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Incidence of Oral Cancer in association with Oral Submucous Fibrosis in Southern Population of Gujarat, India

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Abstract:
Aim: *This study aims at reporting the incidence of oral cancer and its association with Oral Submucous Fibrosis (OSMF) in Southern population of Gujarat, India*
Material and Methods: *Data was collected from the patients who reported to Bharat Cancer Hospital, Surat, Gujarat from March 2018 to September 2018.*
More than 1500 patients reported to the Hospital from which 874 patients were selected for this study. Details regarding patient's age, gender, occupation, habit, site affected with oral cancer and mouth opening was recorded. The data recorded were tabulated in the MS Excel and subjected to statistical analysis using SPSS software 16. Data were analyzed using Chi‐ square test.
Results: *Among the 874 patients, majority of patients were tobacco chewers (91.5%), tobacco smokers (27.5%) and alcoholic (5.7%). Majority of patients were in the age group of 41-50 years (34.4%), followed by 31-40 years (26.3%). Out of 874 patients, 693 were males and 181 were females and buccal mucosa was the most common site followed by tongue. Majority of the cases were seen to have stage 4 cancer along with stage 2 OSMF. Smokeless tobacco consumed in India is one of the most common forms of tobacco, leading to cause oral cancer. People consuming betel nut, areca nut and pan have potency to develop OSMF which can further turn into malignancy.*
Conclusion: *Cancer diagnostic and awareness centers should not be restricted to big cities but also should take into consideration small towns and remote villages. People should be educated about hazardous effects of tobacco, pan, betel nut and areca nut and regular visits as well as follow ups of suspected population should be conducted. There should be regular oral checkup for male and female patients for the early detection of cancer and its prevention.*

Key words: *Buccal mucosa, cancer, Gujarat, India, tobacco, tongue.*

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I. Introduction

Cancers are the most common cause of death in adults. Oral cancer (OC) is a broad term that includes various malignant diseases that are present in oral tissues, which are found on the lip, floor of the mouth, buccal mucosa, gingiva, palate, or in the tongue. The majority (84%–97%) of OCs are squamous cell carcinoma (SCC) which arise from preexisting "potentially malignant" lesions or more often from normal appearing epithelium.[1‐ 3] The term "oral potentially malignant disorders" is recommended by the WHO in 2005. It includes both oral premalignant lesions and conditions. There are number of potentially malignant disorders which constitute a detectable preclinical phase of OC. The most important ones are oral submucous fibrosis, leukoplakia, erythroplakia, candidal leukoplakia, lichen planus, dyskeratosis congenita.

Around 300,000 patients are annually estimated to have OC worldwide.[4] India has world's highest number (nearly 20%) of OCs with an estimated 1% of the population having oral premalignant lesions.[5] Approximately 95% of squamous cell carcinoma occurs in people older than 40 years, with an average age at diagnosis of approximately 60 years.[6]Various factors such as tobacco (smoking and smokeless form), alcohol, human papilloma virus (HPV) 16 and18, dietary factors, and genetic factors are considered etiological factors for squamous cell carcinoma. Clinically, squamous cell carcinoma appears as red or white lesion, proliferative, infiltrative, or ulcerative growth.

Various studies have been conducted across the world to study the incidence and prevalence and factors affecting OC.[7,8] In developing countries like India, the usage of tobacco is more because it is easily available. With this background, the present study was designed to study the prevalence of OC in association with OSMF and its association with habits, age, gender, and site in the Southern population of Gujarat.

II. Materials and methods

An observational, cross sectional study was carried out from March 2018 to September 2018 at Bharat Cancer Hospital, Surat, Gujarat. The data from the patients who reported to the OPD were obtained and 874 patients were selected for the study which includes clinically evaluated and histopathologically diagnosed as Squamous cell carcinoma, who have not taken any treatment and have not undergone chemotherapy or radiotherapy. Habit history of patients including all forms of chewing tobacco, smoking tobacco and alcohol along with quantity and duration was recorded in clinical proforma. Details of patient's age, gender, mouth opening and site of SQUAMOUS CELL CARCINOMA were recorded along with the clinical stage of cancer and OSMF. The data recorded were entered in MS Excel sheet and subjected to statistical analysis.

