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Original Research Article

Histomorphological variants of oral squamous cell carcinoma and their relation with prognosis of the disease

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ABSTRACT

Background: The key to wealth is health but in present days cancer is going to exhaust mental, physical and economic conditions. Oral Cancer is the 6^{th} most common cancer worldwide. Approximately 630,000 new patients diagnosed annually resulting in more than 350,000 deaths every year. Squamous cell carcinoma is by far the most important and the most common malignant mucosal neoplasm of the head and neck accounting for over 90% of all malignancies.
Histomorphological features of oral squamous cell carcinoma (OSCC) and their relation with the pathological prognostic factors i.e. histological stage and grade of malignancy is the key feature, which help early and easy prognosis of OSCC.
Aim: To study the histomorphological features of oral squamous cell carcinoma and their relation with the pathological prognostic factors i.e. histological stage and grade of malignancy.
Objective: Recent reports suggest an increase in oral squamous cell carcinoma (OSCC) frequency. To improve programs in public health, it is necessary to understand the epidemiological conditions.
Study Design: A retrospective review of all OSCC cases diagnosed by the Pathology Department was performed. Demographic data, in addition to anatomic zone and histological degree of differentiation were obtained. Central tendency, dispersion and prevalence rate per 100,000 individuals were determined.
Results: A total of 150 patients were diagnosed with OSCC and majority of them were men 118(79%) were men. OSCC were predominantly observed in the age of 40-60 years. The predominant anatomic zone was the Buccal mucosa, GBS, Angle of Mouth 99(66%), followed by the tongue and lip 42(28%) and Retromolar Triagone 09(06%).
The most frequent histological degree was well differentiated in 110 cases (73.3%). The rates of OSCC prevalence showed similar patterns in terms across time.

1. Introduction

Oral cavity is the visible gateway to the rest of the body and it reflects what is happening inside of one's body. Oral health problems can have a hazardous effect on quality of life in modern times, and are becoming more prevalent. Oral cancer is one of the major health concerns and it is a sixth most common malignant neoplasm in the world.

Around two thirds of oral cancer cases are observed in developing countries, with an annual incidence of approximately 275,000 cases.[1] A large percentage (90%) of malignant tumors of the mouth is oral squamous cell carcinomas (OSCCs).[2] It is the most prevalent form of head and neck cancer associated with high mortality rate, high recurrence rate and less than 50% five-year survival rate

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suggestive of its aggressive and metastatic nature.[3] The cataclysmic features of this malignancy is a consequence of its invading nature.

OSCC is more prevalent in men for obvious reasons. In case of females it is the third most prevalent form of cancer.[1] Men mostly in their fifth and sixth decade of life are found to be predominantly affected by OSCC and it is observed to have lower incidence in patients under 40 years of age.[4,5] There is no clear evidence on the specific location of OSCC in the oral mucosa, but the tongue, gums, palate, and floor of the mouth are principle anatomical zones frequently observed.[6] The lesion is characterized clinically by an ulcerated, necrotic area surrounded by raised boundaries.[7] Tobacco and alcohol consumption were found to be one of the preventable cause of OSCC,[8,9] still a total of 15 -20% people who were not exposed to tobacco and alcohol are increasingly falling prey to OSCC frequently.[8–10] Furthermore, shorter exposure times in younger patients make it difficult to fully understand the role of these risk factors.[11] In this regard further study is suggested to determine whether genetics,[12] diet, or viral agents play a role in the genesis of OSCC.[10]

The conventional form of oral squamous cell carcinoma (OSCC), which makes up between 10% and 15% of all squamous cell carcinomas, has several variants.[13] These variants are listed below;

1. Verrucous carcinoma (VC)
2. Adenoid/ acantholytic/ pseudoglandular SCC (AdSCC),
3. Spindle cell/ sarcomatoid carcinoma (SCSC),
4. Adenosquamous carcinoma (ASC),
5. Basaloid SCC (BSCC),
6. Papillary SCC (PSCC)

There is a distinct histomorphological characteristic to each of these variants. This short article provides a brief overview of the different histopathological variants of OSCC observed in our institute, which allowed for appropriate clinical management. Detailed history and physical examination were performed to detect OSCC. Computer tomography (CT) scanning or magnetic resonance imaging (MRI) were used to confirm the clinical diagnosis and to assess the extent of local and regional tumor spread, invasion depth, and lymphadenopathy.[14,15]

1.1. Histomorphological features of OSCC

In histological terms, a lesion goes through several phases from initial cell injury to cancer formation. An oral carcinoma progresses from simple, moderate, or severe dysplasia to in situ carcinoma and finally to invasive carcinoma.

