

ORIGINAL ARTICLE

Clinico-epidemiological profile of oral potentially malignant and malignant conditions among areca nut, tobacco and alcohol users in Eastern India: A hospital based study

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ABSTRACT

Context: With an increase in the abuse of various oral habitual products in India over the past few decades; the incidence of oral potentially malignant conditions as leukoplakia, oral submucous fibrosis and squamous cell carcinoma (SCC) rates have also increased. No recent study has been conducted reporting the scenario of oral cancer and potentially malignant conditions in Eastern India (specifically Kolkata). **Aims:** The present study was conducted at Dr. R. Ahmed Dental College, Kolkata during 2010-2011 to find a possible correlation between the effects of the different oral habits, age, sex and the different types of oral mucosal lesions among patients reported to the hospital. This study also enabled us to see the predilection of the various histopathological stages of the lesions for different sites of the oral cavity. **Subjects and Methods:** The study group consisted of 698 patients having either oral potentially malignant or malignant lesion. The control group consisted of 948 patients who had reported to the hospital for different oral/dental problems and had the habit of tobacco, areca nut and/or alcohol usage for at least 1 year. **Statistical Analysis:** The unadjusted odds ratio, the 95% confidence interval, and the *P* value were calculated to correlate patients with/without different kinds of habit and having/not having various kinds of oral lesions. **Results:** Our study shows that for males having the habit of taking smokeless tobacco or mixed habit poses the highest risk for developing SCC. For females, significant risk of developing SCC was found in patients habituated to processed areca nut chewing. **Conclusion:** This study presents probably for the first time in recent years the occurrence of oral potentially malignant and malignant conditions amongst patients having deleterious habits in a hospital based population of Kolkata.

Key words: Areca nut, leukoplakia, mixed habit, oral squamous cell carcinoma, oral submucous fibrosis, smokeless tobacco, smoking tobacco

INTRODUCTION

The information obtained from epidemiological studies reveals various patterns of oral habits at different places.

These patterns have provided important data for a number of research studies.

Most commonly observed conditions found associated with deleterious oral habits are erythroplakia, leukoplakia (LKP) [Figures 1 and 2], oral submucous fibrosis (OSF) [Figures 3 and 4], verrucous carcinoma and oral squamous cell carcinoma (SCC) [Figures 5 and 6]. Although many studies have been carried out in different states of India few such studies have been conducted in Eastern India in recent times. Hence, the present study was conducted to find the clinico-epidemiological profile of various oral cancer and potentially malignant cases and their association with various oral habits.

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Figure 1: Clinical photograph of leukoplakia at the angle of the mouth

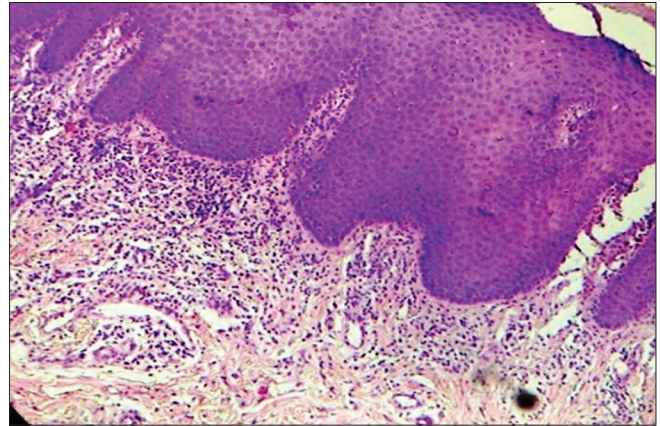


Figure 2: Photomicrograph showing epithelial dysplasia (H and E, $\times 100$)



Figure 3: Clinical photograph of oral submucous fibrosis

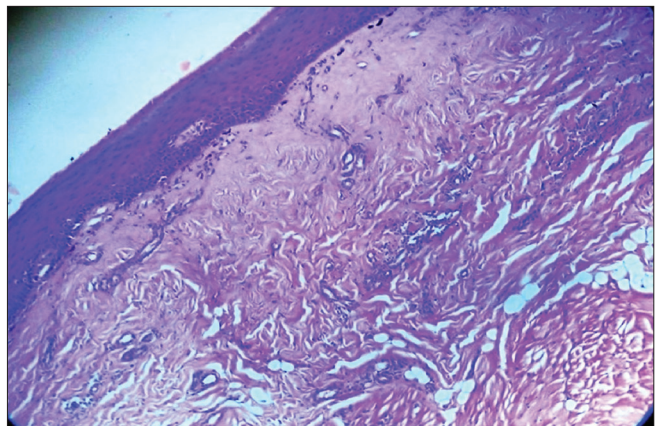


Figure 4: Photomicrograph of oral submucous fibrosis (H and E, $\times 100$)



