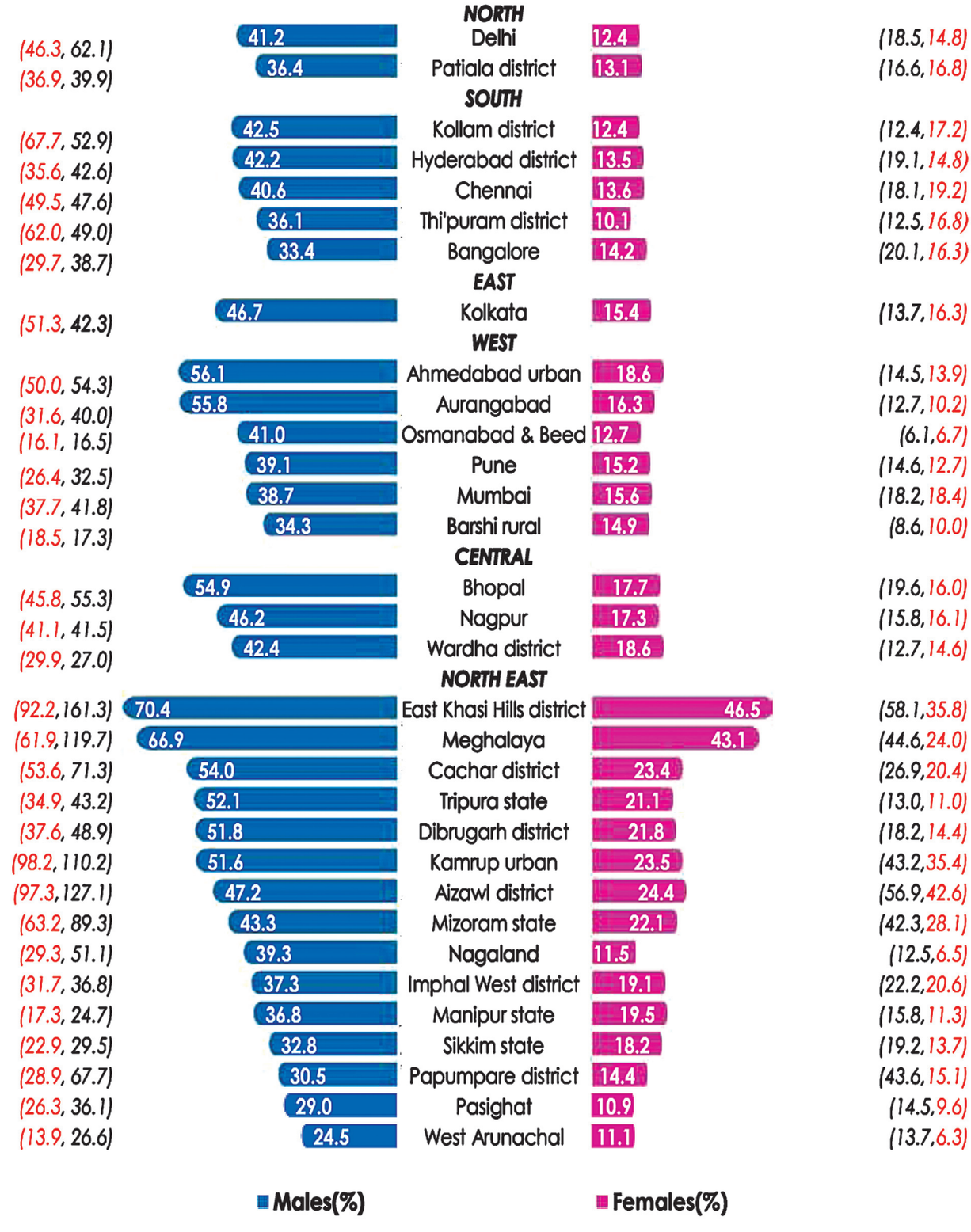

Fig. 7.1: Relative Proportion (%) of Cancer sites Associated with the Use of Tobacco Relative to All Sites of Cancer in 28 PBCRs under NCRP (2012-2016).

