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Clinicopathological Correlation Study of Oral Squamous Cell Carcinoma: A Single Centre Study in Tamilnadu, India

Karthika Panneerselvam [a,b], Rajkumar. K [a], M. Sathish Kumar [b], Mahesh Jagadeson [b] , A. Mathan Mohan [b]

[a] S.R.M. Dental College, Bharathi Salai, Ramapuram, SRM Institute of Science and Technology,

Chennai 600089, Tamilnadu, [b] Karpaga Vinayaga Institute of Dental sciences, Chinna Kolambakkam, Kanchipuram Dist., Madurantagam, Tamil Nadu 603308

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KEYWORDS

Oral squamous cell carcinoma, Tamilnadu, Clinicopathology

ABSTRACT:

Introduction: Oral Squamous Cell carcinoma is a common cancer with increasing incidence every year. The clinicopathological character of OSCC is varied in different studies.

Objectives: The aim of the study is to identify the prevalence of OSCC cases in our Center, Karpaga Vinayaga Institute of Dental Sciences, Tamilnadu and study the clinicopathological characters.

Methods: A total of 300 case histories of patients of oral squamous cell carcinoma were collected. The following details were collected from the reports: age and gender of the patients, site of the lesion and the histological type.

Results: Of 300 cases, 191 (63.7%) were Male and 109 (36.7%) were female. 48 patients were 40 years or less, and 252 patients were more than 40 years. The common sites of occurrence in the oral cavity were buccal mucosa 142 (47.3%), tongue 53 (17.7%), Mandible 44(14.7%), Maxilla (6.3%), retro molar trigone 16 (5.3%), floor of mouth 11 (3.7%), Palate 10 (3.3%), lip 3 (1%) and labial mucosa 2(0.7%). 231 (77%) were well differentiated, 60 (20%) were moderately differentiated, and 9 (3%) were poorly differentiated. There was no correlation between age and the histological grade of the OSCC cases in our study.

Conclusions: In this center, the predominant age of occurrence is more than 40 years, and the main site of the lesion is buccal mucosa. Identifying the specific site of lesion in a population is important to improve the survival rate of the patients.

1. Introduction

Oral squamous cell carcinoma is the 6th most common cancer across the world. The main etiologic factors for OSCC are tobacco and alcohol. Other predisposing factors include genetic factors, bad oral hygiene, persistent irritation, microbial infection, malnutrition, and occupational exposure to chemicals.[1] The incidence of OSCC is considered to occur in the 6th to 8th decade of life more commonly in the male population. The predominant sites of incidence are the tongue, lower lip, and the floor of the mouth.[2] There are variations in the clinicopathological characters of OSCC in different studies done to date, especially associated with the site of occurrence of the lesion and the age of occurrence.

2. Objectives

The aim of the article is to identify the prevalence of OSCC cases in our centre, Karpaga Vinayaga Institute of Dental Sciences, which mainly comprises the South Indian population, and study their clinicopathological characters.

3. Methods

Study design and setting: The study was carried out as a retrospective population based cohort study with a cross sectional analytical design. The investigation took place in the Department of Oral Pathology , Karpaga Vinayaga Institute of Dental Sciences, Kanchipuram, Tamilnadu

Sampling and Study population: The study employed a purposive sampling approach. 300 patient records that were identified as oral squamous cell carcinoma were collected from the department archives. Only histopathologically confirmed primary cases of OSCC were selected. The inclusion criteria were (1) Patients with verified diagnosis of primary OSCC (2) case records that included thorough details on demographics, clinical and histopathological data. The exclusion criteria were (1) secondary or recurrent cases of OSCC (2) Case

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records without complete details on demographics, clinical and histopathological data (3) cases with unclear diagnosis

Data Collection: The following data was collected from the record. Demographic data: age and sex of the patients. Clinical details: site of the lesion. Histopathological detail: grading of OSCC. For the purpose ensuring accuracy in analysis, patients' were categorised into two age groups of less than 40 years and greater than 40 years. The anatomic locations that were taken into account were tongue, lip, floor of the mouth, palate, retromolar trigone, buccal mucosa, labial mucosa, maxilla and mandible. The grading of the lesions were marked as well differentiated, moderately differentiated and poorly differentiated.

Ethical considerations: The study was done according to the ethical norms of the institution of Karpaga Vinayaga Institute of Dental Sciences, Kanchipuram. All patient data were anonymised and only the details pertaining to the study were gathered.

Statistical analysis: Data were input into Microsoft excel and thereafter was analysed using Statistical Package for the Social Sciences (SPSS) software, version XX IBM Corp., Armonk, NY, USA). With all the variables, Descriptive statistics was calculated . The pattern of distribution of age and gender was illustrated in terms of frequencies and percentages. Clinicopathological characters were assessed using Chi-Square test, with a p value < 0.05 regarded statistically significant.

