To Study the Correlation of Duration of Tobacco Intake with Occurrence of Oral Cancer – A Two Year Hospital Based Study in Bihar

Dr. Dilip Kumar[1], Dr. Tripurari[2*], Dr. Sujeet Kumar[3]

1Associate Professor, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.

2Junior Resident, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.

3Junior Resident, Department of Pathology, Patna Medical College and Hospital, Patna, Bihar, India.

Abstract

Objectives: A hospital based study, we conducted to correlate the occurrence of oral cancer with duration of tobacco intake as tobacco consumption practice is widespread throughout the world specially in India leads to oral malignancies.

Methods: Total of 109 patients with oral cancer attending various specialties of Patna Medical College and Hospital, Patna fulfilling the inclusion criteria recruited during two-year period from November 2017 to October, 2019 after obtaining written informed consent. Procedure like FNAC and biopsy from suspected lesions and enlarged lymph nodes were processed in department of pathology.

Results: In our study among 109 cancer patients' average duration of intake of tobacco and occurrence of oral cancer is 30.3±13.1 years with median age of 30 years. Chewing tobacco is most common mode of consumption and buccal mucosa and tongue with 31.2% each are most common sites of cancer, presenting with ulcer (60.55%). More than half of patients have cervical lymph nodes metastasis at the time of diagnosis. Males are more commonly affected than females with M: F ratio 4:1.

Conclusion: we observed that tobacco in any form is carcinogenic and is a leading cause of morbidity and mortality in Indian population. Strict cessation of all forms of tobacco use and follow-up should be implemented to reduce the incidence of oral cancer.

Keywords: *oral cancer; tobacco chewing; paan; alcohol; bidi; gutkha*

Introduction

In 21st century cancer is a leading cause of morbidity and mortality worldwide and is most important barrier to increase life expectancy in all countries. Among all cancers, oral cancer is estimated approximately 354,864 new cases and 177,384 deaths worldwide in 2018 [1]. New data on cancer trends in India shows an alarming 114 % rise in cancers of the lip and oral cavity in the last five years. Total

119992 cases of oral cancer were reported in India which constitutes 11.42% of all cancer incidence and 72611 deaths constituting 10.09% of all deaths due to cancer in year 2018. Incidence among male is 16.1% (92011) and in female is 4.8% (27981) [2].

Male are affected much more commonly than female due to various socio-physiological factors [3]. There are different risk factors associated with premalignant as well as invasive oral cavity cancers. These are tobacco, alcohol, infection, radiation and poor dental hygiene. Among them tobacco and its products are the most common and important risk factor for oral cancer including head and neck cancer. About 90% of oral cancers are associated with tobacco and its different products. There are many different form of tobacco to deliver nicotine to their users. The most common way is tobacco smoking. It contains more than 7000 chemical compounds of which many are known carcinogens. Important carcinogens in smoke are – benzpyrene, tobacco specific nitrosamines, benzene, formaldehyde, carbon mono-oxide, cyanide, acrolein etc.[4,5].

Tobacco can be taken by smoking as cigarette, bidi, cigar, electric cigarette, hookah, kreteks, pipe, reverse smoking etc or as smokeless tobacco which are generally placed inside oral cavity in contact with mucosa like khaini ,betal quid/ paan , mishri/gul ,zarda, gadakhu, mawa, gutka,paan mashala/sweet supari. Trend of taking smokeless tobacco is more common in India than American and European countries [6,7].

Other important risk factor for oral cancer is alcohol which is an independent and synergistic risk factors associated with head and neck cancer[8]. Although tobacco and alcohol synergistically influence the development of oral epithelial dysplasia (OED), exclusive tobacco consumption is more likely than exclusive alcohol consumption to give rise to OED[9] .Among infections HPV, EBV, HSV, and Candida are also considered as important risk factors. HPV16 and HPV18 are most important viral infections which may lead to oral cancer[10]. Radiotherapy for other head and neck subsites and dental factors like Poor oral hygiene, poor dental status, chronic ulceration from ill filled denture are also potential risk factors for oral cancer.

Consumption of either smoke or smokeless form of tobacco causes oral cancer [11]. The direct relationship between tobacco and oral cancer led to the aphorism '*cancer is where tobacco is*'[12].

