

OCCURRENCE OF ORAL SQUAMOUS CELL CARCINOMA IN PATIENTS WITHOUT PREDISPOSING ORAL HABITS

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Running title: Occurrence of oral squamous cell carcinoma in patients without predisposing oral habits.

Kalaivani Natarajan

Graduate student
Saveetha Dental College
Saveetha University.

Gheena S

Senior Lecturer
Department of Oral pathology
Saveetha Dental College.
Saveetha University.

Abstract

Aim

To assess the occurrence of oral squamous cell carcinoma in patients without predisposing oral habits – In a hospital based population.

Materials and methods

This retrospective study was performed on the cases referred to Oral cancer institute –of a reputed University in south India during June 2015 to December 2017. The details of the patients were collected, tabulated and statistical analysis was done.

Results

Non smoking and non drinking female patients are becoming a distinct group in oral squamous cell carcinoma. The male to female ratio (those without habits) is 1:2. The factors that could contribute to this phenomenon could include hormonal or viral infection such as HPV.

Conclusion

There is a relative increase of non smoking, non drinking patients associated OSCC, particularly females. This trend needs to be studied in detail as it is vital for an early diagnosis and this could facilitate a better prognosis.

Keywords: Prognosis, immune response, oncogenic potential, smoking, alcohol consumption

INTRODUCTION:

Oral cancer can be defined as the neoplasm of the oral cavity which begins at the lips and ends at the anterior pillar of the fauces (1). Oral Squamous cell carcinoma is the one of the most common cancer in the world which ranks to be the sixth common. India being called as the capital of the oral cancer among other countries in the world. Oral squamous cell carcinoma is predominantly seen in the middle and old age and is a rarity in those below 45years. Even though there is a debate in regard to the relative importance to some of these factors tobacco and alcohol and smoking are known to play an important role in the pathogenesis of cancer. Effects of these factors are explained in various studies. Yet there are cases reported, in which the patients diagnosed with oral squamous cell carcinoma without any history of smoking, alcohol and tobacco consumption. There can be several other reason which are being studied and have to be studied in detail, those include ultra violet radiation, immune suppression and infections caused by oncogenic viruses [2].

The greatest risk factor is the use of tobacco and alcohol. Although the risk factors are independent, their action seems to be combined (3). Tobacco is used in various forms including betel quid, tobacco with lime, bidi, hookah, etc. Tobacco contains about 4,000 chemical constituents among which more than 24 of the substance are known to be carcinogens which leads to precancerous lesions. Tobacco smoking is associated with 75% of all cases of oral cancer. Although smoking tobacco offers a more pronounced risk of oral cancer, combining tobacco and alcohol results in increased cancer incidence many times greater than the additive effect because of their synergistic action. Oral squamous cell carcinoma is most common in older males, in lower socioeconomic groups and in ethnic minority groups.

Inadequate immune response may lead to cancer development. There is an increased risk of developing OSCC in HIV infected patients and patients who have to undergo organ transplantations and consequently are under immunosuppressive therapy. Other factors include impaired ability to repair DNA damaged by mutagens, impaired ability to metabolise carcinogens, Deficiencies of vitamins A, E or C or trace elements.

More than 100 types of HPV have been identified and are referred as viruses of low or high risk according to their oncogenic potential. Human papilloma virus is the commonest sexually transmitted viral infection (5). The most predominant one is HPV 16. HPV was more frequently detected in OSCCs of the oropharynx and tonsil than at other head and neck sites. HPV associated cancers are common in Asia particularly Japan and very less common in Africa (6). This implies that viral infection may be an important etiological agent and along with dietary habits and a probable genetic predisposition can cause additional mutations leading to malignancy (7).

Hepatitis C Virus can also be the causative agent for oral squamous cell carcinoma but its oncogenic potential is not yet studied in detail. Lichen planus is an extra hepatic manifestation of hepatitis C (8). This Premalignant condition is associated with the development of oral squamous cell carcinoma (9). The progression of lichen planus into SCC of the oral tongue in patients with hepatitis C has been described in several case reports (10).