4. Results

Demographic distribution: A total of 300 cases were reviewed in the study. Of the 300 cases, 191 (63.7%) were male and 109 (36.7%) were female. The male to female ratio obtained in this study was 1.7:1. Patients who were 40 and less than 40 years were 48, and those with more than 40 years were 252.

Histopathological grading: The histological types of cancer were well differentiated 231 (77%), moderately differentiated 60 (20%), and poorly differentiated 9 (3%). The percentages of well, moderately, and poorly differentiated cases in males were 75.9%, 21.5%, and 2.6%, respectively. In females, the percentages of well, moderately, and poorly differentiated cases were 78.9%, 17.4%, and 3.7%, respectively (Table 1). The Chi-square statistical analysis showed no significant association between the histological grading and sex of the patient (p=0.637). (Table 2)

Table 1: Frequency distribution of histological grade by sex.

		GRADE				
SEX			Frequency	Percent	Valid Percent	Cumulative Percent
Male	Valid	Well	145	75.9	75.9	75.9
		Moderate	41	21.5	21.5	97.4
		Poor	5	2.6	2.6	100.0
		Total	191	100.0	100.0	
Female	Valid	Well	86	78.9	78.9	78.9
		Moderate	19	17.4	17.4	96.3
		Poor	4	3.7	3.7	100.0
		Total	109	100.0	100.0	

Table 2: Association between the histological grading and sex of the patient.

Chi-Square Tests			
	1Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	.901[a]	2	.637
Likelihood Ratio	.906	2	.636
Linear-by-Linear Association	.102	1	.749
N of Valid Cases	300		

Anatomical site distribution: The common site of occurrence in the oral cavity in the descending order of frequency was buccal mucosa 142 (47.3%), tongue 53 (17.7%), mandible 44 (14.7%), maxilla (6.3%), retromolar trigone 16 (5.3%), floor of mouth 11 (3.7%), palate 10 (3.3%), lip 3 (1%), and labial mucosa 2 (0.7%). The sex wise distribution showed that the predominant sites of OSCC in males are buccal mucosa 84 (44%), tongue 37 (19.4%), and mandible 29 (15.2%).

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In females, the predominant sites were buccal mucosa 58 (53.2%), tongue 16 (14.7%), and mandible 15 (13.8%). (Table 3) The Chi-square test revealed no significant association between sex and site of lesion (p = 0.403). (Table 4)

Table 3: Frequency distribution of anatomical site by sex.

Site	Male (n=191)	Female (n=109)
Tongue	19.4%	14.7%
Lip	1.0%	0.9%
Floor of mouth	4.2%	2.8%
Retromolar trigone	6.8%	2.8%
Palate	3.1%	3.7%
Buccal mucosa	44.0%	53.2%
Labial mucosa	–	1.8%
Maxilla	6.3%	6.4%
Mandible	15.2%	13.8%

Table 4: Association between anatomical site and sex of the patient

Chi-Square Tests			
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	8.316[a]	8	.403
Likelihood Ratio	9.116	8	.333
Linear-by-Linear Association	1.234	1	.267
N of Valid Cases	300		

Correlation of age and tumor grade: The correlation analysis between the histological grade and the age identified a weak negative correlation by Pearson's analysis (r = –0.086) and Spearman's analysis (ρ = –0.077) and they were not statistically significant (Table 5,6). This suggests that histological grade of OSCC did not vary significantly with age.

Table 5: Pearson's Correlation of age and tumor grade

		age	grade
age	Pearson correlation	1	-.086
	sig. (2-tailed)		.136
	n	300	300
grade	Pearson correlation	-.086	1
	sig. (2-tailed)	.136	
	n	300	300

Table 6: Spearman's analysis of age and tumor grade

			Age	Grade
		Correlation Coefficient	1.000	-.077
	Age	Sig. (2-tailed)	.	.185
Spearman's rho		N	300	300
		Correlation Coefficient	-.077	1.000
	Grade	Sig. (2-tailed)	.185	.
		N	300	300

5. Discussion

Lip and oral cavity cancer case incidence is increasing every year. According to Globocon statistics 2020, the incidence of cancer cases constitutes around 10.3% of the total number of cancer cases in India. The incidence in males and females is 1,046,661:31,268.[3] The main aim of the study was to determine the prevalence of OSCC in the Chengalpet population and study their clinicopathologic characters.