Smokeless tobacco use is more prevalent overall then smoked tobacco and 90% of world's smokeless tobacco uses are found in south Asia specially in India. These risk factors are associated with various Oral potentially malignant disorders (OPMDs) including erythroplakia, erythroleucoplakia, leucoplakia, oral submucosal fibrosis (OSF) etc.

Approximately 95% cancers of head and neck region are squamous cell carcinoma involving oral cavity and oropharynx [13,14,15]. Duration of risk exposure and invasive squamous cell carcinoma are directly proportional to each other.

Pathogenesis of oral carcinoma - It is a highly complex multifocal process that takes place when squamous epithelium is affected by several genetic alterations in response to carcinogens in tobacco and its products. Oral cancer develops over many years, and during this period, there are multiple sites of neoplastic transformation occurring throughout the oral cavity known as field cancerization[16,17,18]

Molecular Biology of Squamous Cell Carcinoma. As with other cancers, the development of SCC is driven by the accumulation of mutations and epigenetic changes that alter the expression and

function of oncogenes and tumor suppressor genes, leading to acquisition of cancer hallmarks, such as resistance to cell death, increased proliferation, induction of angiogenesis, and the ability to invade and metastasize. Tobacco carcinogens induce mutations frequently involving the p53 pathway as well as proteins responsible for the regulation of squamous differentiation, such as p63 and NOTCH1.

Histologic progression of oral cancer – Normal mucosa → Hyperplasia/ Hyperkeratosis → Mild/Moderate dysplasia → Severe dysplasia/CIS → Squamous cell carcinoma [19]

Molecular progression of oral cancer— No knowm genetic alterations →9p21(p16) → 17p13(TP53) → p63,NOTCH 1 → Squamous cell carcinoma [18].

Diagnosis - purely based on biopsy from most accessible suspected lesion and oral exfolietive cytology may act as adjunctive to biopsy but cannot replace biopsy for confirmed diagnosis [8].

Aims and Objective

The present study has been proposed to -

1. Evaluate the average duration between intake of tobacco/tobacco products and occurrence of oral cancer.

2. Histopathological pattern of lesions among patients.

Materials and Methods

The following study, cover all patients of oral cancer attending various specialties of Patna Medical College and Hospital, Patna. A total of 109 patients with oral cancer fulfilling the inclusion criteria recruited during period of 1st of November, 2017 to 31st of October, 2019 after obtaining written informed consent. Accrual of patients was started after ethics approval from the institute ethics committee. Histopathological examinations were done in Department of Pathology, Patna Medical College and Hospital, Patna.

Inclusion Criterias

1. Oral cancer involving oral cavity and oropharynx only.

2. Patient addicted with tobacco and its products.

3. Patient giving informed consent.

Exclusion Criterias

1.Other head and neck cancer extending into oral cavity and oropharynx.

2. Prior history of radiotherapy.

3. Prior history of chemotherapy.

4. Premalignant lesions and or carcinoma in situ.

5. Carcinoma with unknown primary from oral cavity and oropharynx.

6. Oral cancer occurring without addiction of tobacco and its products.

7. Metastasis to oral cavity and oropharynx.

8. Patients refusing to give written informed consent.

Statistical Analysis

Categorical data are presented as number and percentage, normally distributed data are presented as mean with standard deviation (SD), and skewed data are presented as median.

Study Design

This was a single arm cross sectional study. The study aims to enroll only those patients having oral cancer including oral cavity and oropharynx with history of intake of tobacco in any form. In our study, different subsites of oral cavity and oropharynx were included].

Fine needle aspiration cytology (FNAC), biopsy (Bx) and pattern of histopathology were designated as according and finally establishing average duration of intake of tobacco/tobacco products and occurrence of oral cancer.