Oral Submucous staging according to Haider SM et al. -

Clinical staging –

Stage 1: Faucial bands only

Stage 2 : Faucial and buccal bands

Stage 3 : Faucial, buccal and labial bands.

Functional staging –

Stage 1 : Mouth opening >20mm

Stage 2 : Mouth opening 11-19mm

Stage 3 : Mouth opening <10mm

III. Statistical Analysis

Descriptive statistics were computed and mean and standard deviations were calculated for continuous variables and frequency and proportions were computed for categorical variables. Chi square and fisher exact statistics were computed for comparison. A $p<0.05$ is considered significant for statistical inferences.

IV. Results

Table 1 depicts distribution of oral cancer with respect to age and gender. It shows prevalence of oral cancer in males, with male to female ratio being 4:1, and also relatively more number of cases in 41-50yeras of age (34.4%) followed by 31-40 years of age (26.3%). Table 2 shows significant association of gender with site of oral cancer. Buccal mucosa was the most common site accounting for 72.4% of lesions occurring in males and 60.9% in females. Table 3 and table 4 depicts significant association of age with stage of cancer and OSMF. Majority Of patients (79.5%) were having stage 4 cancer whereas 61.1% patients were suffering from stage 2 OSMF. Table 5 and Table 6 depicts association of Gender and age with smokeless tobacco consumption and 28.2% of female patients were found to consume Mishri and 22.1% were found to consume Khaini, whereas, 33.3% male patients were found to consume Gutkha and 27.5% were found to consume Khaini. An association between the stage of OSMF and stage of oral cancer as seen in Table 7 where 119 patients of oral cancer had no OSMF, 81 stage 1 OSMF patients, 534 stage 2OSMF patients and 140 stage 3 patients had oral cancer. Table 8 and table 9 depicts association of Gender with tobacco smoking & alcohol consumption respectively. Table 10 shows significant association of side of lesion with site in oral cavity where
52.6% of cases were seen on left side, 39.4% on right side and 8% bilateral cases.

Distribution of oral cancer with respect to age and gender – Majority of patients were in the age group of 41-50 years (34.4%), followed by 31-40 years (26.3%). Out of 874 patients, 693 were males and 181 were females.

Association of age with stage of OSMF and oral cancer – Majority of the cases were in the age group of 41-60 years, with most of the cases of stage 4 cancer (79.5%) and stage 2 OSMF (61.1%).

Association of stage of OSMF and stage of oral cancer- Majority of the patients in the study were of stage 4 oral cancer (695 patients) out of which 464 patients had stage 2 OSMF.

Association of side and site of oral cancer – Buccal mucosa was the most common site for oral cancer in both males and females constituting 72.4% and 60.9% respectively. Left side buccal mucosa was found to be 52.6% as compared to 39.4% on the right side.