Table 7.2 Number (n) and Relative Proportion (%) of Speciic Sites of Cancers Associated with the Use of Tobacco by Region (Patients treated only at 58 Reporting HBCRs under NCRP)

NORTH

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	207	1.1	60	1.1
Tongue (C01-C02)	2735	14.3	588	10.7
Mouth (C03-C06)	3072	16.0	614	11.2
Oth. Oropharynx (C10)	706	3.7	114	2.1
Hypopharynx (C12-C13)	857	4.5	160	2.9
Pharynx Unspeciied (C14)	67	0.3	17	0.3
Oesophagus (C15)	2551	13.3	1766	32.3
Larynx (C32)	2224	11.6	240	4.4
Lung (C33-C34)	5945	31.0	1769	32.3
Urinary Bladder (C67)	817	4.3	145	2.6
Total	**19181**	**100.0**	**5473**	**100.0**

EAST

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	25	1.1	17	2.3
Tongue (C01-C02)	303	13.3	97	13.1
Mouth (C03-C06)	584	25.6	273	37.0
Oth. Oropharynx (C10)	46	2.0	9	1.2
Hypopharynx (C12-C13)	93	4.1	22	3.0
Pharynx Unspeciied (C14)	7	0.3	2	0.3
Oesophagus (C15)	165	7.2	62	8.4
Larynx (C32)	156	6.8	14	1.9
Lung (C33-C34)	772	33.8	218	29.5
Urinary Bladder (C67)	131	5.7	24	3.3
Total	**2282**	**100.0**	**738**	**100.0**

WEST

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	229	1.4	67	1.6
Tongue (C01-C02)	3076	19.1	791	18.5
Mouth (C03-C06)	5578	34.6	1258	29.5
Oth. Oropharynx (C10)	305	1.9	33	0.8
Hypopharynx (C12-C13)	982	6.1	251	5.9

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Pharynx Unspeciied (C14)	179	1.1	31	0.7
Oesophagus (C15)	1301	8.1	748	17.5
Larynx (C32)	1051	6.5	98	2.3
Lung (C33-C34)	2975	18.5	910	21.3
Urinary Bladder (C67)	436	2.7	83	1.9
Total	**16112**	**100.0**	**4270**	**100.0**

SOUTH

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	149	0.6	131	1.4
Tongue (C01-C02)	3897	16.0	1417	15.5
Mouth (C03-C06)	4747	19.5	3106	33.9
Oth. Oropharynx (C10)	1088	4.5	103	1.1
Hypopharynx (C12-C13)	1906	7.8	667	7.3
Pharynx Unspeciied (C14)	94	0.4	35	0.4
Oesophagus (C15)	2453	10.1	1538	16.8
Larynx (C32)	2914	12.0	248	2.7
Lung (C33-C34)	6352	26.1	1763	19.2
Urinary Bladder (C67)	717	2.9	155	1.7
Total	**24317**	**100.0**	**9163**	**100.0**

CENTRAL

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	90	1.6	41	2.5
Tongue (C01-C02)	1243	21.6	309	18.8
Mouth (C03-C06)	2593	45.0	735	44.8
Oth. Oropharynx (C10)	75	1.3	6	0.4
Hypopharynx (C12-C13)	231	4.0	61	3.7
Pharynx Unspeciied (C14)	42	0.7	15	0.9
Oesophagus (C15)	388	6.7	197	12.0
Larynx (C32)	471	8.2	57	3.5
Lung (C33-C34)	527	9.2	193	11.8
Urinary Bladder (C67)	97	1.7	27	1.6
Total	**5757**	**100.0**	**1641**	**100.0**

NORTH EAST

Anatomical Sites of Cancer	Males		Females	
	n	%	n	%
Lip (C00)	105	1.0	43	1.2
Tongue (C01-C02)	1290	12.1	334	9.7
Mouth (C03-C06)	1360	12.7	717	20.7
Oth. Oropharynx (C10)	351	3.3	58	1.7
Hypopharynx (C12-C13)	2835	26.5	401	11.6
Pharynx Unspeciied (C14)	133	1.2	26	0.8
Oesophagus (C15)	2397	22.4	1179	34.1
Larynx (C32)	864	8.1	160	4.6
Lung (C33-C34)	1262	11.8	525	15.2
Urinary Bladder (C67)	103	1.0	18	0.5
Total	**10700**	**100.0**	**3461**	**100.0**

Males: Lung was the most common site of cancer associated with use of tobacco in the east (33.8%), north (31.0%), and south (26.1%) regions. Cancer mouth had the highest proportion among the cancers associated with use of tobacco in central (45.0%) and western (34.6%) regions whereas cancer hypopharynx was common in the north eastern region (26.5%).