Observations and Results

Total 109 patients were diagnosed for oral cancer at different subsides and mean age of patients was 52 ± 13.58 years. Maximum age at presentation was 85 years while minimum age was 23 years. Maximum no. of patients was belonging to age range of 51-60 years. 85 patients (78%) were male while remaining 24 patients (22%) were females. Sex ratio of male to female was 4:1. 29 (27%) were farmer and 20 patients (18%) were laborer. 80 (73.4%) Patients were belonging to low socio economic status. 48 patients (44%) got exposed at age 16 - 20 years. 86 (79%) were addicted for tobacco in form of khaini. 67 patients(76%) were chewing up to 10 times per day while 14 patients (16%) were chewing 10 to 20 times per day. 12 (14%) were having history of retaining tobacco (khaini) in their mouth for whole night . 28 patients (26%) were bidi smokers and 12 patients (11%) were cigarette smokers. 25 patients (23%) were consuming Gutkha. 16 patients were consuming upto 10 packs of gutkha per day while 2 cases were taking 10 to 20 packs per day . 23 patients (21%) were consuming paan and total 14 patients (13%) were using gul/mishri.49 patients were alcoholic. Among 109 cancer patients, 30 patients (27.52%) developed cancer in 11 to 20 years and 28 patients (25.68%) between21 to 30 years of consuming tobacco. Average duration of intake of tobacco and occurrence of oral cancer is 30.3 ± 13.1 years with median age of 30 years. In our study most common site of oral cancer was buccal mucosa with 34 patients (31.2%) and same for tongue 34 (31.2%) and collectively contributing 62.38%. 66 (60.55%) patients presented with Ulcer at site and next common presentation was growth in 31 (28.44%). cervical lymph nodes were positive for metastasis in 60 patients (55%). Moderately differentiated squamous cell carcinoma (MDSCC) diagnosed in 56 patients (51%) and 50 patients (46%) were reported as Well differentiated squamous cell carcinoma (WDSCC).
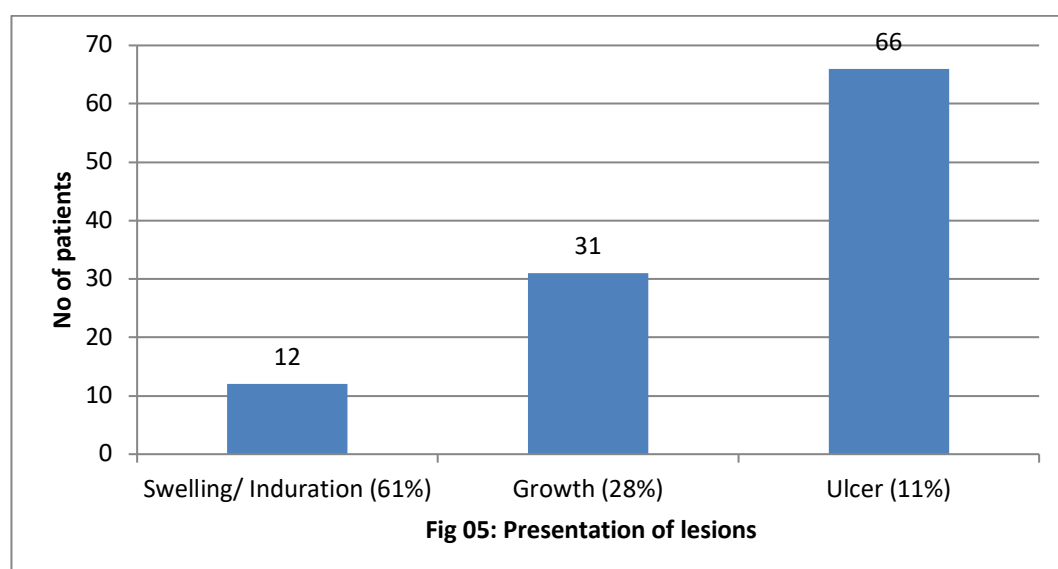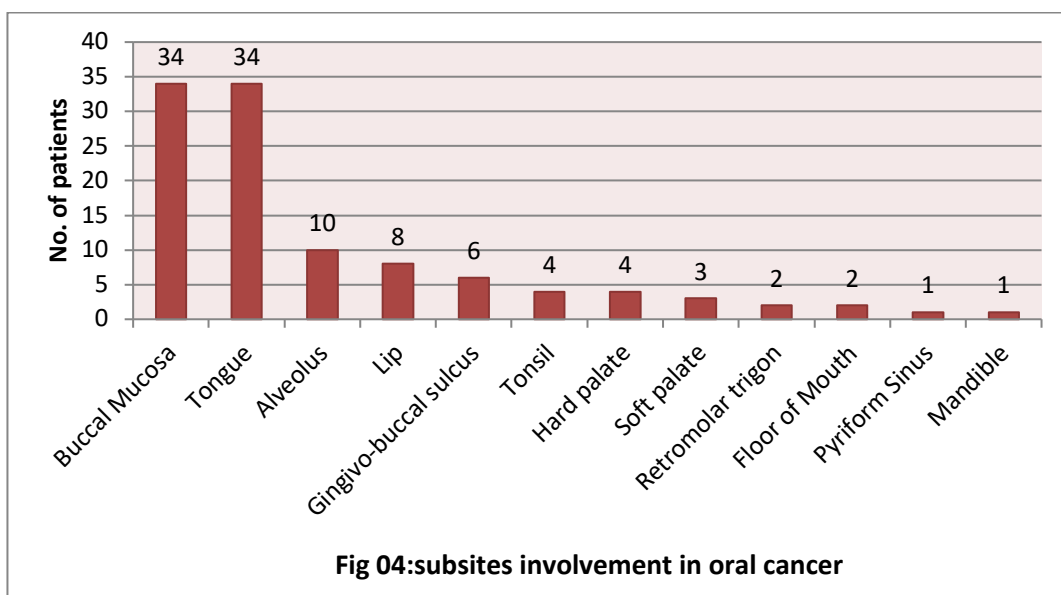

