RISK PROFILE OF ORAL CANCERS AND STRATEGIES TO IMPROVE AWERENESS AND EARLY DETECTION

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Abstract

Fundamentals of implementing any cancer control programs are the understanding of the burden of the disease in the community (incidence trends), risk factor profile and the awareness among the public about the cancer and its risk factors. In this project we attempted to investigate all these three inter related subjects, which would form the basis to implement a systematic oral cancer prevention strategy. In addition, we have investigated the efficacy of a novel oral cancer health education program to improve awareness of oral cancer in the community.

Recent data on the incidence trends from the low incidence, developed countries suggest that the head and neck cancers are increasing especially among young adults. In our study on incidence trends in India of two large tumor registry data, it was observed that there is an overall reduction in the incidence of head and neck cancers in urban and rural populations. However, there was a significant increase in the incidence of tongue cancers among females. An attempt was made to compare the Indian data with the SEER data from US and it was observed that there was an overall reduction of head and neck cancers in India, whereas SEER revealed an increase in the incidence of head and neck cancers among males and an increase of tongue cancers among females. Among young adults, an increased incidence of oral cavity and pharynx cancer was observed among Indian males and tongue cancers among Indian females. Young Americans showed an overall increase in incidence in all head and neck cancer subsites except in the laryngeal cancers.

The incidence trends reflect the risk factor profile of the community. Prior reports suggests that 80% of the oral cancers can be attributable to established risk factors like tobacco in the form of smoking or chewing and alcohol consumption. The rest is attributed to factors like diet, viral etiology and genetic predisposition. There are now reliable economic data to suggest that tobacco consumption in India has decreased significantly over the past decade. The significant reduction in incidence may be attributable to lower prevalence of tobacco habits. In order to determine the current risk profile of head and neck cancers, a retrospective study was carried out in patients who have presented with head and neck squamous cell carcinoma. It was observed that oral cavity cancers formed the majority and 43% of the patients did not have any risk habits.

Therefore an attempt was made to determine the risk factors other than tobacco and alcohol in the subset of individuals.

A case control study to determine causative role of Human Papilloma Virus (HPV) in oral cavity cancer was undertaken. PCR was employed as the gold standard to detect the presence of HPV. In this study, the integration status of the virus was determined by PCR and catalyzed signal amplified *in-situ* hybridization. Also immunohistochemical analysis of the proteins involved in HPV carcinogenesis was carried out. It was observed that 48% of the cases were positive for oncogenic HPV16 among which 83% showed integration by PCR and 67% by *in situ* hybridization. Data from our study has observed that 33% had active E6-p53 pathway and 67%, the E7-pRb pathway and 19% had both the pathways active.

Increased awareness of oral cancer and its risk factors in the community are essential for better compliance

to preventive measures and risk reduction strategies. A survey was carried out to assess the level of oral cancer awareness in a semi-urban population in Kerala. It was observed that the overall awareness of oral cancer and its risk factors is good and is proportional to the educational status though certain gaps exist stressing the need for targeted health education and risk factors cessation counseling.

An attempt was made to improve the awareness and early detection by `oral self examination'. A brochure was developed which gives detailed information on oral cancer, its risk factors, premalignant lesions illustrating the methods to perform oral self- examination. Two Panchayats with a total population of around 30,000 (majority of them are bidimaker with high risk habits) were selected to test this concept. Initially brochures were distributed, public was instructed to perform oral visual examination and report to the local screening clinic if they had any suspicious lesions. Then the health workers performed house-to-house visit to collect information regarding the awareness of oral cancer and its risk factors using a validated questionnaire, provided health education, performed oral visual examination and referred the suspicious cases to the local screening clinic. In this study it was observed that the health education has improved the awareness. The oral cancer awareness was significantly higher among males and in the younger age group and in those without the risk habits. The risk habit awareness was significantly higher among individuals of higher education, females and in the younger age group and in those without the risk habits. Eighty seven percent practiced oral self-examination. Fifty four persons identified lesions on their own out of which 39 were confirmed by health workers and only 8 visited the screening clinic. The program identified 216 pre- cancer and 3 new oral cancer cases in stage I/II through the health workers. Though there is good awareness among the public, there exists poor compliance to seek medical assistance. Further efforts should be channelised towards increased frequency of health education especially to the high-risk individuals, improving the motivation of the public, integration of the early detection into the existing health schemes and educating the school children.

INTRODUCTION

Oral cancer is one of the ten leading cancers in the world. In India, it is the most common cancer among males and third most common cancer in females (Mathew 2007). The primary cause of the very high incidence of oral cancer in South Asia is the widespread habit of chewing betel quid (or paan) and related areca nut use (Bedi 1996). There are reports that the risk profile of head and neck cancer is changing (Schantz 2002) and therefore pattern (incidence and sub-site predilection) of head and neck cancer is also is expected to change. Epidemiological studies have shown that the incidence of head and neck cancers is decreasing except in the young, for whom the etiology remains unresolved (Davis 1987). Because of the well-defined risk factors, long natural history with majority of cancers preceded by pre-cancer lesions and the mouth is easily accessible for visual examination, oral cancers have the vast potential for prevention. This is feasible only if there is increased awareness of the condition in the community, therefore there will be better compliance to preventive measures and risk reductionstrategies.