V. Discussion

In Asia, oral cancer ranks as sixth most frequent malignancy. Developing nations situated in South-central and South- eastern regions such as India, Pakistan, Bangladesh, Taiwan, and Sri Lanka report high incidence rates. In developing countries,OC is the third most common type of cancer after cervix and stomach [8]. Squamous cell carcinoma has a multi-factorial etiology, which includes chronic use of smoking and smokeless form of tobacco, alcohol, and viruses. In India and Southeast Asia, chronic use of betel quid (pan) and tobacco has been strongly associated with an increased risk for squamous cell carcinoma along with alcohol, HPV 16 and HPV 18, dietary deficiency, and poor oral hygiene [9- 13]. The buccal mucosa, gingiva and buccal sulcus are more commonly affected due to placement of tobacco quids such as khaini, gutkha, and betel quid in the oral cavity [16]. Previous studies have shown that the micronuclei cells were found to be significantly higher in smokeless tobacco users than in smokers.[17] Epidemiological studies have shown regional differences in different states of India, with Kerala reporting a lowest incidence[20] and West Bengal reporting a highest[21] incidence of OC. The majority of patients were tobacco chewers (91.5%), followed by patients with habits such as tobacco smoking(27.6%) and alcoholic (5.7%). Previous studies have shown the association of tobacco with OC, which was in accordance with our study[16]. In our study, the highest incidence of oral cancer was seen in the age group of 40-59 years (62.1%) followed by 20-39 years (23%) which was not in concurrence with the previous studies [22-24]. Male to female ratio was 3.8:1 in this study, which was in accordance with various studies where high incidence was noted in males than females which may be due to easy access to tobacco products.[22- 25] The gender-based preponderance of OC in India is also regional, tilting toward men in most parts of the country and toward women in South India owing to the prevailing practice of reverse smoking (chutta).[26] Buccal mucosa was the most common site (63.21%) in our study in both genders, followed by tongue (32.18%) and the least common site was lip (4.59%). The results of our study were in accordance with other studies where they showed buccal mucosal as the most common site. Most of the patients in our study were using chewing form of tobacco which may be the reason for buccal mucosa as the common site.[22,24,25,27] Tongue and floor of the mouth carcinoma are more common in Western countries due to consumption of alcohol and smoking.[28,29] The grade and metastatic status of squamous cell carcinoma at the time of detection are vital as it determines the treatment plan and the prognosis. Various treatments such as radiotherapy, chemotherapy, surgery, and brachytherapy and their combination are available depending on the stage and site of squamous cell carcinoma. Better treatment outcomes are shown if carcinoma is diagnosed in the early stage of development. In India, late diagnosis of carcinoma is one of the major factors, which worsens the disease prognosis.

Table .1. Gender and age-wise distribution of oral cancer

AGE * GENDER Crosstabulation					
			GENDER		Total
			FEMALE	MALE	
AGE	<30	Count	0	41	41
		% within GENDER	0.0%	5.9%	4.7%
	31-40	Count	40	190	230
		% within GENDER	22.1%	27.4%	26.3%
	41-50	Count	30	271	301
		% within GENDER	16.6%	39.1%	34.4%
	51-60	Count	51	131	182
		% within GENDER	28.2%	18.9%	20.8%
	61-70	Count	40	40	80
		% within GENDER	22.1%	5.8%	9.2%
	>70	Count	20	20	40
		% within GENDER	11.0%	2.9%	4.6%
Total		Count	181	693	874
		% within GENDER	100.0%	100.0%	100.0%

Table .2. Association between gender and site of oral cancer

SITE * GENDER Cross tabulation					
			GENDER		Total
			FEMALE	MALE	
SITE	BUCCAL MUCOSA	Count	131	422	553
		% within GENDER	72.4%	60.9%	63.3%
	LIP	Count	0	40	40
		% within GENDER	0.0%	5.8%	4.6%
	TONGUE	Count	50	231	281
		% within GENDER	27.6%	33.3%	32.2%
Total		Count	181	693	874
		% within GENDER	100.0%	100.0%	100.0%
Chi-Square Tests					

	Value	df	P value (significant if <0.05)
Pearson Chi-Square	14.892	2	.001
N of Valid Cases	874		

Table .3. Association between age and stage of oral cancer

Crosstab									
			AGE						Total
			<30	31-40	41-50	51-60	61-70	>70	
Oral Cancer Stage	STAGE II	Count	0	10	0	49	0	0	59
		% within AGE	0.0%	4.3%	0.0%	26.9%	0.0%	0.0%	6.8%
	STAGE III	Count	0	20	70	20	0	10	120
		% within AGE	0.0%	8.7%	23.3%	11.0%	0.0%	25.0%	13.7%
	STAGE IV	Count	41	200	231	113	80	30	695
		% within AGE	100.0%	87.0%	76.7%	62.1%	100.0%	75.0%	79.5%
Total		Count	41	230	301	182	80	40	874
		% within AGE	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	203.645	10	**<0.001**
N of Valid Cases	874		