Fig 01: Age frequencies(years)
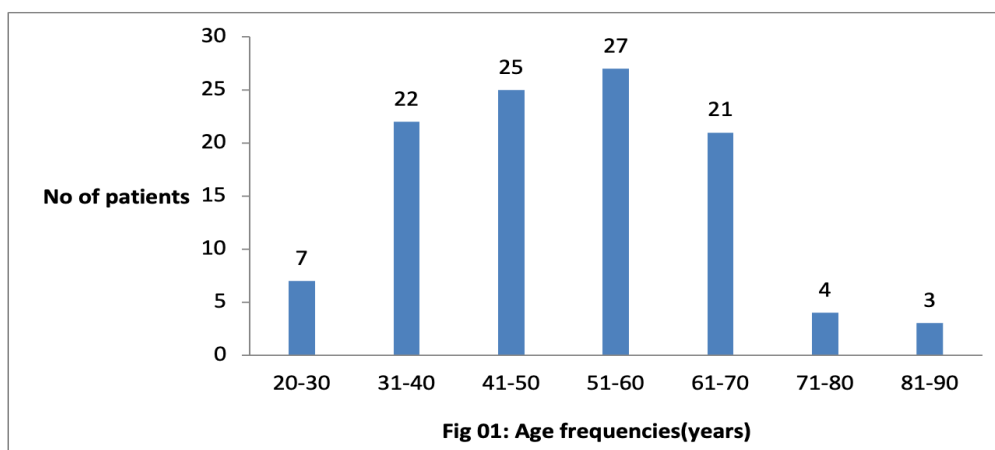
Table 01: Age distribution of patients	
Parameters	Age(years)
Maximum	85
Minimum	23
Median	60
Mean	52
SD	13.58

Table 02: Patient's Sex Distribution		
SEX DISTRIBUTION	NUMBER	PERCENT
MALE	85	78
FEMALE	24	22
Total	109	100
M:F	4:1	

Table 03: Age at 1st exposure to tobacco and its products (yrs)		
Age group	No of patients	Percent
0-10	6	5.5
11-15	19	17.4
16-20	48	44.0
21-25	20	18.3
26-30	12	11.0
31-35	1	1.0
36-40	2	1.8
41-45	0	0
46-50	1	1.0
Total	109	100