The tumors were histologically classified as:

1. Well-differentiated squamous cell carcinoma,
2. Moderately differentiated,
3. Poorly differentiated.

1.1.1. Well differentiated squamous cell carcinoma:

Well differentiated squamous cell carcinomas contain round to polygonal squamous cells, arranged in islands of different shapes and sizes with mild pleomorphism, good amount of intracellular and extracellular keratinization. The islands of tumor cells are seen infiltrating into the stroma.

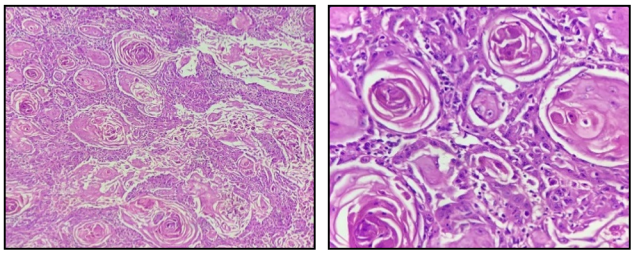

Fig. 1: Conventional OSCC -malignant epithelial islands showing keratin pearl formation. (H&E stain, ×100)

1.1.2. Moderately differentiated squamous cell carcinoma:

The tumoral stroma is infiltrated by islands of neoplastic atypical epithelial cells that are oval-shaped or round in shape. At the peripheral region fibrous stroma or cells of the inflammatory type separate carcinoma islands.

Nuclei of neoplastic cells have different shapes and sizes, most of them

There are various shapes and sizes of nuclei in neoplastic cells, most of which have hypochromic nucleoli and moderate nuclear pleomorphism. The nuclei of neoplastic cells consist different shapes and size, majority of them were hypochromic with large nucleoli and moderate nuclear pleomorphism. In the microscopic examination tumor cells observed as atypical cells diffusely scattered in the stroma with few keratin pearls and mitotic rate of 3/10 Hpf.

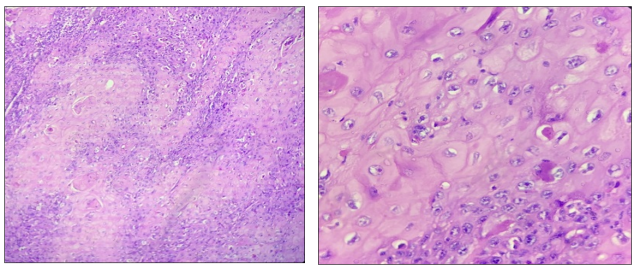

Fig. 2: Conventional oral squamous cell carcinoma- neoplastic atypical epithelial cells showing few keratin pearl formation. (H&E stain, ×100)

1.1.3. Poorly differentiated squamous cell carcinoma

The cells of poorly differentiated squamous cell carcinoma show moderate to marked pleomorphism, lack of intracellular and extracellular keratinization, and increased mitosis >10/10 Hpf.

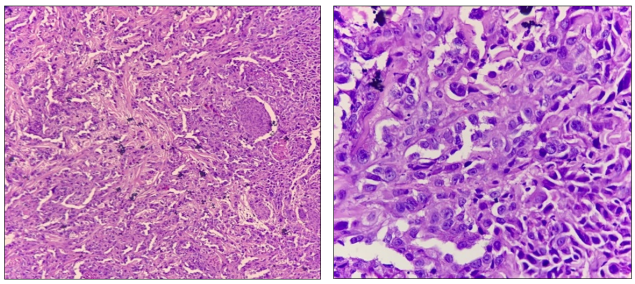

Fig. 3: Poorly differentiated oral squamous cell carcinoma. (H&E stain, ×100)

2. Methodology

The study included radical surgery cases of mandible from patients who were clinically suspected of oral squamous cell carcinoma in the OPD of oncology dept. in Sri Aurobindo Medical College and PG Institute, Indore.

Relevant clinical history including site of lesion, number of lesion, associated symptoms, significant personal and family history including smoking habit were taken and entered in the proforma.

3. Objectives

1. To study the histomorphological patterns of oral squamous cell carcinoma.
2. To study the clinico-epidemiological characteristics including age, gender and smoking habit of patients, comparing different histomorphological types.
3. To find out the association of cancer with site, histopathological grade and stage of squamous cell carcinoma.

3.1. Inclusion criteria

1. All the cases of Radical surgery for oral squamous cell carcinoma (Buccal, Mandibular, Maxillary, Tongue and Oropharynx) specimen that will be received for histopathology study during study period.

3.2. Exclusion criteria

1. Excision biopsy of oral carcinoma.
2. Radical surgery for oral malignancy other than squamous cell carcinoma.

4. Results

The study was undertaken in a tertiary care institution in the specialty of pathology, in the years 2019-2020, 150 participants were assessed. Both male and female students participated in the study.