The overall goal of this project is to define change in incidence trends of head and neck cancer, risk profile of the cancer and develop a strategy to improve awareness of oral cancer in the community. Four inter-related projects were undertaken to address this issue.

Project 1: To investigate the trends in head and neck cancers over a time period in India and compare with data from developed countries and to frame an etiological hypothesis for the change in trends if any.

Project 2: To determine the role of Human Papilloma Virus as a risk factor for oral cancer.

Project 3: To evaluate the status of awareness of oral cancer, its risk factors and to estimate the prevalence of risk factors in a high-risk semi-urban population in India.

Project 4: To assess the efficacy of oral self-examination as a potential tool to improve awareness and early detection of oral cancers in a high-risk rural population

In order to determine the trends of head and neck cancers with special reference to oral cancers in India, cancer registry data was taken from an urban and a rural registry over a period of 13 years and analyzed. Since the data from developed countries report an increase of head and neck cancers particularly in the young adults, comparison of the incidence trends between developed countries was undertaken using the SEER data (1973-97) and data for similar time period from India's first cancer registry –Mumbai. This has demonstrated that the incidence of head and neck cancer is declining in both developed nations and in India, except that of

oral tongue cancer, for which the incidence is on the rise.

To investigate the risk factor profile, a retrospective study was carried out with data obtained from patients presenting with head and neck cancer at Amrita Hospital from January 2004 and December 2006. This has identified that over 50% of oral tongue cancer develop in subjects with no known risk factors. Attempts were made to delineate the role of HPV in oral tongue cancers.

Initially tobacco consumption in the form of chewing or smoking was proposed as the risk factor for oral cancers, later alcohol emerged as an independant risk factor for oral cancer though it has shown to have additive and synergisitic effects with tobacco (Notani 1988; Sankaranarayanan 1989; Franceschi 1990). A study from India showed that 70% of the oral cancers were as the result of either smoking or chewing (Jayant 1977). Later, diet has also been implicated in the etiology of oral cancer (Winn 1984; Notani 1987; La Vecchia 1997). The association between Human Papilloma Virus (HPV) and head and neck cancers was observed as early as 1960. During the past two decades, the data supporting HPV as a causative agent in the development and progression of Head and Neck cancers, particularly that of oropharynx has accumulated. The true prevalence of HPV DNA in HNSCC is uncertain. Studies have estimated up to 60% positivity in HNSCC. The association of HPV with oropharynx was studied extensively, estimating that 45 to 100% tonsillar tumors are HPV positive (Mellin 2000; Gillison 2001; Mellin 2002; Dahlgren 2003; Mellin 2003). It is said that tonsillar crypts act as reservoir for the virus and hence the increase prevalence among tonsillar cancers and relatively decreased or negligible prevalence among other head and neck cancers. Recently it has been suggested that periodontal pockets act as reservoirs for human papilloma virus (Hormia 2005) and a study has shown the association between long-standing periodontitis and risk of tongue cancers (Tezal 2007). Only few studies have studied the role of HPV in oral cavity cancers, particularly that of tongue. Since recent literature suggests the increased incidence of tongue cancers (Schantz 2002), we proposed to determine the prevalence of HPV in oral tongue cancers. This is the first study of its kind with multiple detection techniques employed in detecting the presence of HPV, integration status and further exploring the pathway involved in its pathogenesis. Since HPV 16 is reported to be associated with head and neck cancers, the cases were tested for the presence of the same. The mere presence of HPV does not indicate its role in the causation of cancer, hence detailed molecular studies were also planned to confirm its etiological role in cancer cases. If the role of HPV in these cancers is confirmed, the developmental vaccines – prophylactic and therapeutic would have impact on the incidence of oral cancer if specifically targeted to HPV16.

Though literature suggests that the incidence of oral cancers and the practice of risk habits are decreasing, there is poor public awareness of the signs and symptoms of oral malignant and premalignant lesions (Boyle 1993). Lack of public awareness of oral cancer has been linked to the poor compliance (25.7%) to attend for oral cancer screening following invitation (Jullien 1995). It has also been shown that oral cancer awareness was poor not only among the public but also among the dentists, dental hygienists, nurses, general practitioners. To our knowledge the level of public awareness of oral cancer and its risk factors in India is not known. Hence in order to assess the level of oral cancer awareness, a survey was done in a semi-urban population in Kerala.

Oral cancers have the vast potential for prevention because of its association with known risk factors, long natural history with majority of cancers preceded by precancers, possibility of identifying precancerous and early invasive lesions by visual examination.