Fig 02: Age at 1st exposure with tobacco
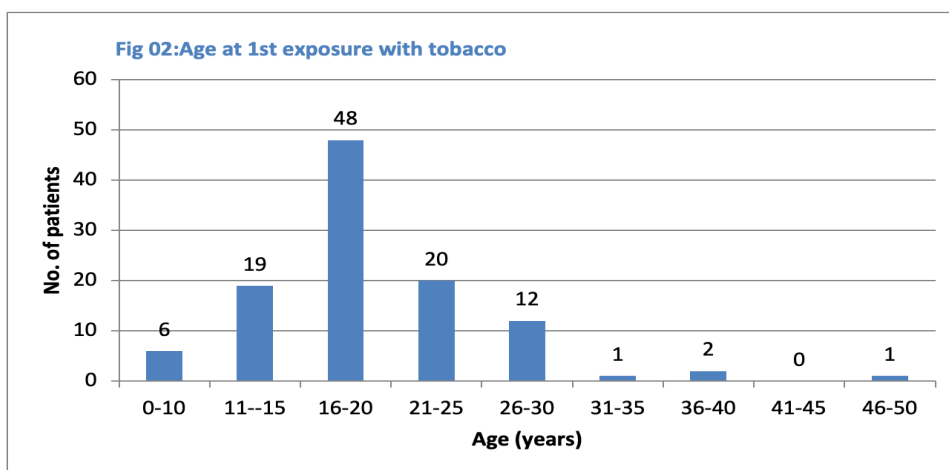
Table 04: average duration of tobacco intake and occurrence of oral cancer		
Duration (years)of tobacco intake	Number of patients	Percent
0-10	3	2.75
11-20	30	27.52
21-30	28	25.68
31-40	23	21.10
41-50	19	17.44
51-60	5	4.59
61-70	1	0.92
Total	109	100
Mean	30.266 years	
Median	30 years	
SD	±13.1	

Fig 03:Duration between intake of tobacco and occurence of cancer (years)

Fig 04:subsites involvement in oral cancer

Fig 05: Presentation of lesions

Fig 06 : Grading/Pattern of Histopathology
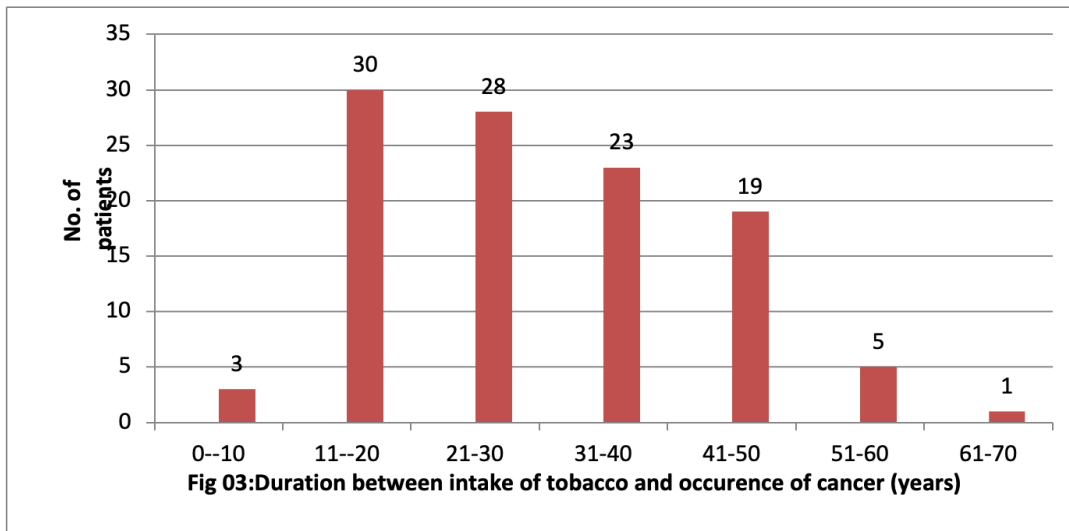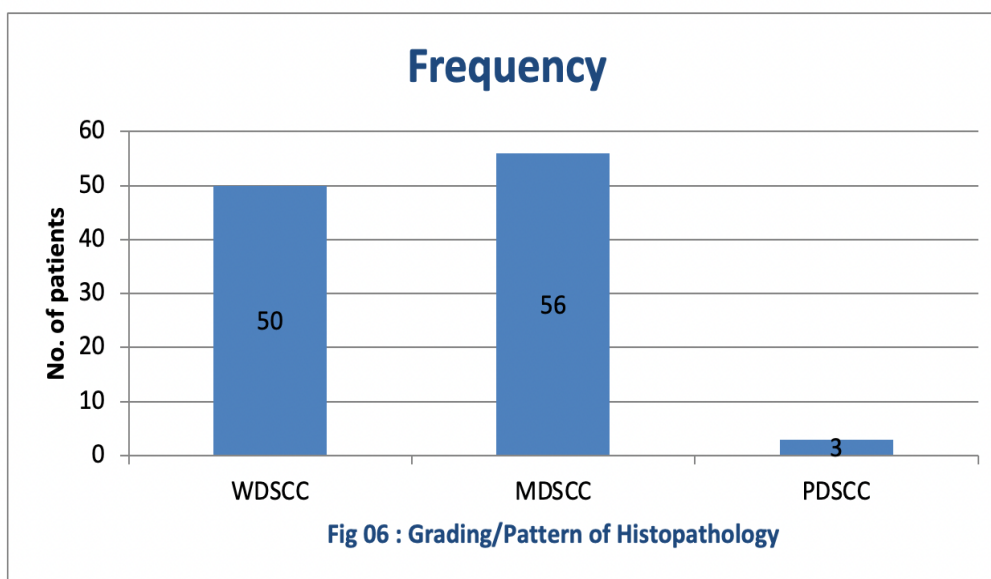
Table 05:Smokeless tobacco users [number(percent)]						
	Khaini	Guthka	Paan	Paan masala	gul/mishri	Khaini+Gutkha+Paan+ paan mashala
YES N(%)	86 (79)	25 (23)	23 (21)	16 (15)	14 (13)	81 (74)
NO, N(%)	23 (21)	84 (77)	86 (79)	93 (85)	95 (87)	28 (26)
TOTAL, N(%)	109 (100)					

