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Original Article

Oncology Section

Clinicopathological Profile of Oral Squamous Cell Carcinoma in Eastern India

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ABSTRACT

Introduction: Head and Neck cancer is most common cancer in developing countries like India. Oral Squamous Cell Carcinoma (OSCC) is the most common site of head and neck malignancy. Various histopathological factors prognosticates the therapeutic outcome. Clinicopathological characteristics of OSCC in Asian countries somehow differ from Western countries.

Aim: To report the different clinicopathological characteristics of OSCC due to paucity of the literature even though it is one of the most common malignancy in India.

Materials and Methods: In this retrospective observational study, the medical records of 1753 patients of OSCC who satisfied the eligibility criteria and were treated at a tertiary cancer centre at Cuttack, Odisha, India, from January 2009 to December 2019. Clinicopathological profile of the included subjects were noted. The data was analysed in the month of March 2021 using descriptive statistics such as mean, median, maximum, minimum value and percentage using International Business Machine (IBM) Statistical Package for the Social Sciences (SPSS) version 23.0.

Results: Total of 1753 patients were analysed with the mean age of 50.55±12.56 years, however, majority 492 (28.1%) were in the age of 40-49 years. Male predominance was observed in 1379 (78.7%) patients. Buccal mucosa was the most common primary site in 731 (41.7%) patients, (41.7%) followed by the tongue in 359 (20.5%) patients. Left side lesion was seen in 1008 (57.5%) patients while 734 (41.9%) patients had lesion at right side. Morphologically, ulceroinfiltrative lesion was the most common presentation constituting in 897 (51.2%) patients. Maximum tumour size was 2.91±1.25 cm. Maximum number of patients i.e., 1529 (87.2%) had grade I disease. Mean Depth of Invasion (DOI) was 8.67±4.50 mm. Lymphovascular Space Invasion (LVI) was positive in 123 (7%) patients and Perineural Invasion (PNI) was observed in 565 (32.2%) patients. Resected margin was positive in 203 (11.6%) patients. Cervical lymph node involvement was found in 691 (39.4%) patients and 28 (1.6%) had extracapsular extension. In the present study, most of the patients presented in advanced stage of the disease i.e., stage III 380 (21.7%) and stage IV 506 (28.9%).

Conclusion: The present study highlights that majority of OSCC presents in younger age groups, as left side buccal mucosal lesion with advanced stages of disease. This scenario is due to poor lifestyle pattern which can be prevented by avoidance of tobacco consumption, active screening, public awareness and early diagnosis.

Keywords: Head and neck neoplasm, Oral cancer, Ulceroproliferative

INTRODUCTION

Head and Neck cancer is one of the most common malignancy in developing countries. Therapeutic management continues to be a great challenge in this disease. OSCC is the most common head and neck cancer with an estimated 53,260 new cases and 10,750 deaths in 2020 [1]. According to Global Cancer Statistics 2020 (GLOBOCON) 2020, the incidence of new cases in carcinoma lip and oral cavity comprises of 16.2% in male and 4.7% in female and occupies second rank with mortality of 8.8% and 5 years' prevalence rate of 21.27% [2].

The OSCC is the most common head and neck neoplasm in India due to lifestyle of tobacco consumption. Clinicopathological information of OSCC is variable from country to country and also from different regions within the same country [3]. Despite advances in diagnosis and treatment, its prognostic landscape has not significantly improved. Locoregional recurrence is the most common failure which puts clinician in dilemmatic situation [4].

Majority of oral cancer patients seek medical attention at the advanced stage of the disease. Paucity of Indian literature specifically at eastern zone inspires us to identify different clinicopathological characteristics which will influence therapeutic management as well as Disease Free Survival (DFS) in OSCC.

This study documents the age, sex, subsite, morphological characteristics, grade, Depth of Invasion (DOI), Lymphovascular Space Invasion (LVI), Perineural Invasion (PNI), margin status, number of lymph node involvement, extracapsular involvement and stage of the diseases in OSCC seen in Odisha, India.