Strategies to improve awareness and early detection will vary in different geographic regions depending upon the life style and habits. Raising public awareness could contribute to achieving a significant reduction in its incidence. Hence an attempt was made to improve awareness and early detection by `oral self examination'. A brochure was developed which gives detailed information on oral cancer, its risk factors, and premalignant lesions illustrating the methods to perform oral self-examination. It was planned to educate the community through the health workers employed from the local community through self-examination brochures. Two Panchayats with a total population of around 57,000 (majority of them are fishermen with high risk habits) were selected to test this concept. Initially brochures were distributed, public was instructed to perform oral visual examination and report to the local screening clinic if they have any suspicious lesions. Then the health workers performed house-to-house visit to collect information regarding the awareness of oral cancer and its risk factors using a validated questionnaire (the same questionnaire used in the awareness survey with little modification in the questions on risk habit awareness), provided health education, performed oral visualexamination and referred the suspicious cases to the local screening clinic.

BACKGROUND

The International Classification of Diseases defines Head and Neck cancers as cancers of the oral cavity and pharynx (ICD-10, C00.0-14.0) and oral cavity cancers include cancers of the tongue, mouth, gum, floor of the

mouth, palate and other and unspecified parts of the mouth (ICD-10, C01.0-06.0). Malignancies arising from the mucosa of the oral cavity are epithelial in origin and are, therefore, classified as squamous cell carcinomas. Oral cancers have much in common with squamous cell carcinomas arising elsewhere in the upper aero digestive tract, sharing common risk factors. Hence studies of head and neck cancer are frequently referred when issues relevant to oral cancer are discussed. Squamous cell carcinoma account for more than 90% of all oral cancers (Zarbo 1988; Silverman 1990). According to the degree of differentiation, three subtypes are defined:

(1) well-differentiated squamous cell carcinoma showing more than 75% keratinization;

(2) moderately differentiated squamous cell carcinoma with 25-75% keratinization; and

(3) poorly differentiated squamous cell carcinoma with less than 25% keratinization. The majority of cases are moderately differentiated carcinomas. The definitions used to categorize cases are "localized" referring to tumor limited to the primary site without known spread to lymph nodes or adjacent tissues; "regional" indicating the presence of invasion of surrounding tissues and/or involvement of lymph nodes; and "distant metastasis" indicating the spread to distant organs.

Oral and pharyngeal cancer is the sixth most common cancer reported globally with the annual incidence of over 300,000 cases, of which 62% arise in developing countries (Parkin 1988). It is very common in countries like India, Pakistan, Taiwan and some areas of France and more common among males than among females. It is predominantly a disease of people over 40 years. In high prevalence areas many patients are less than 40 years old owing to the prevalence of various risk habits. For the past 2-3 decades a rise in the incidence of oral cancer among young adults have been observed (Cusumano 1988; McGregor 1989; Atula 1996; Myers 2000). In industrialized countries men are affected twice or thrice as common as women. But in high incidence countries like India, the incidence of tongue and other intraoral cancer for women is greater than or equal to that of men (Vargas 2000). The incidence in India is one of the highest in the world with the age-adjusted rates of 17.7/100000 among males and 9.3/100000 among females. It constitutes 12% of all cancers in men and 8% of all cancers among women. It has been estimated that 83000 new oral cancer cases and 46000 deaths occur annually in India (Parkin 2002; Ferlay 2004).

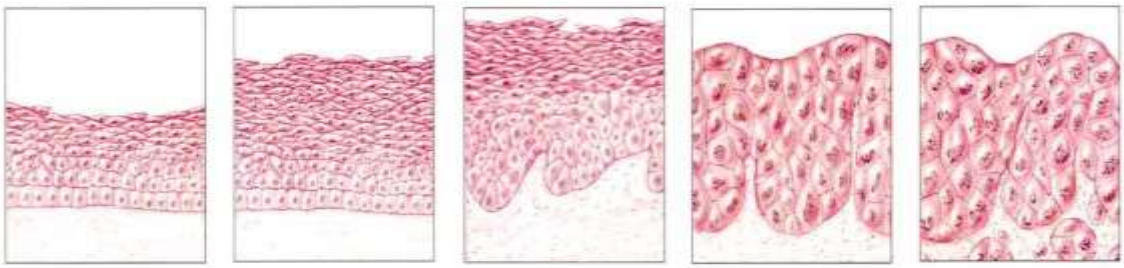
The survival of oral cancers has not significantly improved for the past few decades, the reasons being presentation of cases in the advanced stages and the occurrence of second primaries. Nearly two thirds of all oral cancers are diagnosed only after they become locally advanced (Barry 1989; Vokes 1993; Forastiere 2001).

Oral Carcinogenesis

Oral cancer arises from a premalignant stage, which may be clinically obvious as leukoplakia, or it could be clinically occult; followed by outgrowth of clonal populations associated with cumulative genetic alterations and phenotypic progression to form invasive malignancy. This carcinogenesis process is both a multi-step and multi-stage process.

Multi step carcinogenesis

Cancer development is a multi step process in which exposure to a carcinogen (eg. cigarette smoke) results in repeated damage and repair until the accumulated exposure triggers a transformation from normal to premalignant cells (i.e from normal cells to metaplasia and dysplasia) and eventually to carcinoma. Normal cells are not neoplastically transformed by a single oncogene but rather require two or more cooperating oncogenes and inactivation of multiple tumor-suppressor genes supporting the multistep or multi-hit model of carcinogenesis.