Figure 5: Clinical photograph of oral squamous cell carcinoma of the buccal mucosa

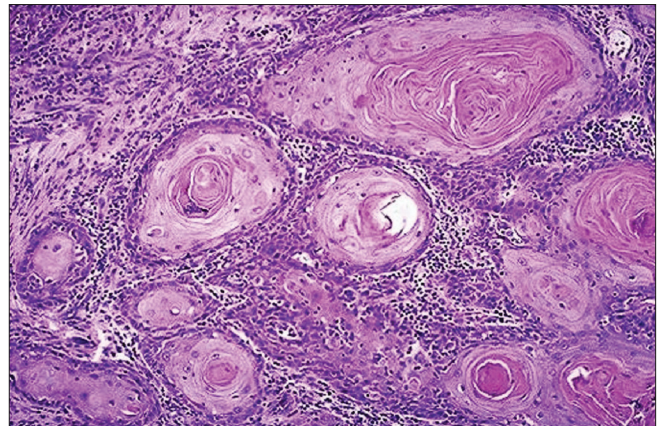


Figure 6: Photomicrograph showing well differentiated squamous cell carcinoma (H and E, $\times 100$)

SUBJECTS AND METHODS

Patients reporting to the Oral Pathology department of Dr. R. Ahmed Dental College and Hospital, Kolkata during 2010-2011 were included as cases in the present study. The study group comprised of 698 (male = 487, female = 211) patients who reported to the Department of Oral and Maxillofacial

Pathology. These patients were clinically diagnosed with malignancy, LKP or OSF. Biopsy was conducted on these patients after having their informed consent, a routine hematological examination and ethical clearance from the concerned institutional ethical committee. These patients were confirmed of having SCC (staged according to early invasive, well differentiated, moderately differentiated or

poorly differentiated), LKP (staged as without dysplasia, mild dysplasia, moderate dysplasia or severe dysplasia) or OSF after histopathological examination. The control group consisted of 948 (male = 647, female = 301) patients who belonged to West Bengal and had reported to the hospital with some dental problem but did not have any oral mucosal lesion. These patients regularly consumed combinations of tobacco, areca nut and alcohol for not less than 1 year. They were counseled to quit their habit(s) and subsequently observed over 2 years 182 of them stopped the habit after the counseling sessions. Hence our final control group consisted of 766 patients who did not quit the habit but also did not develop any oral mucosal lesion at the end of 2 years.

Data was collected using a standard questionnaire protocol (which included name, sex, age, religion, type of habit, duration and frequency of habit, duration of lesion, and socioeconomic background) through in person interview. From the above data, the number of exposed cases, exposed controls, unexposed cases and unexposed controls were extracted. From this data, the unadjusted odds ratio (OR), the 95% confidence interval (CI), and the *P* value were calculated to correlate patients with/without different kinds of habit and having/not having various kinds of oral lesions. The differences between the distributions of the various forms of the diseases among patient of different age groups as well as the various sites have been done on the basis of percentages.

The primary aim of the study was to find out the correlation between the three different kinds of oral mucosal lesions (such as oral SCC, OSF, LKP) and the habit of taking various forms of tobacco, areca nut and alcohol (singularly or in combination). This study was also done for males and females separately to find any significant difference amongst the two.

The secondary aim of the study was to find the effect of age or sex on the different lesions. The study also revealed the predilection of the various histopathological stages of the lesions for the different sites.

RESULTS

Our findings in Table 1 show that OSF is more predominant amongst men and women in the age group of 10-29 years than the higher age groups. The opposite holds true for SCC-whose predominance increases with age group both for men and

women. Smokeless tobacco usage was mainly found to be more popular among the young individuals.

Our study [Table 2] showed that amongst all male patients who developed SCC khaini chewing seemed to be the most predominant habit. Interestingly, chewing betel quid seemed to be the most popular habit among all female patients who have SCC. Bidi smoking was more strongly associated with SCC in case of males as compared to females. This may be because of social stigmas associated with bidi smoking amongst females in India leading to the number of female bidi smokers not being statistically significant. Bidi smoking also was found to be the most predominant habit amongst all LKP patients. Amongst the patients having OSF gutkha chewing was found to be the most popular habit.