In our study population, the male-to-female ratio is 2:1. The incidence matches most oral cancer epidemiology studies worldwide and in India. The main reasons that could be attributed to higher incidence in males are lifestyle factors like smoking, alcohol intake, and betel nut chewing.[4] Kruaysawat et al., in their study about oral cancer incidence in the Thai population, identified that the incidence of squamous cell carcinoma was the major type, and the incidence was higher in females. The male-to-female ratio was 1:1.56.[5] Similarly, a study by Dhanuthai et al, on oral cancer in the Thai population

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found that squamous cell carcinoma constituted around 67% of the tumors studied, and the male-to-female ratio was 0.86:1. The reasons that were attributed to the increased prevalence in females were the higher longevity of life in females, and in their study, increased prevalence was observed in the 7th and the 8th decades. It was also attributed to the fact that females regularly visit dental clinics and hospitals for checkups, unlike the male population, which could have enabled more identification of cases among females.[1] Our study also revealed that the buccal mucosa was the predominant site of incidence in both males and females. (Table 1, 2)

In a study by Rai et al., the maximum cases were seen in the age group between 60 and 69 years, which contributed to 36.20% of OSCC cases.[2] Also, in a study of the Hong Kong population, the average age of incidence of OSCC was 64.14 years.[6] In our study, the average age of incidence was 53.7 $\pm$11.8. Contrary to these studies, in a study of head and neck cancers by Shadab al Aslam et al, where the predominant cases were of the oral cavity and the predominant histological type was squamous cell carcinoma, the majority of the incidence in the oral cavity was noticed in the age group 31 to 40 years with 79 cases and from 41 to 50 years with 74 cases. From 51 to 60 and 61 to 70 years, the cases were 51 and 31 in number.[7] This was attributed to the habits of the patients in the study. Smoking with alcohol consumption and tobacco chewing was very common among the age group less than 50 years in this study. In a study by Singh et al, in tertiary care in North India, the incidence in males was more common in the 40 to 49 years age group with 25.2%, and in the females, the major incidence was noticed in the age group of 50-59 with 26.5%.[8] In our study, the incidence was associated with the age group of 50–59 years, and there was no correlation between the age of the patient and the tumor grade.

In our study (Table 3), we identified the buccal mucosa as the common site of incidence (47.3%), followed by the tongue (17.3%). When seen individually in male and female groups, the main site of occurrence was buccal mucosa, followed by the tongue. In many other studies, various other sites have been recognized as the main site. Choi et al study, which examined a large population of 18-year-olds in Hong Kong, identified the majority of cases in the tongue region almost forming 51.9%.[6] Similarly, in a study by Mneimneh et al, in a study of 150 OSCC patients who were below 40 years, 131 patients had it in the tongue.[9] Different from all the other studies mentioned above, in the study by Chidzonga et al, the majority of the oral malignant tumours, squamous cell carcinoma, was observed in the gingiva.[10] Even within India, in a study done by Alam et al in Western Uttar Pradesh, the main site in the oral cavity was the base of the tongue (16%), followed by buccal mucosa (14.2%).[7] The study attributed this to the patients' habits. Tobacco chewing was linked to the sites of the cancers, but smoking was found to be the main risk factor for tongue cancer. On the other hand, tobacco combined with smoking or alcohol was found to be a risk factor for cancer of the buccal mucosa.[7] In a study of OSCC by Abdullah et al, in a population in the state of Karnataka less than 45 years, the main site was observed as the tongue, constituting 29.07%, followed by buccal mucosa.[11] However, in the elderly population, the primary site was observed as buccal mucosa. The factors that were responsible for the site of occurrence were the lifestyle, customs followed by the population, socioeconomic status, and the easy availability of the substances. Contrary to the above study, Kapila et al, in their research, observed that the buccal mucosa was the most affected site in the population (Karnataka) of both age groups—above and below 40 years.[12] In a study in Odisha, buccal mucosa was the commonest site along with the alveolo-buccal sulcus. The incidence was nearly twice as high in the tongue.[13] In a study by Singh et al, in North India, the predominant site of carcinoma was buccal mucosa.[14]

The incidence of carcinoma at a particular site could be associated with the habits. The common cause of carcinoma in the buccal mucosa is the presence of quid in contact with the mucosa. It is known that betel quid can irritate the epithelium, making it easy for carcinogens and other supra-additive factors to spread through smoking and drinking alcohol, which could lead to cancer. Exposure of the tongue to chemical irritants from smoking and alcohol is responsible for the presence of carcinoma in the tongue. Cancerous growths can form on the sides of the tongue because when the betel quid is moved from the right to the left side, saliva containing chemicals that irritate the tongue comes into contact with the sides.[15] Though all the above reasons are correlated with the site of incidence, in some cases the lesion is also known to arise de novo. In 60% of the cases, the cancer lesion is known to arise de novo.[13] The incidence of carcinoma in young patients with less alcohol consumption or in patients without any habits suggests that factors other than smoking, alcohol, and chewing may also contribute to carcinogenesis. Factors like patients' immune status, genetic susceptibility, and the presence of viral infection should also be taken into consideration while studying carcinogenesis. [12]