In the present study, it was found that 32(21%) were female participants and 118(79%) were male participants. (Table 1)

In the present study it is concluded that oral cancer showed the highest preponderance of occurrence along buccal mucosa, GBS, Angle of mouth that is (n=99) 66%. Tongue and lip followed the same sequence (n=42) 28%. Retromolar triagone was the least chosen area (n=9) 6%. Intrestingly females in these study did not show cancer of tongue and lip retromolar trigone.

Out of 150 OSCC patients maximum number of patients(n=91) 60.67% were reported with T4 tumor which was followed by T2 that is tumor more than 2cm and less than 4cm and then T3 which comprise of tumor more than 4 cm respectively. The study showed only 4% male patients presented with T1 tumor (i.e. tumor less than 2cm) and no female patient presented at this stage. (Table 3) All of the above variations in nuclear & cell size and shape, nuclear hyperchromatism, increased & abnormal mitotic figures.

In the present study the highest cases were reported to be of well differentiated type (n=110) 73.3%, followed by moderately differentiated OSCC (n=35)23.3% and poorly differentiated OSCC (n=5)3.4%.

The overall staging in OSCC in present study were illustrated in the following table, surprisingly 0% female were presented Stage I pathological condition. Majority of participants were male 72 (61%) presenting Stage IV pathological condition.

It was observed in the present study that out of 124 cases of WDSCC around 68 showed positive lymph node whereas 56 were node negative. 7 cases out of 22 cases MDSCC had positive nodes and surprisingly none of the grade III tumor showed nodal involvement.

More than half of the patients who participated in the study were male 55.56%, amongst which 68 were smokers and amongst female cases were 14 patients were smokers. Point to ponder in this study results is significant number of non-smoker female and males who also developed cancer.

5. Discussion

Malignancy follows only one rule that is it follows no rule. Although scientists all over the world are trying tracing the biologic behavior and outcomes of these notorious malignancies still we are falling short of predicting its behavior. Various factors responsible for knowing the prognosis of cancer are being laid down. One of those factors which are authentic and being used are histological variants of oral squamous cell carcinomas.

Table 1: Demographic characteristics of patients

S. No.	Age (In Years)	Male	Female	Total No. of Cases and %.
1.	0-20	-	-	-
2.	20-40	18	00	18(12%)
3.	40-60	67	20	87(58%)
4.	>60	33	12	45(30%)
	Total	118(79%)	32(21%)	150(100%)

Table 2: Clinico-pathological appearance of the reported cases of OSCC variants

S. No.	Site	Male	Female	Total
1.	Buccal mucosa, GBS, Angle of Mouth	68	31	99(66%)
2.	Tongue and Lip	41	01	42(28%)
3.	Retromolar Triagone	09	00	9(06%)
	Total	118	32	150(100%)

Table 3:

S. No.	Tumour Size	Male	Female	Total
1.	T1	06(5.08%)	00	06(4%)
2.	T2	22(18.64%)	10(31.25%)	32(21.34%)
3.	T3	19(16.10%)	02(6.25%)	21(14%)
4.	T4	71(60.17%)	20(62.5%)	91(60.67%)

Table 4: Histological differentiation degree of OSCC

S.No.	Grade	Male	Female	Total
1.	Grade I(Well Differentiated SCC)	90(76.2%)	20(62.5%)	110(73.3%)
2.	Grade II(Moderately Differentiated SCC)	24(20.3%)	11(34.3%)	35(23.3%)
3.	Grade III(Poorly Differentiated SCC)	04(03.5%)	01(03.2)	5(3.4%)
	Total	118(79%)	32(21%)	150(100%)

Table 5: Tumor staging

S. No.	Pathological Stage	Male	Female	Total
1.	Stage I	06 (05%)	00	06 (04%)
2.	Stage II	16 (14%)	02 (06%)	18(12%)
3.	Stage III	24 (20%)	06 (19%)	30(20%)
4.	Stage IV	72 (61%)	24 (75%)	96 (64%)
	Total	118(79%)	32(21%)	150 (100%)

Table 6: Lymph node status

S. No.	Grade	Lymph Node Status		Total
		Positive	Negative	
1.	Grade I (WDSCC)	68	56	124
2.	Grade II (MDSCC)	7	15	22
3.	Grade III (PDSCC)	00	4	4
	Total	75	75	150

There are multiple histological variants each having different behavior, these predictors provide accuracy many of the times but still they are not used and reported regularly by pathologist. The present paper tries to shed light on this already known, but less explored part of oral cancer.

OSCC entails quite noteworthy morbidity and mortality rates among all other cancers. The incidences of OSCC were probably more in males than females (2:1), which was due to greater-exposure of this group to carcinogenic agents such as alcohol and tobacco.[16] In the present literature more than half of the patients who participated in the study were male 55.56%, amongst which 68 were smokers while amongst females 14 patients were smokers. Point to ponder in this study is the significant number of non-smoker females and males who also developed cancer.

