Clinicopathological Prognostic Parameters in Oral Squamous Cell Carcinoma

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Abstract: _Aim: To determine the prognostic parameters in oral squamous cell carcinoma (OSCC)._ _Methods: All cases were retrospectively and prospectively analyzed from August 2014 to July 2018 for various prognostic parameters. The parameters were divided into demographic, clinical and pathological groups. TNM pathological stage was determined in each case._ _Results: 53 cases were included. Male to female ratio was 1.3:1. Mean age was 58.9 years. Males reported greater risk prone habits to oral cancer than females. Tobacco usage was the predominant habit, with maximum number of cases showing duration of 20- 30 years of that habit. Medium socioeconomic and primary educational status was the commonest. Maximum number of patients presented within 6 months of onset of symptoms. Buccal mucosa and lower gingiva i.e. gingivobuccal sulcus was the most common affected site. Majority of patients presented in Stage III (49.1%). Staging by the current AJCC TNM system was done. Tumor size of >2 and </= 4 cm and tumor thickness > 10 mm was the commonest. Moderately differentiated OSCC (45.3%) was predominant histological grade. 6 cases came out to be OSCC variants. Close surgical margins, PNI and LVI were identified more commonly in advanced stages. 40% cases had lymph node metastasis and 20% had extranodal extension._ _Conclusions: TNM classification had significant correlation with clinical and histopathological parameters. These highly significant results indicated that histologically invasive areas may be primarily responsible for clinical behaviour of the tumor and this may be important for therapy of choice for OSCC. The current AJCC TNM system of staging appears to be a better mechanism for assessment of tumor volume and predict the prognosis of OSCC. Analysis of the TNM system has been adopted to plan treatment and provide better evaluation of patient's evolution._

Keywords: Oral cancer, Oral squamous cell carcinoma, Clinicopathological, Prognosis

1. Introduction

Carcinoma of oral cavity is one of the most frequent malignant tumors worldwide with major predominance in South East Asia and India. Among oral cancers, 95% are squamous cell carcinomas (SCC), ranking sixth in the world and ranks among the top three types of cancer in our country. Age-adjusted rates of oral cancer in India are high at 20 per 100,000 population and accounts for over 30% of all cancers in the country. [1] Oral squamous cell carcinomas (OSCC) originate from squamous epithelium in the oral cavity. They are aggressive cancers with a tendency to recur and metastasize.

Despite advances in the diagnostic and therapeutic modalities, the prognosis of epithelial tumors in the oral cavity is still very unpredictable. The prognostic determinants in OSCC have been broadly classified into patient and tumor related factors. Patient related factors are age, gender, habits, socio-economic status, education and diagnostic delays. Tumor related factors are site, tumor thickness, resection margins, degree of differentiation, perineurial invasion (PNI), lymphovascular invasion (LVI), angiogenesis, lymph node metastasis and TNM (tumor, node, metastasis) staging. Despite voluminous information on the subject of OSCC the prognosis remains uncertain with marginal changes in mortality rates. Thus this study aims to correlate prognostic parameters in OSCC in the Indian context with pathological TNM stage.

2. Materials and Methods

This was a prospective and retrospective study conducted on all successive cases of surgical resection of oral squamous cell carcinomas received at the Department of Pathology of our Medical College and Hospital, for histopathological study, during the period from August 2014 to July 2018. Cases received from August 2014 to July 2016 were studied retrospectively. Cases from August 2016 to July 2018 were studied prospectively. Archival records for retrospective cases were procured from hospital database and archives of Department of Pathology and relevant details were noted. Old paraffin embedded blocks was retrieved from records of Department of Pathology and fresh histological sections prepared. Specimens of cases were studied prospectively for gross details and clinical demographic details noted. Appropriate sections were prepared and processed for histopathological examination.

All sections were stained by haematoxylin and eosin technique and studied microscopically. Histopathological details pertaining to suggested prognosis as recorded in the literature were identified and tabulated in each case. These parameters were divided into demographic, clinical and pathological groups. TNM pathological stage carried out by American Joint Committee on Cancer (AJCC) manual guidelines was determined in each case. [2]

3. Results

53 cases of resection for oral squamous cell carcinoma were included in this study. 30 (56.6%) were from males and 23 (43.4%) were from females. Male female ratio was 1.3:1. Most number of patients was seen in the age group of 60- 69 years (39.6%). The mean age of the patient was 58.9 years. The personal habits revealed that 30 (56.6%) of the patients had a tobacco alone followed by 6 (11.3%) patients with tobacco and alcohol habit and 4 (7.5%) patients with tobacco

and betel quid. Habit of alcohol intake alone and betel quid alone was not found in any of the patients. Duration of tobacco habit in these cases revealed that the largest number of cases (17/42.5%) was of duration 20-30 years. However, it was not possible to analyze tobacco, alcohol and betel quid use in terms of quantity and frequency of use. (Table 1)