Some sites get easily affected when compared to the others due to the thickness of the epithelium in that region. The thickness of epithelium at the buccal mucosa, labial mucosa, gingiva, dorsum, and ventral surface of

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the tongue, as well as the floor of the mouth, has been identified as 659.79 mm, 405.56 mm, 650.02 mm, 318 mm, and 100.07 mm, according to an optical coherence tomography study.[16] In a study by Farhood et al, it was identified that compared to carcinoma of the floor of the mouth, retromolar trigone and upper gum had better survival rates than the carcinoma of the tongue.[17] Similarly, the Taiwanese population study revealed that the survival rates varied depending on the location of the lesion. The 5-year survival rate for lip, buccal cancer, tongue cancer, floor of mouth, and gingiva was 78%, 67.8%, 64.8%, 63.3%, and 61.3%, respectively.[18] The studies show that the predominant site of incidence varies from one population to the other, and more studies are now focusing on the site of OSCC cases, as they are known to influence the survival rate too.

Molecular changes in the different sites of OSCC have been observed. In the study by Linda Boldrup et al. with 3 miRNAs—miR-21, miR-125b, and miR-203—it was identified that miRNA levels varied across different sites, and the tongue tumour had deregulation of all the three miRNAs. The gingival tumors exhibited deregulation solely of miR 125b, while the tumors of the tongue and the floor of the mouth demonstrated deregulation of both miR 21 and 125B. [19] In the study by Frohwitter et al, in the study of 17 genes associated with specific sites, X-linked inhibitor of apoptosis (XIAP) exhibited increased expression in the floor of the mouth relative to the tongue and other sites in the oral cavity. Although the expression of other genes was different, they were not statistically significant. In all cases of OSCC, the elevated expression of XIAP was associated with reduced overall survival.[20] These studies indicate that the molecular profiles may vary across different intraoral subsites, and that these molecules could play a significant role in determining the survival rate. Further studies are recommended to elucidate their potential influence and clinical relevance.

Our study observed the buccal mucosa as the primary site correlating with the patients' tobacco chewing habit. Tobacco chewing and smoking were the predominant habits, followed by alcohol intake in the research population. Riika et al., in their study demonstrated that the influence of alcohol and smoking on the incidence of OSCC is different between different regions in the oral cavity. In their study, smoking and alcohol habits were more correlated with the incidence of OSCC in the floor of the mouth and were less correlated with buccal and gingival tissues.[21] Tobacco is considered a principal cause of premature mortality globally. Tobacco displays varied functions like epigenetic modifications of oral epithelial cells, interaction with viruses, modulation of oxidative stress, and suppression of various immunologic processes.[22] Alcohol induces tumorigenesis through its metabolite, ethanol. It induces carcinogenesis by disrupting DNA synthesis, creating DNA adducts, and modifying the expression of oncogenes. They also function as a solvent and enhance the permeability of the mucosa, facilitating the action of other carcinogens.[23] The study by Worakhajit et al. identified that betel quid, followed by alcohol, is a potential risk factor. In the study, the greatest significant synergistic activity was observed in the group exposed to smokeless tobacco, betel quid, and alcohol. [24] The recurrence rate for OSCC is 26%, with a range of 15–41.7%.[25] The study by Reichal et al. correlating the site of oral squamous cell carcinoma incidence with recurrence revealed that the buccal mucosa had the highest recurrence rate. [26] Different studies depending upon the staging, grading, and the margins have presented different recurrence rates .[27] The survival rate for OSCC is approximately 50% .[28] PMODs(potentially malignant oral disorders) can develop into oral cancer, and it is crucial to acknowledge that the majority of PMODs are also affected by habits.

The study identifies that habits significantly influence the prevalence and location of OSCC. This underscores the critical role of prevention in the process. Primary prevention aims at eliminating the risk factors like tobacco and alcohol. It aims at improving diet and nutrition. Secondary prevention at identifying potential malignant oral disorders or early OSCC. Tertiary prevention aims at preventive strategies to reduce disease recurrence and complications in treated patients.[29] Knowing early detection can increase the 5-year survival rate from less than 30% when detected at an advanced stage to 80% when detected early. [30]

6. Conclusion

OSCC is known to occur at different sites specific to geographic conditions or the habits associated with it. The main site of occurrence in Southern India, according to this study, is identified as buccal mucosa. Identification of specific sites of OSCC lesions in a population, along with prevention measures and research work, could greatly prevent the incidence of OSCC. This may also influence the clinical outcome and the mortality associated with it.

The clinical significance of the study is the understanding that OSCC occurs in buccal mucosa in individuals more than 40 years old in this population, which will help clinicians adopt a targeted screening methodology. Smokers and betel quid chewers, who are high risk individuals should be screened to detect and treat OSCC early. This population specific knowledge could enhance preventive measures and patient survival.

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