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## RESEARCH ARTICLE

### ORAL CANCER EPIDEMIOLOGY – INDIAN BASED REVIEW

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#### ABSTRACT

Oral cancer is the 6<sup>th</sup> most common cancer worldwide. However the incidence of oral cancer is increasing day by day. It may involve any anatomical site of the oral cavity. It is estimated around 43% of cancer death are due to usage of tobacco in any forms, unhealthy diet, alcohol consumption, change in lifestyle, and infections. It is known that over one-third of cancers are preventable and one-third are potentially curable provided they are diagnosed and treated in the early stage of the disease. This requires multidisciplinary approach to prevent and manage the disease.

## INTRODUCTION

Oral cancer is a major health problem in the Indian subcontinent, which ranks first among the top three types of cancer. Oral cancer is the 6<sup>th</sup> most common cancer worldwide. Oral squamous cell carcinoma represents from 90-95% of all malignant neoplasms of the oral cavity. The incidence and prevalence of oral cancer varies in various geographic regions due to various different etiological factors and influencing factors. Most frequently observed cancer in the Indian population are Lung, breast, colon, rectum, stomach and liver. Presently in India oral cancer is the 4<sup>th</sup> most common cancer in male while it is 5<sup>th</sup> most common in female. (Imran Ali *et al.*, 2011; Krishnan Nair, 2015) Oral cancer ranks second and third positions in Goa and Assam states respectively. Identification of the high risk factors in patients also helps in prevention of the development of the oral cancer. (Imran Ali *et al.*, 2011) It is estimated around 43% of cancer deaths are due to usage of tobacco in any form, unhealthy diets, alcohol consumption, changing in lifestyle and infections. It is known that over one-third of cancers are preventable and are one-third are potentially curable provided they are diagnosed and treated in the early stage of the disease. (Krishnan Nair, 2015) This requires multidisciplinary approach to prevent and manage the disease. In recent times the incidence of oral cancer is increasing in Asian countries. (SreeVidya Krishna Rao and Gloria Mejia, 2013) Future research should be aimed in

improving the quality of the data for early detection and prevention of oral cancer.

### Etiology of oral cancer

The use of tobacco in any form is considered as one of the main etiology for oral cancer. Epidemiological studies show that there is 5-9 times increased risk of oral cancer for tobacco smokers compare to non-smokers, and as much as 17 times increased risk in heavy smokers. (Brad W Neville, 2002) Snuff and chewing tobacco have also been associated with the increased risk for oral cancer which shows 4 times increased risk to develop a cancer. Alcohol use has been identified as a major risk factor which shows 3 times increased risk of developing of oral cancer. High exposure to ultraviolet light increases the chance of developing cancer of the lower lip. Diets with low levels of vitamins A and C or inadequate consumption of vegetables and fruits may contribute to the risk of oral cancer (Helbock *et al.*, 1998). (Imran Ali *et al.*, 2011) In India, the chronic use of betel quid is strongly associated with an increased risk for oral cancer. In recent studies it had been identified that HPV-16 is seen in almost 22% of oral cancer and HPV-18 is seen in 14% of the case which also increases the risk for cancer development. Aging and immunosuppression appears to predispose and increase the risk. (Shafer's textbook of "Oral Pathology" 6<sup>th</sup> edition)

### Risk Factors and Socioeconomic condition

Oral cancer is one of the disease which exhibits a social gradient. A meta-analysis of 41 case-control studies done in

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2008 across the globe had demonstrated that low socioeconomic condition is an independent risk factor for development of oral cancer. People who are self-employed such as agriculture, labouring, and working in industries are at high risk for oral cancer development. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Itsuochiba, 2001)

### Quid Chewing

It is an ancient ethnic practice that can be found in Southeast Asian countries where betel quid is chewed due to its medicinal properties. Areca nut which is used in quid contains arecoline specific nitrosamines that are known carcinogens. Lime a constituent of quid acts as a tumour promoter by hydrolysing alkaloids present in areca nut. (SreeVidya Krishna Rao and Gloria Mejia, 2013)

### Tobacco use

#### Smoking

Tobacco use is widespread in almost all over the world especially in the Asian countries. Tobacco smoking includes use of cigarettes, bidi and hookah. Smoking bidi increases the cancer risk upto 4 times in India, Bangladesh, Nepal, Pakistan and Sri Lanka. A meta-analysis in 2003 done by Rahman *et al* proved that dose-response relationship for the duration of bidi smokers in developing oral cancer. Local brand cigarettes that contain high tar and nicotine can pose a high risk for these patients. It is well appreciated that tobacco chewing has a high risk compared to smoking bidi. However the study results differ which shows 7.45% increased risk in smoking and 4.10% in chewing. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Raghu Radhakrishnan, 2012)