Our present study showed [Table 3] that amongst male patients having a habit of using smokeless tobacco, chances of having SCC was significantly more as compared to patients having no habits (OR [95% CI] =2.876 [1.537-5.421], *P* = 0.001). The chance of developing SCC was significantly increased in male patients having mixed habit as compared to patients having no habit.(OR [95% CI] =3.66 [1.936-6.974], *P* = 0.0001). Similarly, for male patients taking areca nut, the chances of having OSF is significantly more as compared to patients having no habit (OR [95% CI] =15.049 [2.188-298], *P* = 0.0001). Male patients are also at significantly increased risk of developing OSF if having mixed habits (OR [95% CI] =17.18 [2.343-352.410], *P* = 0.0001). Hence for male patients it can be said that having smokeless tobacco or mixed habits increases the chances of having SCC 3-4 times, the latter having a more deleterious effect, whereas having areca nut or mixed habits increases the chances of developing OSF 15-17 times, the latter causing a worse effect. Chances of developing LKP are not significantly related to any one particular habit. For the female patient, the scenario is a bit different. Female patient having smokeless tobacco are much more likely to develop SCC as compared to the female patient having no habit (OR [95% CI] =6.405 [3.043-13.585], *P* = 0.0001). Similarly, chances of developing SCC are much increased in female patients who consumed areca nut as compared to patients who had no habit (OR [95% CI] =3.482 [2.026-6.019], *P* = 0.0001). It was also found that the chances of developing SCC is very significantly found to be higher in patients having mixed habit as compared to patients having no habit at all (OR [95% CI] =9.09 [2.755-31.075], *P* = 0.0001). Another very significant finding for the female

Table 1: Demographic variations of the study population

Age group	Control (%)		OSF (%)		SCC (%)		LKP (%)	
	Men	Women	Men	Women	Men	Women	Men	Women
10-29	156 (65.82)	46 (75.4)	69 (29.11)	12 (19.67)	8 (3.37)	1 (1.64)	4 (1.69)	2 (3.27)
30-49	294 (67.43)	95 (60.5)	28 (6.42)	10 (6.37)	93 (21.33)	44 (28.02)	21 (4.82)	8 (5.09)
50-69	131 (37.22)	41 (27.89)	5 (2.04)	3 (1.6)	186 (52.84)	88 (59.86)	30 (8.52)	15 (10.2)
70-99	3 (6.52)	0	0	0	37 (80.43)	27 (96.43)	6 (13.04)	1 (3.57)

OSF: Oral submucous fibrosis, SCC: Squamous cell carcinoma, LKP: Leukoplakia

Table 2: Distribution of oral habits among controls and patients of the study sample

Habits	Controls		SCC		LKP		OSF	
	Male n (%)	Female n (%)	Male n (%)	Female n (%)	Male n (%)	Female n (%)	Male n (%)	Female n (%)
Smokeless tobacco								
Khaini	33 (5.1)	7 (2.32)	68 (20.98)	19 (11.87)	11 (18.03)	2 (7.69)	8 (7.84)	1 (4)
Gudhaku	20 (3.09)	10 (3.32)	12 (3.7)	11 (6.87)	0	1 (3.84)	0	0
Snuff	45 (6.95)	7 (2.32)	5 (1.5)	1 (0.625)	0	0	0	0
Smoking tobacco								
Bidi	95 (14.68)	21 (6.97)	42 (12.96)	2 (1.25)	22 (36.06)	1 (3.84)	7 (6.86)	2 (8)
Cigarette	67 (10.35)	0	26 (8.02)	0	5 (8.19)	1 (3.84)	6 (5.88)	0
Arecanut								
Betel quid	55 (8.5)	35 (11.63)	25 (7.71)	60 (37.5)	3 (4.91)	7 (26.92)	14 (13.72)	10 (40)
Gutkha	192 (29.67)	96 (31.89)	42 (12.96)	32 (20)	9 (14.75)	9 (34.61)	45 (44.12)	10 (40)
Smokeless+smoking	7 (1.08)	1 (0.33)	12 (3.7)	1 (0.625)	1 (1.63)	0	2 (1.96)	0
Smoking+arecanut chewing	36 (5.56)	2 (0.66)	14 (4.32)	1 (0.625)	3 (4.91)	0	9 (8.82)	0
Smokeless tobacco+arecanut	5 (0.77)	0	21 (6.48)	7 (4.375)	0	1 (3.84)	9 (8.82)	1 (4)
Smokeless+alcohol	13 (2)	3 (0.1)	3 (0.925)	0	0	0	0	0
Smoking+alcohol	13 (2)	0	25 (7.71)	1 (0.625)	3 (4.91)	0	0	0
Smokeless+smoking+alcohol	2 (0.3)	0	5 (1.54)	0	0	0	1 (0.98)	0
Smokeless tobacco+smoking+arec	1 (0.15)	0	5 (1.54%)	1 (0.625)	0	0	0	0
No habits	63 (9.73)	119 (39.53)	19 (5.86)	24 (15)	4 (6.55)	4 (15.38)	1 (0.98)	1 (4)

SCC: Squamous cell carcinoma, LKP: Leukoplakia, OSF: Oral submucous fibrosis

patient was that those who had the habit of taking areca nut were very highly predisposed to develop OSF as compared to those who did not (OR [95% CI] =18.168 [2.526-369.1], $P = 0.0001$). As in case of males, similarly for females the chances of developing LKP was not significantly related to one particular habit only.