Table 06: Frequency of taking smokeless tobacco		
Frequency/day	khaini chewers Number (%)	Gutkha chewer No. (%)
occasional	6 (7)	6 (24)
Less than 10 times	67 (76)	16 (84)
11-20 times	14 (16)	2 (11)
More than 20	1 (1)	1 (5)
Total	88(100)	25(100)

Table 07: Average duration of contact with tobacco and its products		
Average duration of contact(minutes)	Number	Percent
Less than 15	68	77
15-30	18	20
More than 30	2	3
Total	88	100

Table 08: Tobacco smoking [Number (percent)		
	Cigarette N(%)	Bidi N(%)
Yes	12 (11)	28(26)
No	97 (89)	81 (74)
Total	109 (100)	109 (100)

Table 09: Smoking Frequency (Pack years)		
(pack years)	Cigarette N(%)	Bidi N(%)
occasional	5 (42)	9 (32)
<10	4 (34)	14 (50)
10-20	2 (17)	5 (18)
>20	1 (8)	0
Total	12(100)	28 (100)

Table 10: Alcohol consumption		
Alcohol consumption	Number	Percent
Occasional drinker	36	73
Moderate drinker	2	4
Heavy drinker	11	23
total	49	100

Table 11: Paan mashala/Paan/Gul consumption frecuency			
(pack/day	Paan mashala	Paan	Gul/Mishri
Occasional	10 (63)	9 (38)	1 (7)
<5	5 (31)	10 (44)	5 (36)
>5	1 (6)	4 (18)	8 (57)
Total	16 (100)	14(100)	14 (100)

Discussion

Tobacco and its product consumption are well established risk factors for oral cancer. Average duration between intake of tobacco and tobacco products are one of the important determinants for occurrence of oral cancer. Multiple epidemiological studies showed that the incidence of oral cancer varies considerably between different parts of the world with the highest levels in the Indian subcontinent and the lower ones in western countries

Our study on 109 patients shows that median age of diagnosis of oral cancer is 60 years with mean age 52± 13.58 years. Peak age group is 51-60 years followed by 41-50 years.Males are more commonly affected than females with M:F ratio 4:1.Similar studies done by Khetchandra S wasnik et al (1998) found that most common age at presentation was 51-60 years with M:F ratio 3:1 [20]. Bhawna et al (2017) did hospital based study at Pune on 187 oral cancer patients and reported as mean age (yrs) at presentation was 56.49 ±11.96 with M:F ratio 4:1 [21]

In our study we found that average duration between intake of tobacco and occurrence of oral cancer is 30.3 ± 13.1 years. Most patients present with oral cancer after 20 years of tobacco consumption. Peak duration of consumption is 11 to 20 years followed by 21 to 30 years before occurrence of oral cancer.