Sunlight is a continuous spectrum of electromagnetic radiation that is divided into three major spectrums of wavelength namely ultraviolet, visible and infrared (11). The UV is the most significant spectrum of sunlight that causes photo aging and skin cancer. It produces DNA damage, gene mutation, immune suppression, oxidative stress and inflammatory responses which all help in cancer development (12)

MATERIALS AND METHODS:

This retrospective study was performed on the cases referred to Oral cancer Institute – of a reputed University in South India, during June 2015 to December 2017. The institution is situated in the suburban region of Chennai, in Southern part of India. The patients attending the institution are from adjoining rural, suburban, and urban regions. From the department archives, biopsy details of all cases diagnosed with OSCC were retrieved. The details of the patient's age, gender, site of occurrence of the lesion and habit profile of the patients were collected and tabulated. Broadly habits were classified as those with habits and those without habits. Habits were further classified into smoking, pan chewing, alcohol and multiple habits. Statistical analysis was performed.

RESULTS:

There were 84 patients referred to the Oral cancer institute during June 2015 to December 2017, who were diagnosed with squamous cell carcinoma, among which 26 were female patients and 58 were male patients. They were subdivided into two groups those with habits and those without habits.

The age of the patients ranged from 30years to 70years, while the mean age was calculated to be 53 years.

Among the females 15 did not have any predisposing oral habits while 11 female patients had predisposing oral habits predominantly pan chewing. Among the male patients only 7 presented without any predisposing oral habits while the rest 51 were further classified into tobacco, alcohol, smoking and few others had multiple habits. Table 2 shows the frequency of habits in which pan chewing is of more frequency which ultimately proves to be the major risk factor for oral squamous cell carcinoma with 33.3%, followed by pan chewing added up with alcohol consumption, with 15.5% where alcohol is believed to have synergistic effect in the pathogenesis of cancer. Multiple factors that include smoking, alcohol and pan-chewing together cause carcinoma which stands to be the third frequent etiological factor, followed by smoking and alcohol. Smoking and alcohol consumption is least frequent with 1 and 2 respectively. The mean value and standard deviation of the age of male and female patients of those with and without habits are shown in Table 3 and Table 4. Among the female patients the mean age for those without habits is 58 and those with habits is 59

Table 5 is the cross table between gender and habits in which it was found that the frequency of females without predisposing oral habits was higher than that of males without predisposing oral habits. On comparing both the gender the percentage of females without habits accounts to be 68.2% while that of male is 31.8% which is to be taken into consideration and studied further. To find the significant difference between the two groups chi square test was done. The p value was found to be 0.00 (p value = 0.00) which indicates it is highly significant.

Table 1: Age range, mean, minimum and the maximum age

N	Valid	84
	Missing	0
Mean		53.07
Median		52.50
Std. Deviation		13.179
Range		52
Minimum		28
Maximum		80

Table 2: Frequency of the habit groups

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Alcohol	2	2.4	2.4	2.4
	No habits	22	26.2	26.2	28.6
	Panchewing	28	33.3	33.3	61.9
	Panchewing,Alcohol	13	15.5	15.5	77.4
	Panchewing.Alcohol	2	2.4	2.4	79.8
	Smoking	1	1.2	1.2	81.0
	Smoking,Alcohol	7	8.3	8.3	89.3
	Smoking,Panchewing,Alcohol	9	10.7	10.7	100.0
	Total	84	100.0	100.0	

Table 3: Habit wise distribution of female patients.