Mixed habit is more significantly related in causing SCC as compared to single habits. So it might be concluded that having a mixed habit might actually have a synergistic effect as compared to having a single habit in causing SCC.

In our study population, [Table 4] well differentiated, moderately differentiated as well as poorly differentiated SCC was found more predominantly in the lower alveolus and gingival region. Early invasive SCC was most commonly found in cheek mucosa. Varying degrees of dysplasia in the form of mild, moderate and severe forms or without dysplasia was predominantly seen in buccal mucosa.

DISCUSSION

Oral cancer prevalence exists within a country due to the familial and genetic predisposition of certain ethnic groups. Geographic/regional variations cause the risk factors to differ from country to country as well as from state to state, for example, chewing of tobacco/areca-nut/betel quid is popular in developing countries whereas cigarette smoking and high consumption of alcohol is popular in developed countries. In Eastern India, different forms of tobacco and areca nut are in popular use amongst the general population

such as khaini, gudakhu, snuff, bidi, paan and gutkha. With variation in the different habits, the prevalence of the diseases also varies. In India, a remarkable variation has been observed in the prevalence rate of oral habits amongst the different states with 0.2% in Bihar and 4.9% in Andhra Pradesh.^[1] Gujarat has shown a prevalence rate of 11.7% owing to the high consumption of tobacco or gutkha chewing practices.

The prognosis of the lesions also varies. In a study conducted in Mumbai, amongst the untreated cases of LKP amongst the tobacco chewing group, 42.5% disappeared in 5 years and 45.3% in 10 years.^[2] Similarly in a study conducted in Gujarat where the LKP patients were re-examined after 2 years showed that 11% of lesions had increased in the size, 31.6% had decreased in size or disappeared and 57.3% had remained unchanged.^[3] A 10 year follow-up study conducted in the developed world showed that only 20.1% had disappeared, 17.8% had reduced in size and 3.3% had increased in size.^[4] Several studies have shown that the frequency of dysplastic or malignant alterations in oral LKP has ranged from 15.6% to 39.2%. In India studies have shown that the rate of malignant transformation ranges from 0.13% to 2.2% per year.^[2,3] In a Swedish study, rate of transformation of oral cancer was 0.2% in 2 years, 0.4% in 5 years for tobacco users whereas 1.15% and 3.1% at 2 and 5 years respectively for non-tobacco users.^[5] In the systematic review by Dr. Petti the global transformation rate for oral LKP was 1.36% per year.^[6] The lesions that are present in the floor of mouth, lateral tongue and lower lip are more likely to show dysplastic or malignant changes.

Table 3: Correlation of various oral habits to the risk of developing oral potentially malignant and malignant lesions

Sex	No habit	Smokeless tobacco	OR (95% CI)	P value	Smoking	OR (95% CI)	P value	Areca nut	OR (95% CI)	P value	Mixed habit	OR (95% CI)	P value
Male	Control	98	Ref		162	Ref		247	Ref		77	Ref	
	SCC	85	2.876 (1.537-5.421)	0.001	68	1.392 (0.747-2.611)	0.334	67	0.899 (0.486-1.675)	0.835	85	3.66 (1.936-6.974)	0.0001
	LKP	4	1.768 (0.490-6.923)	0.501	27	2.622 (0.828-9.244)	0.115	12	0.765 (0.219-2.921)	0.893	7	1.432 (0.354-6.140)	0.410
	OSF	1	5.143 (0.628-112.281)	0.182	13	5.056 (0.668-105.673)	0.162	59	15.049 (2.188-298.005)	0.0001	21	17.18 (2.343-352.416)	0.0001
Female	Control	24	Ref		21	Ref		131	Ref		6	Ref	
	SCC	31	6.405 (3.043-13.585)	0.0001	2	0.472 (0.071-2.302)	0.496	92	3.482 (2.026-6.019)	0.0001	11	9.09 (2.755-31.075)	0.0001
	LKP	4	3.719 (0.611-21.532)	0.212	2	2.833 (0.335-19.830)	0.525	16	3.634 (1.098-13.262)	0.031	1	4.958 (0.182-64.36)	0.641
	OSF	1	4.958 (0.13-189.397)	0.712	2	11.33 (0.7583-323.01)	0.106	20	18.168 (2.526-369.12)	0.0001	1	19.833 (0.469-858.06)	0.223