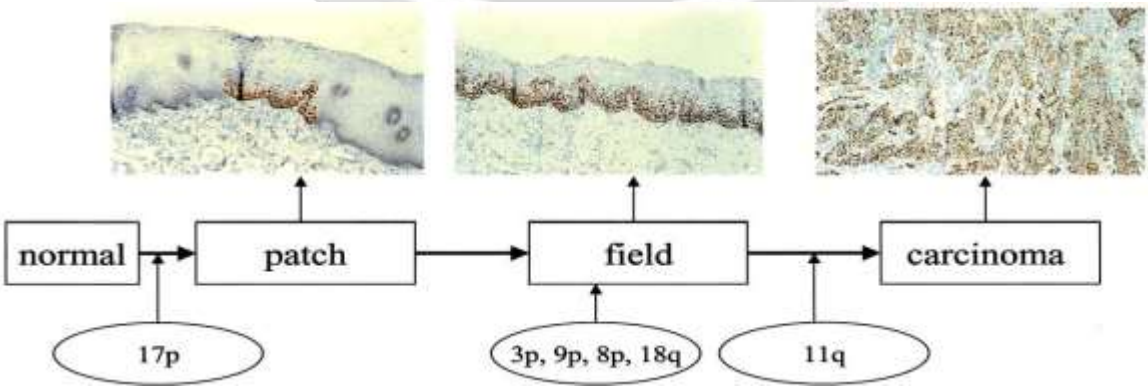
Normal mucosa → Hyperplasia → Dysplasia → Carcinoma in situ → Carcinoma

Histological progression model of oral squamous cell carcinoma

The histological progression model for oral Squamous cell carcinoma (SCC) is well established. It is generally believed to develop through sequential stages of premalignant /pre-invasive lesions: hyperplasia, mild, moderate, severe dysplasia, carcinoma *in situ* (CIS), and finally invasive SCC. Califano and his colleagues were the first to develop a molecular progression model for oral carcinogenesis, using findings from microsatellite analysis of archival tissue (Califano 1996). Eighty-seven lesions of the head and neck-preinvasive lesions and benign lesions associated with carcinogen exposure, were tested using microsatellite analysis for allelic loss at 10 major chromosomal loci -9p21, 3p21, 17q13, 11q13, 13q21, 14q 31-32.1, 6p, 8q, 8p, 4q 26-28 which have been defined previously. In this model, allelic loss has been used as a molecular marker for inactivationof putative tumor suppressor genes.

Field Cancerisation

Head and neck cancer patients often present with premalignant lesions and Multiple Primary Tumors (MPTs) in their Upper Aerodigestive tract (UADT). This led Slaughter *et al.* in 1953 to postulate the concept of field cancerization. Head and Neck Squamous cell carcinoma (HNSCC) results from a multistep carcinogenesis process, which occurs over large areas of the upper aerodigestive tract epithelium exposed to carcinogens. This condemned mucosa contains multiple transformed clones that can develop into new primary tumors at a rate of 30% over five years. This process is called “field cancerization” (Slaughter 1953). It could be the result of either independent molecular events affecting multiple cells separately or as molecular event in a single clonal progenitor that gives rise to this phenomenon, *via* mechanisms of widespread clonal expansion or an alternative means of undergoing lateral spread across the mucosa of the upper aero digestive tract.



Genetic Explanation of Slaughter’s Concept of Field Cancerization (Boudewijn 2004)

Genetic Alterations

The genetic alterations include gene amplification, over expression of oncogenes such as *MYC, ERBB-2, EGFR, RB, RASSF1A, FHIT, CCND1* and mutations, deletions and hypermethylation leading to *p16* and *p53* TSG inactivation. And loss of heterozygosity in several chromosomal regions is frequently observed, suggesting that other tumor suppressor genes not yet identified could be involved in the tumorigenic process of head and neck cancers. Genetic polymorphisms of carcinogen metabolizing genes or DNA repair genes influence susceptibility of individuals to cancer development.

Loss of Heterozygosity (LOH)

Deletion of specific chromosomal regions is one of the most common genetic events observed in solid tumors and the deleted regions are believed to contain potential tumor suppressor genes.

Oncogene activation

Mutation of *H-ras* oncogene is less common in Western countries (<5%) (Yarbrough 1994). In India, a high incidence of about 35% has been reported in OSCC in which betel- quid and reverse smoking are probable initiators (Saranth 1991; Field 1992). Yet another study has shown significant risk (odds ratio 1.6) associated with an H-ras gene polymorphism in the Indian population (Sathyan 2006). A nodal example is the ras gene family that includes the H-, K- and N-ras oncogenes. Indeed, constitutive activation of the K-ras protein in a mouse model is sufficient to induce oral tumor formation.

Risk factors/Etiological agents

Several etiologic agents are involved in the development of Head and neck cancers including oral cancers. They include tobacco and alcohol consumption, diet, genetic susceptibility, certain chemicals, and radiations in addition to viral infections such as exposure to human papilloma virus (HPV).