Females: Mouth was the most common site of cancer associated with use of tobacco in the central (44.8%), eastern (37.0%), southern (33.9%) and western (29.5%) regions. Cancer oesophagus and cancer lung had the highest proportion among the cancers associated with use of tobacco in north (32.3%) whereas cancer oesophagus was common in the north eastern region (34.1%).

Gene expression profile and copy number variation has been studied by genome-wide approaches in esophageal cancer patients from Assam and Kamrup districts showing high incidence (AAR of 33/100,000) and familial clustering (29%) with aim to identify the molecular functional pathways and link between tobacco use and genetic variation. Up-regulation of β-cell receptor signaling pathway genes (PRKCB1) and down regulation of natural killer cell mediated cytotoxicity genes (NFAT5, KLRC1) in familial ESCC suggests that immune response contribute significantly to familial esophageal cancer. Down regulation of genes associated with xenobiotic metabolism viz. GST & EPHX1 and mutations in BRCA2 gene were found associated with risk for familial ESCC and can help in screening. Up-regulated GPCR activity gene NPY and MAPK activity gene FGF12 and down-regulated ribosome proteins S4, L32 and cytokeratin genes KRT4 were found important prognostic factors for both familial and non-familial tobacco and betel quid associated esophageal cancer. DHFR was found important drug target for this cancer. A high through put tissue micro array containing esophageal squamous cell carcinoma from the patient pool was constructed to validate the gene expression profile.

Gastric Cancer in North East India

Frequency of gastric cancer (GC) is very low in India compared to that in Japan and China. However in Mizoram, one of the NE states in India, a very high age adjusted incidence of stomach cancer has been recorded. Epidemiologic studies indicate that the risk of gastric cancer is significantly elevated among current smokers and in *meiziol* (a local cigarette) smokers (OR>2). The risk increased with increasing

cumulative dose of tobacco smoked. Use of locally prepared *Tuibur* (tobacco smoke–infused water) in Mizoram, seemed to increase the risk of stomach cancer (OR, 2.1). There is no report so far on the genetic profile of the patients with gastric cancer from this high-incidence region of Mizoram in NE India.

Although CYP and GST enzymes are involved in the activation and detoxification of N-nitrosamines which are some of the most potent carcinogens present in smokeless tobacco, snuff and tobacco smoke and related compound, studies on the relationship between genetic polymorphisms of CYP1A1, GSTT1, and GSTM1 and the risk of gastric carcinoma (GC) have not been carried out in this high risk region of India so far and the previous reported studies from other part of the world are conflicting.

To evaluate the association between polymorphic detoxifying genes and GC risk, a case-control study including histologically confirmed 134 Gastric Cancer patients and 282 healthy controls was conducted in a gastric cancer patients and healthy controls in a gastric cancer in north east region of India to screen the GST, CYP1A1(2A,2C) genes and p53 codon 72 polymorphisms.

The frequency of *GSTT1* and *GSTM1* null genotypes did not show significant differences between cases and controls. Variant genotypes (*Ile/Val* and *Val/Val*) of *GSTP1* were found more frequent in cases of gastric cancer as compared to controls but the difference was not statistically significant (OR=1.25, 95% CI 0.77-2.03, P=0.37). No significant difference in frequency distribution of CYP1A1 2A genotypes (ww,wv,vv) and CYP1A1 2C genotypes (II,IV,VV) was found in cases and controls, suggesting no associated risk for gastric cancers with GST and CYP1A1 genes. Conditional logistic regression analysis of frequency distribution of p53 codon 72 Arg/Arg, Arg/Pro and Pro/Pro in the cases and controls showed higher risk associated with Arg/Pro genotype whereas the Pro/Pro appeared to be a protective genotype. These observations were represented both by OR1 and OR2 but lacked statistical power. No significant interactions of risk habits was found with *P53* genotypes, however, interaction of betel quid chewing with Arg/Pro genotype reached a near significance level with a 2 fold risk for gastric cancer (OR2=2.40 95% CI=0.91-6.26; p=0.07).