Socio-economic status revealed that most of the patients (25/47.2%) were of medium category followed by low category which included 24 patients (45.3%). None of the patients were of high socio-economic status. 32 (60.4%) patients attained primary education alone followed by higher secondary in 10 (18.9%) patients. 41 cases (77.4%) presented with < 6 months, 10 (18.9%) cases with 6- 12 months and 2 cases (3.8%) with > 12 months duration of symptoms. (Table 1)

Majority of patients were in Stage III (49.1%) followed by Stage II (22.6%), Stage IV A (15.1%) and Stage IV B (11.3%) cases. (Table 2) Site distribution revealed that buccal mucosa and lower gingiva (gingivobuccal sulcus) was the most commonly involved site, accounting for 27 (50.9%) cases. (Table 3)

Tumor size revealed that 29 (54.7%) cases had tumor size >2 and </=4 cm and 35 (66%) cases had tumor thickness > 10 mm. Histologically, 24 (45.3%) cases were of Grade II followed by 20 (37.7%) cases of Grade I and 3 (5.7%) cases of Grade III. Grading was not applied in 6 cases as they were reported as variants of squamous cell carcinoma. Majority of the cases were of higher stage (Stage III and IV). Of 6 cases of OSCC variants, 3 (50%) cases were verrucous type, 2 (33.3%) cases spindle cell variant and 1 (16.7%) case was papillary variant. 32 (60.4%) cases revealed close margin (1-5mm), 17 (32.1%) cases negative margin (>5mm) and 4 (7.5%) cases as positive margin (<1mm). PNI and LVI was seen in 15 (28.3%) and 14 (26.4%) cases respectively. (Table 4)

18 (40%) cases showed nodal involvement, of which 9 cases showed extranodal extension (ENE). (Table 5)

Table 1: Demographic features of oral squamous cell carcinoma cases studied

Parameters	Number of cases	Percentage (%)
Gender (n=53)		
Male	30	56.6
Female	23	43.4
Age (in years) (n=53)		
<50	11	20.8
50-59	11	20.8
60-69	21	39.6
>70	10	18.9
Habits(n=53)		
Nil	13	24.5
Tobacco alone	30	56.6
Tobacco + Alcohol	6	11.3
Tobacco + Betel quid	4	7.5
Duration of habits (in years) (n=40)		
<20	14	35.0
20-30	17	42.5
>30	9	22.5
Socioeconomic status (n=53)		
Low	24	45.3
Medium	25	47.2
N.A.	4	7.5
Education(n=53)		
Uneducated	4	7.5
Primary	32	60.4
Higher secondary	10	18.9
Graduate	1	1.9
N.A.	6	11.3
Onset of symptoms (in months) (n=53)		
<6	41	77.4
6-12	10	18.9
>12	2	3.8

Table 2: Pathologicalstaging wise distribution of the cases

Pathological staging	Number of cases	Percentage (%)
I	1	1.9
II	12	22.6
III	26	49.1
IVA	8	15.1
IVB	6	11.3
Total	53	100.0

Table 3: Site wise distribution of the cases

Tumor Site	Number of cases	Percentage (%)
Buccal mucosa, lower gingiva	27	50.9
Buccal (cheek) mucosa	7	13.2
Mucosa of lower lip	5	9.4
Lateral border of tongue	5	9.4
Retromolar area	2	3.8
Others	7	13.2
Total	53	100.0

Table 4: Histopathological features of oral squamous cell carcinoma cases studied

Parameters	Number of cases	Percentage (%)
Tumor size (in cm) (n=53)		
</=2	17	32.1
>2 and </=4	29	54.7
>4	7	13.2
Tumor thickness (in mm) (n=53)		
</=5	5	9.5
>25 and </=10	13	24.5
>10	35	66.0
Histological Grade (n=53)		
I	20	37.7
II	24	45.3
III	3	5.7
N.A.	6	11.3
Histological Variant (n=6)		
Verrucous variant	3	50.0
Spindle cell variant	2	33.3
Papillary variant	1	16.7
Surgical Margins (in mm)(n=53)		
Negative (>5)	17	32.1
Close (1-5)	32	60.4
Positive (<1)	4	7.5
PNI (n=53)		
Absent	38	71.7
Present	15	28.3
LVI (n=53)		
Absent	39	73.6
Present	14	26.4

Table 5: Distribution of involvement of lymph nodes and extranodal extension in the studied cases

Lymph Nodes(n=45)	Number of cases	Percentage (%)
Involved	18	40
Not involved	27	60
Extranodal Exension (n=45)		
Absent	36	80
Present	9	20

4. Discussion

Oral squamous cell carcinoma (OSCC) is a major problem in the Indian subcontinent. It is therefore important to know the various clinical and pathological factors that can affect the prognosis of these patients in order to reduce the morbidity and mortality.