Tobacco and alcohol usage are the major risk factors, which lead to nutritional deficiencies, and susceptibility to various carcinogens and thus lead to immune suppression. Seventy five percent of oral cancers are attributed to tobacco and alcohol usage. Heavy alcohol drinkers are frequently heavy smokers as well (WHO. 1984; Gupta1996; Yeole 1999; Gupta 2000). The risk for development of oral cancer is 3 to 9 time greater in those who smoke or drink and as much as 100 times greater in those who both smoke and drink heavily than in those who neither smoke nor drink (Neville 2002). A wide variety of tobacco habits like bidi smoking, tobacco chewing, and cigarette smoking, in that order, account for a large majority of these cancers (Sanghvi 1989).

Tobacco

WHO estimate has shown that 91% of oral cancers are due to tobacco usage (WHO. 1995).

Chewing (Smokeless tobacco)

Some of the common forms of smokeless tobacco used in India are pan, betel quid, khaini (tobacco & lime), mishri (burned tobacco), zarda (boiled tobacco), gadakhu (tobacco & molasses), mawa (tobacco, lime & areca)

Smoking

In India, smoking of bidis, cigarettes, pipe, cigar, etc. is common. Over 300 carcinogens have been identified in tobacco smoke or its water-soluble compounds. The most studied are aromatic hydrocarbon benzopyrene and the tobacco specific nitrosamines (TSNs), N- nitrosonornicotine (NNN), N-nitrosopyrrolidine (NPYR), N-nitrosodimethylamine (NDMA) and 4-methylnitrosamino-1-3-pyridyl-1-butanone (NNK) (Hecht 1993). These agents act locally on keratinocyte stem cells and are absorbed. They produce DNA adducts, principally O-6 methyl guanine and these interfere with the accuracy of DNA replication leading to mutations which contribute to the molecular chain of events leading to malignant transformation of a cell and its clonal derivatives.

Alcohol

Alcohol by itself is not a carcinogen (Doll 1981). Alcohol promotes carcinogenesis in a variety of ways. The proposed mechanisms are i) Acetaldehyde, which is the alcohol metabolite, has been identified recently as a tumor promoter (Blot 1992; Harty 1997), ii)Alcohol may act as a solvent and enhance the penetration of

carcinogens into the target tissues (Stenback 1969), iii) nutritional deficiency associated with heavy drinking (Harris 1997), iv)alcoholic liver disease is common in heavy drinkers and that reduces the detoxification of active carcinogens (Kato 1994).

Genetic polymorphisms

Majority of drinkers and smokers do not develop cancers suggesting a genetic cause. Single nucleotide polymorphisms (SNPs) of genes coding for carcinogen metabolism enzymes or for DNA repair genes may explain individual differences in the susceptibility to carcinogens. These could include genes that may influence behavior, which might lead to increased alcohol or tobacco consumption, as well as phase I and phase II metabolizing genes (such as *ADH*, *ALDH*, *CYP*, *GST* and *N*-acetyl transferase genes) that are likely to be important in determining internal carcinogenic dose. The subsequent development of DNA mutations, repair of these errors, or cell apoptosis might also be regulated by DNA repair genes or tumor suppressor genes.

Human Papilloma virus (HPV)

HPV has been detected in 31% to 74% of oral cancers and is also associated with papillomas, condyloma, verrucous leukoplakia, and carcinoma (Kashima 1990; Chang 1991; Vokes 1993; Franceschi 1996; Steinberg 1996).

Combination of risk factors

The combined effect (tobacco and alcohol) is greater than the sum of the independent effects and probably multiplicative (Elwood 1984; Tuyns 1988; Franco 1989). The combination of smoking and HPV infection and of alcohol and HPV infection may have an additive effect.

Diet

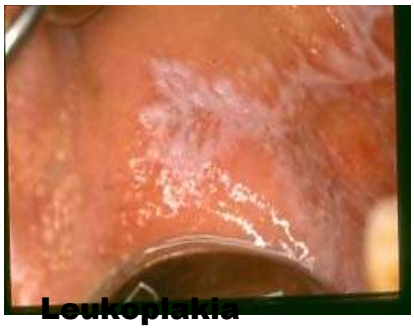
A diet rich in fruits and vegetables, particularly fruit, reduces the risk of oral cancer and premalignant lesions (Mucci 2002). Several studies have shown that higher levels of vitamin C or carotene consumption reduce the risk of oral cancer. The potentially increased risk associated with meat consumption is less clear (Mehrotra 2006). Results of intervention studies involving dietary change or dietary supplements have shown no clear evidence of benefit (Mayne 2006). La Vecchia and his colleagues estimated that approximately 15% of oral and pharyngeal cancer cases in Europe could be attributed to dietary deficiencies or imbalances (La Vecchia 1991).