Risk estimates for *H. pylori* status, tobacco, betel quid and alcohol consumption habits in cases and healthy age matched controls showed significant association of tobacco chewing with risk of development of GC, while there was no significant association with *H. pylori* as reported earlier. However, tobacco chewers who were also *H. pylori* positive showed a seven fold risk (OR2=7.12, 95% CI=5.02-36.31, *p* 0.0001) whereas betel quid chewers who were also *H. pylori* positive showed a four fold risk (OR2=3.52, 95% CI=1.16-10.86, *p*=0.026) for developing gastric cancer.

To understand the molecular mechanism underlying the development and progression of GC in this high-risk region in NE India, the gene expression profiles of tumor tissue from patients having history of tobacco/ betel quid chewing, alcohol consumption and sero positivity for IgG antibody against *H. pylori* were studied and compared with normal appearing pooled gastric mucosal tissues. A total of 170 genes were found to be differentially expressed. Of the 108 significantly up-regulated genes, genes involved in apoptosis (*RYK, SH2D2A, CSNK1E, LRP12, HSPE1, FGB, PXN, CHP*), proinflammatory response (*IL9*), angiogenesis (*SH2D2A, ANG*), cell adhesion (*CD151, PXN, WASF1*), cell proliferation (*CDC2L1, JAG2, IL9), r*egulators of I-kappa B kinase / NF-kappa B cascade (*CXXC5*), Wnt signaling (*CHP, CSNK1E, RYK*), Notch signaling (*JAG2*), Hedgehog signaling (*CSNK1E, BMP7*), metobolic pathway (*LDHB*), thyroid cancer (*RET)* andepithelial cell signaling in *H. pylori* infection (*ATP6V1G2*) were found

to be biologically relevant in tumorigenesis. Of the 62 significantly down-regulated genes, genes involved in base-excision repair (*RAD51L3*), inhibition of cellular proliferation (*INSM1*), immune response (*RFX1, CXCL10, C3AR1, MALT1*), viral response *(ATP6V1G2, HBXIP, ACE2*), epithelial cell signaling in *H. pylori* infection (*JAM3*) were found to be relevant in tumorigenesis . Analysis of the molecular functional pathways by Genowiz™ identified four different potential relevant molecular functional pathways that were deregulated in these patients including mainly Hedgehog signalling (*CSNK1E, BMP7)*, Wnt signalling (*CHP, CSNK1E, RYK*), Notch signalling (*JAG2)* and epithelial cell signaling in *H. pylori* infection pathways (*JAM3*, *ATP6V1G2)*. It is reported that a balance between Wnt-FGF-Notch and BMP-Hedgehog signaling network is important to regulate the homoestasis among stem and progenitor cells and disruption of the signaling network results in cancer.

Validation of *LDHB, PXN, RYK, RET, ANG, BMP7, RAD51L3* and *CXCL10* genes by real time PCR in cases of gastric cancer including *H. pylori* positive and *H. pylori* negative cases showed significant down-regulation in expression of *RAD51L3 (p=0.0013), CXCL10 (p=0.0038) and BMP7 (p=0.0002)* genes whereas significantly up-regulation in expression of *PXN (p=0.0077), ANG (p=0.0015), LDHB (p=0.019), RYK (p=0.044) and RET (p<0.0001)* genes in *H. pylori* positive cases compared to adjacent normal tissue. The *H. pylori* negative cases showed a significant up-regulation of expression of *RET* (*p=0.024*) and a significant down-regulation of expression of *BMP7 (p*=0.018) as compared to its adjacent normal tissue. The gene expression of *PXN (p=0.039)* was alone found to be significantly up-regulated in *H. pylori* positive Gastric Cancer cases on comparison to *H. pylori* negative Gastric Cancer cases. A significant direct correlation of expression of *PXN* with *RET* (0.523, *P=0.05*) was observed in *H. pylori* positive patients while *H. pylori* negative cases did not show any correlation in the expression of any of the genes studied.