In the present study the mean age of patients was 58.9 years which is in contrast to the figures of Pires FR et al which was 62.3 years. [3] OSCC was found to predominantly affect males than females in the present study (M: F = 1.3: 1) which was comparable with the studies of Singh et al. [4] This is postulated to be due to the easier acceptance of habits in males than females. 40 (75.5%) patients were associated with habits of tobacco, alcohol consumption and betel quid. Tobacco usage was found to be the predominant habit in 30 (56.6%) cases of which 17 cases were of duration 20- 30 years. This is in accordance with the study by Shenoi et al who also found tobacco chewing was the major cause for the development of OSCC. [5] Petti et al also reported in their studies that 74.9% of oral cancers occur due to concurrent smoking, alcohol intake and betel quid chewing in Southeast Asia. [6] Most patients (47.2%) were found to belong to medium socio-economic status followed by low socio-economic status (45.3%) and strongest association was with Stage III in both groups. Hence socio-economic status can be considered as a potential risk factor in OSCC. Lohe et al in their study of 120 OSCC cases also found socio-economic status as a potential risk factor in the development of OSCC. He concluded that measures to improve socio-economic status and education are important to improve the awareness about the disease. [7] In the present study, 77.4% of the patients presented within 6 months of onset of the symptoms which was in contrast with the studies of PIRES et al. [3] Most of these patients presented in advanced stages. Various numbers of reasons of delayed presentation were noticed. Financial barrier was the most common factor. Other reasons noticed were lack of knowledge and education, habit of taking self medication, fear of cancer or lack of faith in the medical treatment. This resulted in the worsening of the symptoms leading to presentation in more advanced stages of the disease.

Buccal mucosa and lower gingiva (27 cases) was found to be the most common involved site in the present study. This is likely to be due to the habit of retaining tobacco in the lower gingivobuccal sulcus during chewing. This is in accordance with the results of Fang et al who found buccal mucosa, the most common tumor site, followed by gums in their studies. [8] In the present study, 29 (54.7%) cases had tumor size >2 and </=4 cm. Tumor thickness revealed that 35 cases had tumor thickness >10 mm irrespective of tumor size. This is in accordance with PIRES et al, who found in their studies

that most OSCC (149 cases) were diagnosed with up to 4 cm in their greater diameter. [3] In the present study, 24(45.3%) cases were moderately differentiated tumors followed by 20 (37.7%) cases of well differentiated tumors and the majority of these cases were in advanced stages. 6 cases were OSCC variants, 3 (50%) cases verrucous type, 2 (33.3%) cases spindle cell variant and 1 (16.7%) case was papillary variant of OSCC. These figures were comparable with those of PIRES et al. [3] In the present study 32 (60.4%) cases revealed close surgical margin, negative margins in 17 (32.1%) cases and positive margins in 4 (7.5%) cases Maximum cases with close margins were of advanced stages. Priya et al in their study of 306 patients found 190 (62.1%) patients had negative margins of resection (≥5 mm), 102 (33.3%) patients had close margins (1-5 mm), while 14 (4.6%) patients had positive margins (≤1 mm). [9] In the present study, 28.3% (15 of 53) cases showed PNI and maximum number of these positive cases were of advanced stages. Lymphovascular invasion was identified in 14 (26.4%) cases. 13 of these 14 positive LVI cases, were of advanced stages. Thus, PNI and LVI are considered as an important prognostic factor. PNI along with lymphatic and vascular invasion represents the third mode of metastatic spread. Varsha et al studied 117 cases of OSCC and found that 40.5% showed evidence of PNI and 59.5% of the patients showed no PNI histopathologically which was higher in this study. [10]

In the present study, 40% cases had lymph node metastasis and half of them also showed extranodal extension. Salian et al in a study of 61 cases of OSCC found lymph node metastasis in 20% cases which was half of the values found in this study. [11] Extranodal extension was also seen in smaller (<3 cm size) lymph nodes. Wreesmann et al in their study found extracapsular spread in 44% patients. [12] Thus nodal status is considered as another prognostic marker. Also prognosis is further affected by presence of number of metastatic lymph nodes and extranodal extension.