Table 7:

S. No.	Parameters	Name of the Study	Incidence	Present Study
1.	M:F Ratio	Jyoti Verma et al.	3:1	3.68:1
		Garima Sharma et al.	4:1	
		Yue Jing et al.	1.04:1	
2.	Most Involved Site of the Lesion	Jyoti verma et al.	Buccal mucosa>Tongue>Retromolar trigone	Buccal mucosa>Tongue> Retromolar Trigone
		Garima Sharma et al.	Tongue>Buccal mucosa	
		Arush Agrawal et al.	Buccal mucosa>Tongue	
3.	Most common Grade	Jyoti Verma et al.	I>II>III	I>II>III
		Garima Sharma et al.	II>I>III	
		Arush Agrawal et al(142)	I>II>III	
4.	Most common Stage	Jyoti Verma et al.	IV>II>I>III	IV>III>II>I
		Atif Ali Hashmi.	II>I>III=IV	
		Arush Agarwal et al.	II>I>III>IV	
5.	Lymph Node Status	Atif Ali Hashmi.	Positive-0.9% Negative-99.1%	Positive-50% Negative-50%
		Arush Agrawal et al.	Positive-44% Negative-48%	

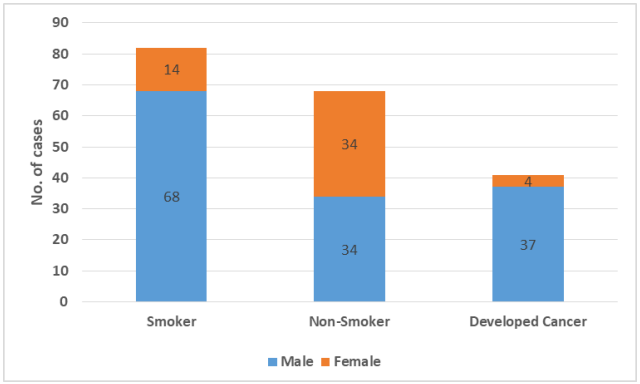

Fig. 4: Demographic data smokers with respect to gender

OSCC is characterized by two important characteristics: the anatomic zone and histological differentiation degree. These features could indicate its future biological behavior, treatment, and prognosis.[16–18]

In our study, the buccal mucosa, tongue, and retromolar trigone were identified as the most affected anatomic zones. (Table 2) Although, the study done by Sánchez-Garca et al.[19] and Durazzo et al.[20] have reported that the tongue is the most affected anatomic area in higher volume medical centers in Mexico and Brazil, respectively.

In contrast, Asian populations reported a higher incidence of buccal cancer than other zones. Variation in anatomic zone frequency can somewhat be attributed to the difference/change in exposure to risk factors, such as cigarette smoking, cigars, pipes or chewing tobacco.[1,19,20] Classifying tumor differentiation degrees gives some indication of their aggressiveness, which may then influence the prognosis or treatment.[17] Our results indicated that 35 OSCC were MD (moderately differentiated), followed by WD in 110 cases, and PD in 5 cases only. As reported, aggressiveness is inversely related to differentiation level; consequently, our study suggests that many patients with MD carcinomas might not experience a good quality of life or a long survival time. (Table 4)

Based on the findings of Bagan J et al. and Neville BW et al.[16] OSCC occurs more frequently in alcohol drinkers and smokers and showed propensity for early and extensive lymph node metastases and predominantly,[2,16] which is similar to findings of the present study.[3,4] Since each of these tumors has a different prognosis, it is crucial for clinicians to identify each tumor accurately.

This entails that oral cavity frequently affected by variants of OSCC. As the prognosis of each of them differs greatly, accurate histopathological identification is crucial to precise treatment. In most cases, after five years, survival rates for OSCC post treatment is around 50%. It is important to consider invasion mode, surgical margins, lymph node metastases, extra capsular spread and invasive tumor front grade, which play a vital role in determining survival success. The pathologist may evaluate deeply invasive margins when grading by gross histological differentiation, but this will not affect prognosis. In this study, we focus on the histological variants of OSCC, which will aid in the early and easy prognosis of the condition.

Table 7 is a brief literature review of the past significant studies regarding incidence of male female ratio, most involved site of the lesion, most common grade, most common Stage and lymph node involvement and their comparison with our study.

6. Conclusion

OSCC variants that are histopathologically challenging/ difficult to diagnose, such as SCSC and AS, required immunohistochemistry and special stains for accurate diagnosis. As a result, each variant is unique in terms of prognosis, metastatic potential, survival rate and treatment.

7. Source of Funding

None.

8. Conflict of Interest

None.

9. Acknowledgement

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