International Head and Neck Cancer Epidemiology Consortium (INHANCE)(2019) pooled analysis suggest that increased head and neck cancer (HNC) risks observed with earlier age at starting tobacco smoking are largely due to longer duration and higher cumulative tobacco exposures [22]. Khetchandra et al (1998) reported close association between average duration of smoking and duration

of tobacco chewing with occurrence of oropharyngeal cancer [20]. Ariana Znaor et al (2003) also reported similar finding between different age group of patients of Chennai and Trivandrum.[23]

In our study, most common site for occurrence of oral cancer is buccal mucosa and tongue. Boyle P (1993) reported that more than 50% of the cancer arises from the ventro-lateral aspects of the tongue and the floor of the mouth in Western countries [24]. The World Health Organisation Report (1997) and Ezzati et al (2006) reported that, oral cancer is significantly high in the buccal and commissural mucosa in the Southeast Asian countries. The reason behind is the used of unrefined topical smokeless tobacco in mouth for long periods.[25,26]

Bidi smoking is more popular than cigarette smoking in our region because of cheaper and easy availability. Gutkha, paan, paan mashala and gul/mishri are another form of tobacco which are more popular among young people. Prabha balaram et al (2002) reported as paan-masala/ Gutkha is an alternate type of tobacco which is an independent risk factor.[27]

Bhawna Gupta et al (2017) reported that excessive alcohol consumption are well established risk factors for oral cancer in India[21]. Similar results are obtained by P. Balaram et al. (2002) from south india patients[28]. Pooled analysis in the INHANCE consortium by T.N. Toporcov et al (2015) found a dose–response relationship between oral cancer and alcohol.[22]

Summary

Oral cancer is a leading cause of morbidity and mortality in Indian population. Its occurrence depends on many factors among which tobacco is the most important. Chewing tobacco is most common mode of consumption. Analysis of 109 patients shows median age of diagnosis of oral cancer is 60 years with mean age 52 ± 13.58 years. However it is uncommon below 30 years of age. Males are more commonly affected than females with M: F ratio 4:1. Peak age group of 1st exposure to tobacco and its products is 16 to 20 years. Average duration between intake of tobacco and occurrence of oral cancer is 30.3 ± 13.1 years. Most patients present with oral cancer after 20 years of tobacco consumption. Buccal mucosa and tongue with 31.2% each are most common sites of cancer, presenting with ulcer (60.55%). More than half of patients have cervical lymph nodes metastasis at the time of diagnosis. Half of the patients diagnosed as moderately differentiated squamous cell carcinoma (MDSCC) followed by well differentiated squamous cell carcinoma (WDSCC).

Two third (73.4%) of patients are belonging to low socio-economic class among which 45% are farmers and laborers. These patients are more exposed to tobacco chewing and smoking. Chewing tobacco is not popular among females. However 21% of oral cancer patients are females working as home maker, using gul/mishri for cleaning their teeth and few are addicted to bidis due to cheap and easy availability.

Use of smokeless tobacco is most popular than smoking in our region. It is popular among drivers and shopkeepers. More than 3/4th patients are addicted for khaini and 2/3rd are chewing up to 10 times per day.

Alcohol is synergistic as well as independent risk factor for oral cancer. Approximately half of patients are mild drinkers and 1/4th are heavy drinkers.

Bidi smoking is equally popular among male and females. It is more popular than cigarette smoking in our region because of cheaper and easy availability . Gutkha, zarda and paan mashala are another form of tobacco which are more popular among young people.

Conclusion

In conclusion, our present study offers an up-to-date picture of major causes of oral cancer in relation with average duration of exposure with causative agents . Lack of any documentary and supportive evidences related to this regional area regarding etiopathology, causative factors and unawareness among people prompted us to carry out this study. we observed that tobacco in any form is carcinogenic. Age at first exposure, duration of contact with tobacco in each dose, frequencies of tobacco intake per day are strongly associated with occurrence of oral cancer. Strict cessation of all forms of tobacco use and follow-up should be implemented to reduce the incidence of oral cancer. Widespread use of these and other products by children, as well as adolescents, is mostly due to their pleasant taste, low cost, and easy availability. Oral cancer rates are increasing due to use of tobacco particularly among the lower socioeconomic levels, that constitute the large majority of the population. It is therefore important to establish appropriate data management, monitoring, and evaluation systems. In addition, oral cancer control policies should be implemented to change the lifestyle and behavior of high-risk populations through focused legislation and regulation such as pictorial health warnings on chewing tobacco, cigarette & bidi packets, creation of smoke-free areas, bans on tobacco advertising and promotion, provision of cessation services, increased tobacco taxes as well as building a health infrastructure aimed at enhancing the health promotion awareness and periodic screening.

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