In the present study, the majority of the cases were of Stage III (49.1%) followed by Stage II (22.6%) and Stage IV A (15.1%). Shenoi et al in a retrospective study of 295 patients found majority of patients in Stage III (82.3%). [5] This study showed that the tumor staging done by assessing the primary tumor volume (size and thickness) correlate with other patient demographic and tumor characteristics particularly histological parameters. Detailed histological analysis is therefore required to prognosticate the patient.

To conclude, this study has shown that oral squamous cell carcinomas occur most commonly in elderly age groups and in males. Long term tobacco usage especially by chewing was found to be an important etiological factor. The disease tends to occur in the relatively poorly educated and medium and poor socioeconomic strata of society. However patients were found to present early within the onset of symptoms. The common site of involvement in the gingivobuccal sulcus is again strongly related to the tobacco chewing habit and retention of the tobacco in the sulcus. Most tumors were found to be of high volume with most of them being of great thickness. Histological grade did not correlate with the pathological staging. Close surgical margins were very commonly seen in the study suggesting the need for more

ample margins. Nodal assessment should include numbers, size and extranodal extension.TNM classification is one of the most used systems to predict the prognosis of OSCC. TNM classification had significant correlation with clinical and histopathological parameters. Analysis of the TNM system and the histological staging has been adopted to plan treatment and provide better evaluation of patient's evolution.

References

[1] Coelho KR. Challenges of the oral cancer burden in India. Journal of cancer epidemiology. 2012;2012.

[2] Protocol for the Examination of Specimens from Patients with Cancers of the Lip and Oral Cavity. College of American Pathologists (CAP).8th Edition, AJCC Staging Manual. 2017 June Lip Oral Cavity 4.0.0.0. p. 1-22. Available from :http://www.cap.org/ShowProperty?nodePath=/UCMCon/Contribution%20Folders/WebContent/pdf/cp-lip-oralcavity-17protocol-4000.pdf

[3] Pires FR, Ramos AB, Oliveira JB, Tavares AS, Luz PS, Santos TC. Oral squamous cell carcinoma: clinicopathological features from 346 cases from a single oral pathology service during an 8-year period. Journal of Applied Oral Science. 2013 Oct;21(5):460-7.

[4] Singh MP, Kumar V, Agarwal A, Kumar R, Bhatt ML, Misra S. Clinico-epidemiological study of oral squamous cell carcinoma: A tertiary care centre study in North India. Journal of oral biology and craniofacial research. 2016 Jan 1;6(1):32-5.

[5] Shenoi R, Devrukhkar V, Sharma BK, Sapre SB, Chikhale A. Demographic and clinical profile of oral squamous cell carcinoma patients: A retrospective study. Indian journal of cancer. 2012 Jan 1;49(1):21.

[6] Petti S, Masood M, Scully C. The magnitude of tobacco smoking-betel quid chewing-alcohol drinking interaction effect on oral cancer in South-East Asia. A meta-analysis of observational studies. PloS one. 2013 Nov 18;8(11):e78999.

[7] Lohe VK, Bhowate RR, Sune RV, Mohod SC. Association of socioeconomic risk factor with patients delay in presentation of oral squamous cell carcinoma. Journal of DattaMeghe Institute of Medical Sciences University. 2017 Jan 1;12(1):75.

[8] Fang KH, Kao HK, Cheng MH, Chang YL, Tsang NM, Huang YC, *et al*. Histological differentiation of primary oral squamous cell carcinomas in an area of betel quid chewing prevalence. Otolaryngology—Head and Neck Surgery. 2009 Dec;141(6):743-9.

[9] Priya SR, D'Cruz AK, Pai PS. Cut margins and disease control in oral cancers. Journal of cancer research and therapeutics. 2012 Jan 1;8(1):74.

[10] Varsha BK, Radhika MB, Makarla S, Kuriakose MA, Kiran GS, Padmalatha GV. Perineural invasion in oral squamous cell carcinoma: Case series and review of literature. Journal of oral and maxillofacial pathology: JOMFP. 2015 Sep;19(3):335.

[11] Salian V, Dinakar C, Shetty P, Ajila V. Etiological trends in oral squamous cell carcinoma: A retrospective institutional study. Cancer Translational Medicine. 2016 Mar 1;2(2):33.

[12] Wreesmann VB, Katabi N, Palmer FL, Montero PH, Migliacci JC, Gönen M, *et al.* Influence of extracapsular nodal spread extent on prognosis of oral squamous cell carcinoma. Head & neck. 2016 Apr;38(S1):E1192-9.