Group Statisticsa					
HABITS		N	Mean	Std. Deviation	Std. Error Mean
AGE	No habits	15	58.07	12.407	3.203
	With habits	11	59.18	13.029	3.928

a. GENDER = Female

Table 4: Habit wise distribution of male patients

Group Statisticsa					
HABITS		N	Mean	Std. Deviation	Std. Error Mean
AGE	No habits	7	59.00	15.695	5.932
	With habits	51	49.47	12.160	1.703

a. GENDER = Male

Table 5: Cross table between Gender and Habits

			HABITS		Total
			No habits	With habits	
GENDER	Female	Count	15	11	26
		% within HABITS	68.2%	17.7%	31.0%
	Male	Count	7	51	58
		% within HABITS	31.8%	82.3%	69.0%
Total		Count	22	62	84
		% within HABITS	100.0%	100.0%	100.0%

Table 6: chi square test

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi Square	19.330a	1	.000		
Continuity Correctionb	17.042	1	.000		
Likelihood Ratio	18.458	1	.000		
Fisher's Exact Test				.000	.000
N of Valid Cases	84				

DISCUSSION:

Many Literature suggest that tobacco and alcohol plays a major role among all the etiological factors in the pathogenesis of oral squamous cell carcinoma. It is believed when these substances are combined, the carcinogenic effect becomes potentiated because of their synergistic effect [20,21]. It is not clear whether the presence or absence of these habits affect the clinicopathological, molecular characteristics and prognosis of the patients. However such patients, without typical risk factors for developing squamous cell carcinoma of the oral cavity may have a worse prognosis compared with patients with usual risk factors like tobacco and alcohol (13,14). The non smoking and non drinking population accounts for 13-35% of the oral squamous cell carcinoma population and were more likely to be female (15). They are emerging as a unique subset (16). The factors that could contribute to this phenomenon could include hormonal or viral infection such as Human papilloma virus. Tachezy et al demonstrated HPV positive tumours in all non smokers and 69% of non drinkers in his study. The nonsmokers with oral squamous cell carcinoma contain a lower frequency of genetic alteration, suggesting that underlying changes in these cancers remains undiscovered.

In our study the patients with no habits diagnosed with squamous cell carcinoma were predominately females. There are several articles supporting this, a study conducted by Agudelo et al, they reviewed 933 patients with squamous cell carcinoma out of which 31 patients had no history of alcohol and tobacco, predominantly females, they had better prognosis and survival [22]. In a study conducted by Constantnides et al, they found 10 patients with no history of smoking and alcohol out of which 9 were women. It was likely to occur in the later age when compared to the women who have history of smoking and alcohol [23], which is not in concordance with our study where the mean age of women with habits is 59.18 and the mean age of females without habits is 58.07.

It is also found that patients with no history of habits have lower p53 mutations and have higher rate of HPV infections [24]. Whereas other studies based on the patients with habits suggest that there is dysregulation of cell cycle control and that leads to carcinogenesis as there is involvement of p53 mutation. Hence there is lower p53 mutation in no habits patients, ultimately concludes that there is a different pathogenesis in these patients that has to be studied in detail.

Epidermal Growth factor receptors are amplified and over expressed in certain cancers which is associated with poor prognosis. Non-smoking status is a positive predictor of tumour epidermal growth factor receptor expression in oral squamous cell carcinoma [17]. Ryott et al found there was no correlation between EGFR status and survival, but significant expression of EGFR in early stages compared to that of smokers [19]. Farshadpour et al explained non-smoking and non-drinking patients present differentially expressed genes which possibly indicate the presence of a different cellular response to carcinogenic events in such patients (18). Despite the lack of exposure to tobacco and alcohol and for the reasons not yet understood people have the tendency to develop cancer. Hence, further studies are required to validate this and provide different therapeutic implications to improve prognosis for these patients.

Conclusion and clinical significance:

Not much work is done in non smokers and non drinkers with oral squamous cell carcinoma group thus we suggest that such group should be evaluated and further investigations are required to identify the unknown pathogenesis and this may guide us the treatment plan of oral cancer as overall prognosis of oral cancer is not very good.

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