SCC: Squamous cell carcinoma, LKP: Leukoplakia, OSF: Oral submucous fibrosis, OR: Odds ratio, CI: Confidence interval

Table 4: Sites of occurrence of potentially malignant and malignant lesions among the study population

Site	SCC					LKP					OSF	
	Well diff n (%)	Mod diff n (%)	Poorly diff n (%)	Early inv n (%)	W/o dys n (%)	Mild n (%)	Mod n (%)	Severe n (%)	Severe n (%)	n (%)	n (%)	
Cheek mucosa	124 (36.26)	37 (29.13)	1 (14.28)	7 (26.92)	5 (38.46)	17 (41.46)	14 (50)	8 (42.10)	119 (93.7)			
Retromolar area	15 (4.38)	2 (1.57)	0	1 (3.85)	0	0	0	0	0			
Vestibule	44 (12.86)	19 (14.96)	0	3 (11.54)	1 (7.69)	7 (17.07)	2 (7.14)	1 (5.26)	8 (6.3)			
Mucosa of upper lip	14 (4.09)	9 (7.08)	0	0	0	1 (2.44)	0	0	0			
Mucosa of lower lip	6 (1.75)	7 (5.51)	2 (28.57)	0	0	2 (4.88)	2 (7.14)	1 (5.26)	0			
Commissures	19 (5.56)	1 (0.78)	0	3 (11.54)	2 (15.38)	5 (12.19)	3 (10.71)	5 (26.31)	0			
Upper alv and gingiva	22 (6.43)	19 (14.96)	1 (14.28)	2 (7.69)	1 (7.69)	0	0	1 (5.26)	0			
Lower alv and gingiva	130 (38.01)	43 (33.85)	2 (28.57)	4 (15.38)	0	1 (2.44)	3 (10.71)	2 (10.53)	0			
Hard palate	25 (7.3)	10 (7.87)	0	2 (7.69)	1 (7.69)	3 (7.32)	0	1 (5.26)	0			
Tongue												
Dorsal surface and ant 1/3 rd	48 (14.03)	19 (14.96)	0	4 (15.38)	3 (23.08)	3 (7.32)	4 (14.28)	0	0			
Ventral surface	10 (2.92)	1 (0.78)	1 (14.28)	0	0	2 (4.88)	0	0	0			
Floor of mouth	17 (4.97)	8 (6.29)	0	0	0	0	0	0	0			

SCC: Squamous cell carcinoma, LKP: Leukoplakia, OSF: Oral submucous fibrosis

In India, 0.2-1.2% of an urban population attending dental clinics are affected by OSF.^[7] There is a positive association between the incidence of LKP and oral cancer with OSF. The frequency of malignant change has been reported to a range from 3% to 6%. The potentially malignant nature of OSF was first described by Paymaster, who observed SCC occurring in one third of his patients with OSF.^[8] In 17 years long-term follow-up study conducted by Murti *et al.*, the annual malignant transformation rate was found to be approximately 0.5-7.6%.^[9]

Oral SCC ranks number one in terms of incidence among men and third among women. It has one of the lowest 5-years survival rates of all cancers, probably because most lesions are not diagnosed in the initial stages. However, if detected early, the probability of survival from oral cancer is remarkably better when compared to most other types of cancers.^[10] In a study reported from Allahabad (North India) the malignant oral lesions were found to be highly prevalent in patients visiting tertiary level hospitals.^[6] A similar study conducted in Manipuri district of India reported an annual incidence rate of oral cancer to be 21.4/100,000 individuals.^[1]

In conclusion, we can say that apart from the correlation of different types of habit to oral potentially malignant and malignant lesions, the diet and genetic disposition of a patient might also predispose the patient to such lesions.^[11] Since the present study emphasizes on the correlation of the different types of deleterious oral habits and oral potentially malignant and malignant lesion, spread of awareness forms the most important pillar on which the prevention of oral cancer depends.^[12] Patients should be encouraged to go in for a bi-annual oral screening. Both the governmental and non-governmental organizations in India are making efforts to educate the masses regarding the risk factors and early signs and symptoms of the disease. With this combined effort in the coming years hopefully we can reduce the number of oral cancer cases to a minimum.

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