Familial & Genetic predisposition

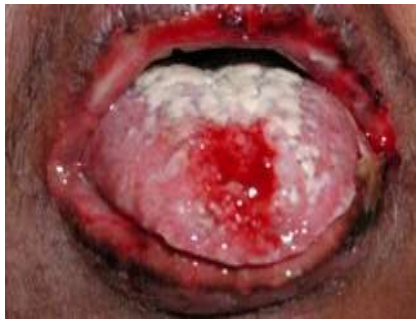
There is little evidence to suggest family history/genetic predisposition as a risk factor for oral cancer. Genetic predisposition has been suggested due to the fact that not all exposed to the risk factors develop oral cancer and sporadic cases of oral cancer occur in non-users of tobacco and alcohol and in young adults. Recently, many genetic events produced by chromosomal alterations caused by these risk factors have been proposed to underlie the histopathologic progression of oral squamous cell carcinoma (Califano 1996; El-Naggar 1996).

Dental factors

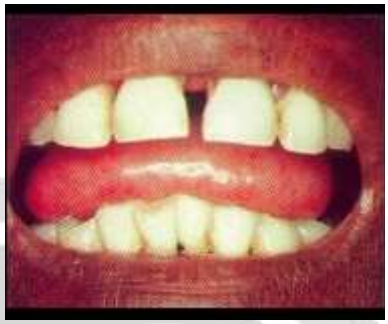
Wearing dentures *per se* is not a risk factor but chronic ulceration due to ill fitting dentures may promote a neoplasm in the presence of other risk factors (Lockhart 1998; Schildt 1998; Velly 1998).



Leukoplakia



Erythroplakia



Submucous

Treatment

Premalignant lesions

Various modes of treatment include surgery, radiotherapy, chemotherapy and combined modality treatments based on the site of the primary tumor, size, depth of infiltration, proximity to the bone, regional lymph node, and histology status.

Single modality treatment like either surgical resection or radiotherapy is preferred for early stage tumors (T1, T2). Patients with advanced stage of disease are candidates for combined modality treatment. Currently the role of chemotherapy is still investigational. Factors related to the patient like age, tolerance, general physical condition, occupation, socio-economic status, and factors related to the physician like surgical or radiotherapy skills, support and rehabilitation services influence the selection of initial treatment.

Prevention

Primary

Aims at elimination of risk factors from the community thereby minimizing the incidence. Physicians, dentists, health workers could play a major role in the elimination of risk habits. Also interventions can be made via schools, mass media, integrating health education with the existing community based programmes.

Secondary

Aims at detecting the disease at an early stage thereby reducing morbidity and mortality. Screening for oral cancer and precancers and chemoprevention come in this category. Oral cancer meets some of the criteria for disease screening. Oral visual screening is an effective tool because of the asymptomatic nature of the lesions, precedence by premalignant lesions and the detection of conditions like leukoplakia, erythroplakia and submucous fibrosis by simple visual examination. Population based screening cannot be recommended, but screening in high risk individuals is highly recommended (Sankaranarayanan 2005).

The over expressions of cyclooxygenase-2 (COX-2), phospho-epidermal growth factor receptor (pEGFR), activation of NFKB, RAR, and PCNA/Ki67 HPV gene expression and integration are important events in oral carcinogenesis and are the basis of targetedprevention strategies.

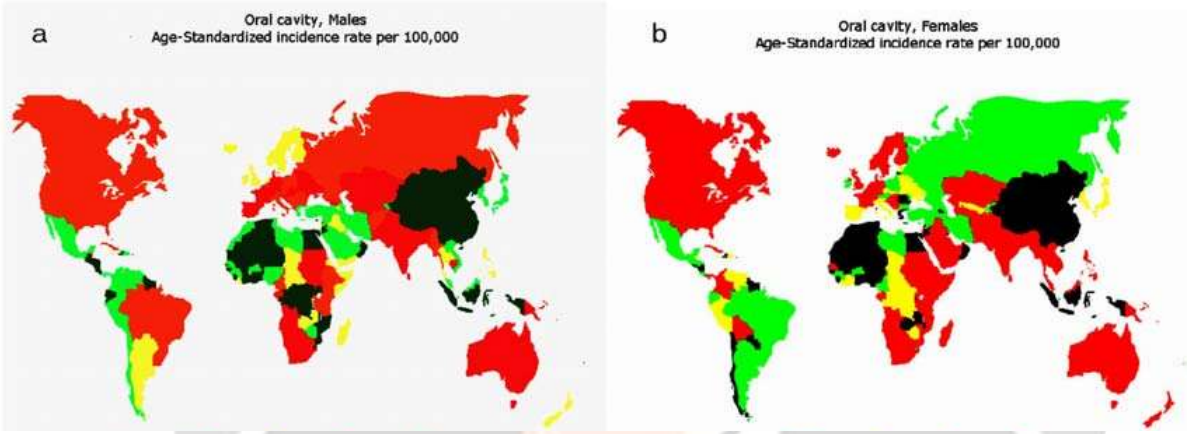
Tertiary

Aims at reducing the recurrence after treatment and reduction of morbidity after treatment.

RESULTS WITH EPIDEMIOLOGIC TRENDS OF HEAD AND NECK CANCERS

Head and neck cancers are among the 10 most common cancers globally. In India, it accounts for one fourth of male cancers and one tenth of female cancers (Yeole 2001). The sub-site predilection of head and neck squamous cell carcinoma (HNSCC) reflects the risk profile of a community and there are suggestions that these are changing over time.