#### Smokeless tobacco

Smokeless tobacco are available in various forms such as panmasala, gutkha, tobacco flakes and sometimes as a whole leaf. The combination of ingredients are strongly genotoxic and carcinogenic. The dose response relationship in development of oral cancer is also observed in various studies. Comparatively smokeless tobacco has high risk when compared to smoking but the study results are different. (SreeVidya Krishna Rao and Gloria Mejia, 2013)

### Alcohol consumption

Alcohol consumption is also an important risk factor in developing oral cancer. Many studies had revealed that alcohol also shows synergistic effects when it is consumed along with tobacco. A prospective study in India conducted by Cancela *et al* in 2009 showed alcohol consumption had increased the development of cancer about 49%. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Raghu Radhakrishnan, 2012)

### Diet

The complexity of the diet makes it difficult in evaluating its role in development of cancer. A few studies had shown the actual relationship with diet and cancer. Polycyclic aromatic hydrocarbons, a carcinogen is found to be present in meat products which might increase the risk in development of cancer in non-vegetarians compared to vegetarians and

deficiency in intake of fruits and vegetable also increase the risk. (SreeVidya Krishna Rao and Gloria Mejia, 2013)

### Viral infections

Viruses also plays a role in the development of oral cancer. Viruses such as Epstein Bar virus, herpes simplex virus-1 and Human papilloma virus 16 & 18 were found in association with oral cancer. In recent studies it had been identified that HPV-16 is seen in almost 22% of oral cancer and HPV-18 is seen in 14% of the cases which also increase the risk for cancer development. HPV acts synergistically with betel quid chewing to cause high morbidity. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Raghu Radhakrishnan, 2012)

### Oral hygiene

Poor oral hygiene is also included in the risk factor since it can increase the incidence about 32% in males and 64% in females.<sup>3</sup> In long term denture wearers using ill-fitting dentures, the oral mucosa is subjected to chronic irritation which increases the risk of oral cancer. In India a study conducted by Guneri *et al* in 2005 reported that patient with ill-fitting denture for more than 15 years are at high risk for developing oral cancer. Also an unusual repeated manipulation includes self-inflicted biting or by sharp teeth can increase the risk of development of cancer. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Shafer's textbook of "Oral Pathology" 6<sup>th</sup> edition)

### Epidemiology of oral cancer

#### Incidence

Oral cancer ranks the 6<sup>th</sup> most common cancer world-wide. High incidence rates are reporting from the south-central and south-east regions like India. In India 8-10% of all cancers occur in the oral cavity. The incidence rate of oral cancer in Indian's is more than 10 per 100,000 people in 2001 and it has increased to 12-14 per 100,000 people in recent years. In South Asia Oral cancer accounts for one fourth of all the cancer in male and also the incidence is about 3-7 times more common when compare to the other developed countries. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Shafer's textbook of "Oral Pathology" 6<sup>th</sup> edition; Arvind Krishnamurthy, 2013)

#### Age and Gender

Oral cancer is considered to be a disease that occurs mainly in older individuals, however most of the cases occurred in between 50 and 70 years. Children as early as 10 years old also have been reported without any known risk factors. The mean occurrence of the cancer in different parts of the oral cavity in the country usually ranges from 51-55 years. In India a study conducted by Halboub *et al*. (SreeVidya Krishna Rao and Gloria Mejia, 2013) in 2011 had reported that 17 % of the patients are younger than 40 years. In India oral cancer affects males when compare to female with a ratio of 1.5 : 1 this is because male are commonly involved with deleterious habits. (SreeVidya Krishna Rao and Gloria Mejia, 2013) Age adds further dimension of age-related mutagenic and epigenetic changes leading to increased incidence of oral cancer below the age of 45. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Poul Erik Petersen, 2008)

## Site of occurrence in Oral Cavity

Site of occurrence depends on the predominant risk factors in that particular geographical region. In India tongue is the foremost common site of occurrence for oral cancer which accounts for about 42% in adults of all age group. It has been confirmed in various studies conducted in 2000, 2007, 2008, 2011. The carcinoma of floor represents 15-30% and also the sites like buccal mucosa and alveolar regions have increasing incidence due to direct exposure of smokeless tobacco. (SreeVidya Krishna Rao and Gloria Mejia, 2013; Poul Erik Petersen, 2008)

## Clinical features

The clinical feature of oral cancer varies in each patient which ranges from small asymptomatic oral lesion to a large symptomatic lesion. A high index of clinical suspicion is needed to diagnose small lesion, especially if the patient has any risk in development of oral cancer. The clinical symptoms such as pain from the lesion, referred pain to the ear, malodour from the growth, difficulty in speaking, discomfort while chewing, pain with swallowing, weight loss, swelling in the neck are common in oral cancer. In advanced case of oral cancer the neck nodes become enlarged and fixed to the underlying structure. Intra orally the advanced case will have ulceroproliferative growth with areas of necrosis and extension into the surrounding structures. Occasionally orocutaneous fistula, intractable bleeding, severe anaemia and cachexia may be present with trismus. (Raghu Radhakrishnan, 2012)