Table .4. Association between age and stage of OSMF

Crosstab									
			AGE						Total
			<30	31-40	41-50	51-60	61-70	>70	
OSMF Stage	NO OSMF	Count	10	30	30	29	0	20	119
		% within AGE	24.4%	13.0%	10.0%	15.9%	0.0%	50.0%	13.6%
	STAGE I	Count	0	10	30	31	10	0	81
		% within AGE	0.0%	4.3%	10.0%	17.0%	12.5%	0.0%	9.3%
	STAGE II	Count	21	130	211	102	60	10	534
		% within AGE	51.2%	56.5%	70.1%	56.0%	75.0%	25.0%	61.1%
	STAGE III	Count	10	60	30	20	10	10	140
		% within AGE	24.4%	26.1%	10.0%	11.0%	12.5%	25.0%	16.0%
Total		Count	41	230	301	182	80	40	874
		% within AGE	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0 %

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	129.409	15	**<0.001**
N of Valid Cases	874		

Table .5. Association between gender and smokeless tobacco in oral cancer

Crosstab					
			GENDER		Total
			FEMALE	MALE	
HABIT	NO HABITS	Count	0	31	31
		% within GENDER	0.0%	4.5%	3.5%
	GUTKHA	Count	30	261	291
		% within GENDER	16.6%	37.7%	33.3%
	GUTKHA+MAWA	Count	0	20	20
		% within GENDER	0.0%	2.9%	2.3%
	KHAINI	Count	40	200	240
		% within GENDER	22.1%	28.9%	27.5%
	MAWA	Count	0	171	171
		% within GENDER	0.0%	24.7%	19.6%
	MISHRI	Count	51	0	51
		% within GENDER	28.2%	0.0%	5.8%
	MISHRI+GUTKHA	Count	10	0	10

		% within GENDER	5.5%	0.0%	1.1%
	TAPKIR	Count	20	10	30
		% within GENDER	11.0%	1.4%	3.4%
	TAPKIR+MISHRI	Count	30	0	30
		% within GENDER	16.6%	0.0%	3.4%
Total		Count	181	693	874
		% within GENDER	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	466.541	8	**<0.001**
N of Valid Cases	874		

Table .6. Association between age and smokeless tobacco in oral cancer

Crosstab									
				AGE				Total	
			<30	**31-40**	**41-50**	**51-60**	**61-70**	**>70**	
HABIT	NO HABITS	Count	0	10	10	11	0	0	31
		% within AGE	0.0%	4.3%	3.3%	6.0%	0.0%	0.0%	3.5%
	GUTKHA	Count	41	40	120	60	30	0	291
		% within AGE	100.0%	17.4%	39.9%	33.0%	37.5%	0.0%	33.3%
	GUTKHA+MAWA	Count	0	20	0	0	0	0	20
		% within AGE	0.0%	8.7%	0.0%	0.0%	0.0%	0.0%	2.3%
	KHAINI	Count	0	90	110	30	10	0	240
		% within AGE	0.0%	39.1%	36.5%	16.5%	12.5%	0.0%	27.5%
	MAWA	Count	0	50	51	40	10	20	171
		% within AGE	0.0%	21.7%	16.9%	22.0%	12.5%	50.0%	19.6%
	MISHRI	Count	0	20	0	11	10	10	51
		% within AGE	0.0%	8.7%	0.0%	6.0%	12.5%	25.0%	5.8%
	MISHRI+GUTKHA	Count	0	0	0	10	0	0	10
		% within AGE	0.0%	0.0%	0.0%	5.5%	0.0%	0.0%	1.1%
	TAPKIR	Count	0	0	10	10	10	0	30
		% within AGE	0.0%	0.0%	3.3%	5.5%	12.5%	0.0%	3.4%
	TAPKIR+MISHRI	Count	0	0	0	10	10	10	30
		% within AGE	0.0%	0.0%	0.0%	5.5%	12.5%	25.0%	3.4%
Total		Count	41	230	301	182	80	40	874
		% within AGE	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	463.488	40	**<0.001**
N of Valid Cases	874		