The diverse patterns of expression of tumourigenesis related genes in *H. pylori* positive and negative patients suggest the probability for the existence of different and distinct molecular pathways in the pathogenesis of gastric cancer. It is possible that factors other than *H. pylori* infection including high tobacco consumption and food habits such as high salt intake interact with and contribute significantly to the initiation of inflammation in gastric cancer. This is a novel protumorigenic mechanism of inflammation in Gastric Cancer in which tumor-related pathways such as Wnt (*CHP, CSNK1E, RYK*), Notch (*JAG2*), Hedgehog (*CSNK1E, BMP7*) and epithelial signaling pathway in *H. pylori* (*ATP6V1G2, JAM3*) may play an important role in the development of gastric cancer in *H. pylori* infected and non-infected individuals via distinct molecular pathways.

Global Knowledge Hub on Smokeless Tobacco (KHSLT)

As per recommendation of Conference of Parties in its sixth conference (COP6) Global Knowledge Hub on Smokeless Tobacco Hub (KHSLT) has been established in National Institute of Cancer Prevention and Research by WHO Framework Convention on Tobacco Control (WHO FCTC) Secretariat and Ministry of Health and Family Welfare, Government of India in 2016.

The first objective of KHSLT is to generate and share expertise, information and knowledge on smokeless tobacco through information collection, analysis and exchange of information on smokeless tobacco and dissemination of these information through web portal, individual and group consultation, meetings and international conferences.

Second objective of the KHSLT is to assist Parties of the WHO Framework Convention on Tobacco control (FCTC) in the area of SLT control by identifying laboratories and investigators working on SLT in the South-East Asia region and beyond; strengthen communication and collaboration between laboratories through developing platforms for sharing data, information and expertise; nucleate and support collaborative projects on molecular and related social and economic aspects of SLT; develop standard operating procedures for analysis of SLT products; and generate and assess the existing data on specific SLT products and their constituents.

Second Policy project: Searching for the most recent literature and preparing a background paper to address smokeless tobacco products and the policies to control their use; the paper shall propose draft recommendations on how to strengthen the control of smokeless tobacco products in the South-East Asia region; engage with Parties from the South-East asia region, discuss the draft recommendations from the paper and develop strategies for their implementation in each Party of the region through an expert meeting organized for the Parties in the South-East Asia region.

White Paper on Electronic Nicotine Delivery System (ENDS)

ENDS or e-cigarettes are battery-powered devices used to smoke or 'vape', a flavoured solution containing varying concentration of nicotine and other ingredients as flavouring agents and vaporizers, which are too found to be harmful for health. Use of e-cigarettes adversely affects almost all the human body systems, especially severe respiratory disease. It also poses risk to foetal, infant, and child brain development and are harmful to non-users when exposed to second-hand vapours. Passive exposure to vapours during pregnancy can severely affect the health of both the mother and foetus. There are reports of poisoning due to accidental swallowing by children and also can cause fire and explosion. There is an increasing trend of the use of ENDS or e-cigarettes amongst the youth and adolescents in countries where these products were introduced. Thus, the increasing use of e-cigarettes by youth is a significant public health concern since the extent of potentially long term harmful effects are still to be fully revealed. Based on the currently available scientific data from multiple streams of research, the ICMR recommends complete prohibition on ENDS or e-cigarettes in India in the greater interest of protecting public health, in accordance with the precautionary principle of preventing public harm from a noxious agent.

White Paper on Smokeless Tobacco & Women's Health in India

Smokeless tobacco (SLT) use is widespread across many nations and populations, and India shares more than three-quarters of the global burden of SLT consumption. Tobacco use in India has been largely viewed as a male-dominant behaviour. However, evidence from medical, social and behavioural sciences show significant SLT use among women and young girls. The paper highlights key dimensions of SLT use among women in India including prevalence and determinants, the health effects arising from SLT use and cessation behaviours. The paper concludes by providing recommendations with the aim of setting research priorities and policy agenda to achieve a tobacco-free society. The focus on women and girls is essential to achieve the national targets for tobacco control under the National Health Policy, 2017, and Sustainable Development Goals 3 of ensuring healthy lives and promote well-being for all.

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