## Relevant diagnostic procedures

Early detection of oral cancer is the most effective way in reduction of mortality and morbidity. There are several tumour markers which aid in the risk assessment. Screening for the oral cancer should include a thorough history and examination. The clinician should be skilled enough to detect the lesion by clinical examination which includes the digital palpation of the lesion as well as the neck node regions. The diagnosis is confirmed with a biopsy. The specimen should be taken from the active and suspicious area, avoiding thenecrotic and ulcerated areas. (Raghu Radhakrishnan, 2012) Imaging such as Orthopantomography, CBCT, CT, MRI also plays a vital role in visualizing the bony involvement and also it provides additional information of the extent of the lesion, nodal involvement and distant metastasis from oral cancer. (Raghu Radhakrishnan, 2012)

## Prevention

As we all know "Prevention is Better than Cure". An ounce of prevention is worth more than a million pounds of cure. It is an inexpensive long term method of cancer control. The above statements prove that when there is sufficient and constant motivation to the people to quit the deleterious habits and encouragement to lead a healthy life style will prevent the occurrence of oral cancer to a maximum extent.

## Primary prevention

It refers to the avoiding carcinogens in the environment or in the dietary elements that are closely associated with increase in the risk of cancer development. Patients are also advised to

quit using tobacco and encouraged to undergo management if necessary.

## Secondary prevention

In India, Randomized intervention trials to evaluate oral visual inspection for the early detection and prevention of oral cancer started in 1986. In secondary prevention the subjects who have potentially malignant disorder are identified and closely monitored as well as treated in a possible way. In a study conducted in India which consisted of 36,471 tobacco chewers and smokers from rural population showed a reduced incidence of oral-precancerous lesions after secondary prevention. (Itsuoichiba, 2001; Liviu Feller and Johan Lemmer, 2012)

## Chemoprevention

Early chemoprevention is beneficial in patients who are at high risk for cancer development. Many studies with chemopreventive agents such as vitamin A, Vitamin E, Retinoids, Curcumin, Betacarotene and other newer agents have been extensively studied for cancer prevention. Studies shows various significant results. (Itsuoichiba, 2001; Liviu Feller and Johan Lemmer, 2012)

## Treatment

The treatment of Oral cancer generally requires a multidisciplinary approach. The primary aim of the treatment is always the eradication of the cancer to prevent recurrence and if possible to restore the form and function. The selection of the treatment modality depends on the nature of the carcinoma, and the general condition of the patient. The salient features in selection of the cases includes the site affected, the clinical size, the extent of local invasion, histopathological features, regional lymph node involvement and distant metastasis. Patient factors include age, general health status, a history of previously treated oral cancer and high-risk habits. Various treatment modalities include surgery, systemic cytotoxic chemotherapy and radio-therapy or combination of any of these. (Liviu Feller and Johan Lemmer, 2012)

## Palliative care

Palliative care is a specialized area of health care that focuses on relieving and preventing the sufferings of a terminally ill patient where definitive treatment is not possible. The distressing symptom in the patients suffering from oral cancer is because of the disease itself or a consequence of the treatment. Oral cancer can cause symptoms such as pain, trismus, difficulty in chewing, difficulty in swallowing, difficulty in speaking. Following treatment such as radiotherapy can cause consequences such as mucositis, xerostomia, loss of taste, candidiasis, nausea, vomiting, trismus, osteoradionecrosis and dental related problems. Pain management in palliative care may be local, systemic or both. In severe pain condition the parental opioid therapy can be recommended. Pain can also be managed with topical analgesics to relive somatic pain. In few cases management of infection or other co-morbid conditions may relive pain for many patients. (Krishnan Nair, 2015; Shubhavinyasa and Shraddha, 2014) Kerala is the place where many palliative care centres are present with a good intension to care for the people as well as all over in India palliative care centres have come up both in government and private sectors.