Table .7. Association between stage of oral cancer and stage of OSMF

Oral Cancer Stage * OSMF Stage Crosstabulation							
			OSMF Stage				Total
			NO OSMF	STAGE I	STAGE II	STAGE III	
Oral Cancer Stage	STAGE II	Count	29	10	20	0	59
		% within OSMF Stage	24.4%	12.3%	3.7%	0.0%	6.8%
	STAGE III	Count	40	30	50	0	120
		% within OSMF Stage	33.6%	37.0%	9.4%	0.0%	13.7%
	STAGE IV	Count	50	41	464	140	695
		% within OSMF Stage	42.0%	50.6%	86.9%	100.0%	79.5%
Total		Count	119	81	534	140	874
		% within OSMF Stage	100.0%	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	208.617	6	**<0.001**
N of Valid Cases	874		

Table .8. Association between gender and smoking tobacco in oral cancer

Crosstab					
			GENDER		Total
			FEMALE	MALE	
SMOKING TOBACCO	NO	Count	181	453	634
		% within GENDER	100.0%	65.4%	72.5%
	YES	Count	0	240	240

		% within GENDER	0.0%	34.6%	27.5%
Total		Count	181	693	874
		% within GENDER	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	86.413	1	**<u>≤0.001</u>**
N of Valid Cases	874		
b. Computed only for a 2x2 table			

Table .9. Association between gender and alcohol in oral cancer

Crosstab					
			GENDER		Total
			FEMALE	MALE	
ALCOHOL	NO	Count	181	643	824
		% within GENDER	100.0%	92.8%	94.3%
	YES	Count	0	50	50
		% within GENDER	0.0%	7.2%	5.7%
Total		Count	181	693	874
		% within GENDER	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	13.852	1	**<u>≤0.001</u>**
N of Valid Cases	874		
b. Computed only for a 2x2 table			

Table .10. Association between side and site of lesion with oral cancer

RIGHT/ LEFT * SITE Cross tabulation						
			SITE			Total
			BUCCAL MUCOSA	LIP	TONGUE	
RIGHT/ LEFT	L	Count	351	0	109	460
		% within SITE	63.5%	0.0%	38.8%	52.6%
	R	Count	192	0	152	344
		% within SITE	34.7%	0.0%	54.1%	39.4%
	R/L	Count	10	40	20	70
		% within SITE	1.8%	100.0%	7.1%	8.0%
Total		Count	553	40	281	874
		% within SITE	100.0%	100.0%	100.0%	100.0%

Chi-Square Tests			
	Value	df	P value (significant if <0.05)
Pearson Chi-Square	527.354	4	**<u>≤0.001</u>**
N of Valid Cases	874		

VI. Conclusion

In a short span of 7 months, such a large number of patients reported to one center! Hence, we can estimate the huge number of cases suffering with Oral cancer and OSMF in India.

In India, because of easy availability of smokeless tobacco, there is increase in the number of people suffering from OSMF and oral cancer. Also because of low awareness of people regarding the hazardous consequences of tobacco use, the cases of cancer are not decreasing. Smokeless tobacco consumed in India is one of the most common forms of tobacco abuse leading to cancer and death. Depending on the form of tobacco usage, site of cancer in the oral cavity differs. There is need to spread awareness about this tobacco- related cancer and immediate consultation on suspicion of cancer. Early detection of oral cancer always helps the patient treatment and survival rates.

Cancer diagnostic and awareness centers should not be restricted to big cities but also should take into consideration small towns and remote villages. People should be educated about hazardous effects of tobacco, pan, betel nut and areca nut and regular visits as well as follow ups of suspected population should be conducted. There should be regular oral checkup for male and female patients for the early detection of cancer and its prevention.

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COMPLIANCE WITH ETHICAL STANDARDS
There is no conflict of interest. This article does not contain any studies with animals performed by any of the authors. All procedures performed in studies involving human participants were in accordance with the ethical

standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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