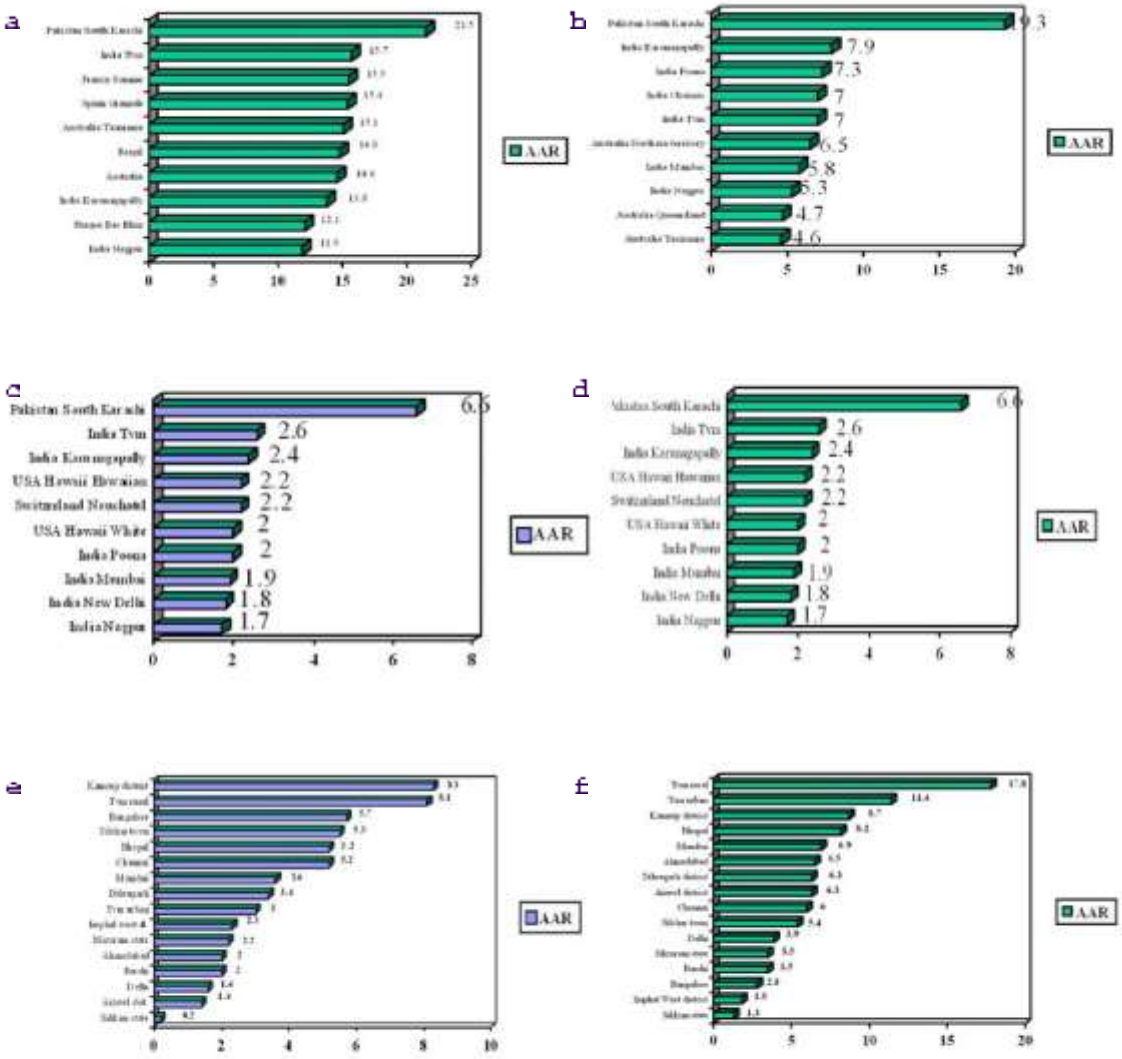
1. To determine the trends in incidence of head and neck squamous cell carcinoma over a time period in India.



2. To compare change in the trends of head and neck squamous cell carcinoma of India and US populations.

3. To evaluate etiologic basis for the change in trends (if any) of head and neck squamous cell carcinoma.

Figure 3.2: Population Incidence of AAR of Oral Cancers (C00-06) Males and Females