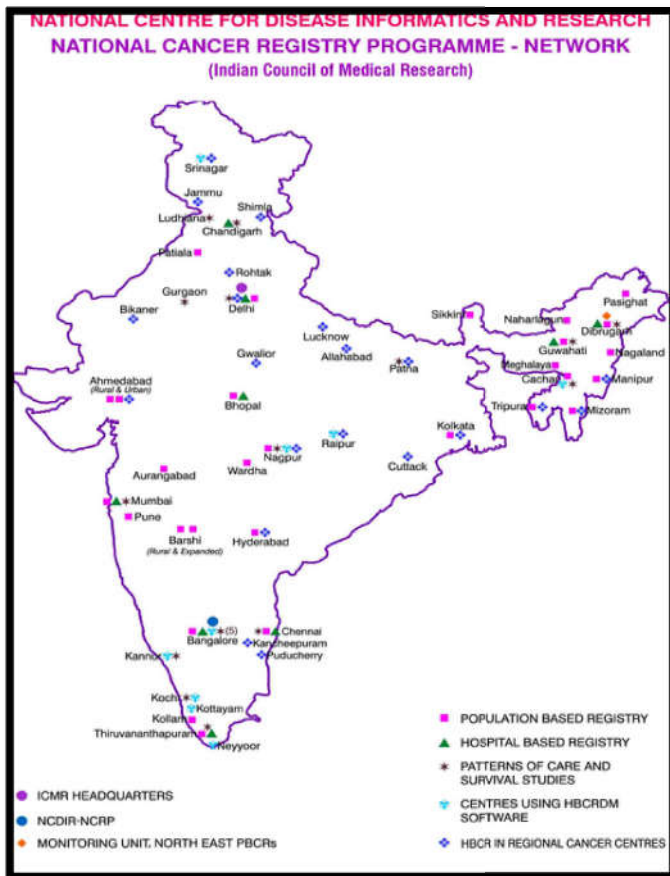


Fig.1. National Cancer Registry - 2012-14

## Recurrence

It is an important aspect of the treatment outcome which indicates a poor prognosis. According to an institutional study conducted by Priya *et al* in 2012 in India, the average disease free survival time is around 35 months. Recurrence can be local, regional, locoregional or second primaries. The recurrence rates vary between 25-40% after a follow-up period of 2-4 year. T1-T2 lesions are often associated with a risk of regional metastasis of 10-30% respectively whereas the tumour stage of T3 & T4 has a significantly greater risk of regional lymph node involvement. Loco-regional lymph node involvement indicates poor prognosis. (Juliana Nogut, 2012)

## Mortality and survival

Despite many advanced treatment modalities the 5 year survival rate had been reported as low for oral cancer. This is mainly because about two-third of the person with oral cancer were in advanced stage at the time of diagnosis. (Poul Erik Petersen, 2008) In India, oral cancer accounts for 1<sup>st</sup> most common cause of fatality in men which account for more than 70% during their productive age i.e, between 30-69 years of age, (Cancer scenario in India, 2015) while it accounts for 4<sup>th</sup> most common fatality in women. Other than cancer, various factors influence the mortality such as continuing habits like tobacco use, betel quid chewing and alcohol consumption. This situation may be further complicated by poor socio-economical conditions. (Imran Ali *et al.*, 2011; Ken Russell Coelho, 2012)

## National centre for disease informatics and Research

The National Cancer Registry Programme (NCRP) was commenced by the Indian Council of Medical Research

(ICMR) with a network of cancer registries across the country (Fig.1). The main objectives of this Programme were:

1. To generate reliable data on the magnitude and patterns of cancer
2. Undertake epidemiological studies based on results of registry data
3. Help in designing, planning, monitoring and evaluation of cancer control activities under the National Cancer Control Programme (NCCP)
4. To develop training programmes in cancer registration and epidemiology.

With these objectives three Population Based Cancer Registries (PBCRs) at Bangalore, Chennai and Mumbai and three Hospital Based Cancer Registries (HBCRs) at Chandigarh, Dibrugarh and Trivandrum were commenced from 1<sup>st</sup> January, 1982. The PBCRs had gradually expanded over the years and as of now there are around 23 PBCRs under the NCRP network. The NCRP is a long term activity of the ICMR and the office of the NCRP is located in Bangalore. It is assisted by a Steering Committee and a Monitoring Committee that meets periodically to oversee and guide its functioning.

## Conclusion

Oral cancer is the most common cancer in India. Site of occurrence and tobacco is a major health related and socio-economical burden in India and its subcontinents. Tobacco products are the main etiology for oral cancer, which directly proportionate the risk of oral cancer, which directly proportionate the risk of oral cancer. India has world's highest number of oral cancers which accounts for 20%. The common site of occurrence varies in different geographical regions however tongue appears to be the most common site in the oral cavity. Being a developing country, India needs special attention on this issue because Indian economy plays a vital role in global economy and had been affected tremendously by the alarming rise of cancer in the last few decades. In India "late diagnosis" is the major factor which worsens the disease prognosis this is due to lack of awareness in the community based population. Hence early detection and prevention of oral cancer is important to reduce the occurrence of oral cancer. Creating awareness among public about physical activities, healthy life style, reducing occupational and environmental exposures to tobacco reduced the risk of oral cancer. Our education should focus on harmful effects of tobacco, alcohol usage and to motivate people towards healthy life style.

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