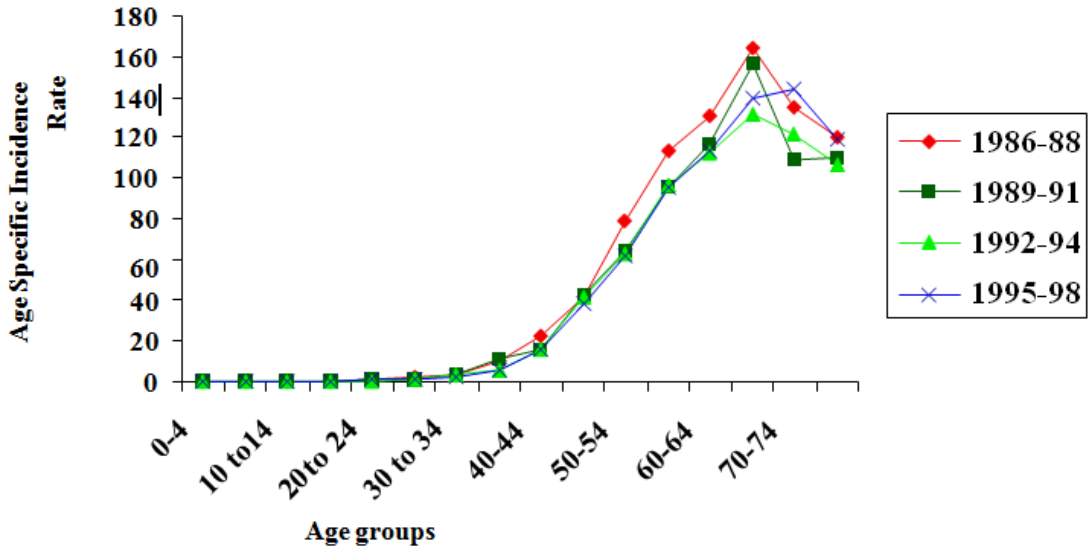
a: Oral cancers males, b: Oral cancers- females
c: Tongue cancers males, d: Tongue cancers females
e: Oral cancers India males, f: Oral cancers India females

Source: Cancer Incidence in five continents Vol. IX pVIX-IX)

Habit	Ingredients	Population
Pan/paan/betel quid	Areca nut, betel leaf, slaked lime, catechu,condiments, with or without tobacco	Indian subcontinent, South-east Asia, Papua,New Guinea, part of South America
Khaini	Tobacco and lime	Bihar –India
Mishri	Burned tobacco	Maharashtra-India
Zarda	Boiled tobacco	India and Arab countries
Gadakhu	Tobacco and molasses	Central India
Mawa	Tobaco, lime and areca	Bhavnagar –India
Nass	Tobacco, ash, cotton or sesame oil	Central Asia, Iran, Afghanistan, Pakistan
Naswar/niswar	Tobacco, lime, indigo, cardamom, oil, menthol,etc.	Central Asia, Iran, Afghanistan, Pakistan
Shammah	Tobacco, ash, lime	Saudi Arabia
Toombak	Tobacco and sodium bicarbonate	Sudan

Common forms of oral smokeless tobacco in developing countries (Johnson 2003)

Site	Urban								Rural							
	Male		Female		Young male		Young female		Male		Female		Young male		Young female	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Tongue	1019	21	298	14	123	22	47	13	44	16	12	23	6	15	4	29
Oral cavity	1252	26	1175	57	140	25	181	48	59	22	21	40	15	39	2	14
Larynx	863	18	104	5	100	18	24	6	43	16	5	9	5	13	3	21
Pharynx	1643	34	503	24	198	35	122	33	126	46	15	28	13	33	5	36



Age Specific Incidence Rates of Head and Neck Cancers in India

Site	LTR				CIRP			
	Urban		Rural		Urban	Urban	Rural	Rural
	M	F	M	F	M	F	M	F
Head & neck	27	64	54	494	4% (3.433-4.036)	1.6% (1.444-1.716)	2% (1.565-2.438)	0.34% (0.203-0.463)
Tongue	136	458	459	1250	.76% (0.657-0.864)	.23% (0.199-0.259)	0.33% (0.188-0.483)	0.07% (0.007-0.138)
Oral cavity	102	111	422	1068	1% (0.902-1.102)	.94% (0.816-1.065)	0.33% (0.213-0.522)	0.12% (0.079-0.162)
Larynx	150	1386	-*	-*	.69% (0.611-0.766)	.08% (0.064-.092)	0.24% (0.210-0.451)	0.003% (-.012-.066)
Pharynx	80	313	130	1304	1.27% (1.154-1.413)	.3% (0.287-0.386)	0.97% (0.676-1.261)	0.11% (0.055-0.168)

CONCLUSIONS

1. Epidemiological studies have shown that there is an overall reduction in the oral cavity cancers in India. This may be attributed to the decreased prevalence of tobacco use. The increase in tongue cancer incidence may suggest factors other than tobacco and alcohol in its genesis.
2. Human Papilloma Virus plays a major role in tongue carcinogenesis. Forty eight percent of the tongue cancer samples were positive for HPV16. Eighty-three percent showed integration. Both E6-p53 and E7-pRb pathways are involved in carcinogenesis with a preponderance of the later. Koilocytosis alone could not be
recommended as a screening method.
3. The assessment of awareness of oral cancer in a high-risk population revealed that the overall awareness of oral cancer and its risk factors was satisfactory, though gaps exist stressing the need for targeted health education and risk factors cessation counseling.
4. It is identified that oral self-examination is a potential cost-effective health education and screening tool to improve awareness of oral cancer in a high-risk community.

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