The present study was undertaken to report the different clinicopathological characteristics of OSCC due to paucity of the literature in Cuttack, Odisha even though it is one of the most common malignancy in India.

MATERIALS AND METHODS

It was a retrospective observational study, conducted at a tertiary cancer care hospital at Cuttack, Odisha, India, that renders the services to 30 different districts of Odisha. Besides, it renders its services to neighbouring states like West Bengal, Jharkhand and Andhra Pradesh.

Relevant data of 1753 eligible patients of carcinoma oral cavity who were treated from January 2009 to December 2019 were collected and analysed in the month of March 2021.

Inclusion criteria: Histopathologically proven carcinoma of oral cavity, patient who had undergone surgery without any prior chemotherapy or radiotherapy were included in the study.

Exclusion criteria: Patients having upfront metastatic disease, those who have received neoadjuvant chemotherapy and patient's record having missing data were excluded from the study.

STATISTICAL ANALYSIS

After collecting the necessary records, the data were collected and analysed using descriptive statistics such as mean, median,

maximum, minimum value and percentage using International Business Machine (IBM) Statistical Package for the Social Sciences (SPSS) version 23.0.

RESULTS

The complete data regarding clinicopathological profile of eligible OSCC patients were collected from clinical case records of medical record section of the Institute as well as Patholab, Cuttack. It documented age, sex, subsites, morphological features, grade, DOI, LVI, PNI, margin status, number of lymph node involvement, extracapsular involvement and stages of diseases in OSCC. The mean age of presentation of being was 50.55±12.56 years [Table/Fig-1]. Maximum number of patients i.e., 492 (28.1%) were in the age group 40-49 years, followed by 443 (25.3%) in the age group 50-59 years. There was a male predominance with 1379 (78.7%) patients while 374 (21.3%) patients were female. Majority of patients i.e., 1008 (57.5%) had lesion at left side of oral cavity, 734 (41.9%) patients had lesion at right side of oral cavity and only 11 (0.6%) patients presented as midline lesion. Among 1753 patients in the study, the most common subsite of OSCC was buccal mucosa with 731 (41.7%) patients followed by oral tongue 359 (20.5%) while only 9 (0.5%) patients had lesion at floor of mouth.

Parameters	Mean±SD || Median (IQR) || Min-Max
Age (Years)	50.55±12.56 || 50.00 (42.00-60.00) || 20-92
Age	Frequency (n) and Percentages (%)
20-29	55 (3.1)
30-39	285 (16.3)
40-49	492 (28.1)
50-59	443 (25.3)
60-69	328 (18.7)
70-79	131 (7.5)
80-89	18 (1)
≥90	1 (0.1)
Gender	
Male	1379 (78.7)
Female	374 (21.3)
Tumour side	
Right	734 (41.9)
Midline	11 (0.6)
Left	1008 (57.5)
Tumour site	
Buccal mucosa	731 (41.7)
Tongue	359 (20.5)
Lower buccogingival sulcus	351 (20.0)
Combined	186 (10.6)
Retro molar trigone	65 (3.7)
Upper buccogingival sulcus	34 (1.9)
Lip	18 (1)
Floor of mouth	9 (0.5)

[Table/Fig-1]: The clinicodemographic data of patients of OSCC.

On evaluation of gross morphology in [Table/Fig-2], maximum i.e., 897 (51.2%) patients had ulceroinfiltrative type of lesion followed by 596 (34%) patients who presented with ulceroproliferative lesion while only 81 (4.6%) patients had verrucous type of lesion.

Gradewise analysis of lesion showed majority i.e., 1529 (87.2%) patients had grade I lesion while 203 (11.6%) patients and 21 (1.2%) presented with grade II and grade III disease, respectively. Mean tumour size was 2.91±1.25 cm means DOI in this study was 8.67±4.50 mm. Maximum patients i.e., 1022 (58.3%) had deep and infiltrating type of stromal involvement while only 3 (0.2%) patients had deep and pushing type of stromal involvement each.

Parameters	Mean±SD || Median (IQR) || Min-Max || Frequency (n) and Percentages (%)
Gross appearance	
Ulceroinfiltrative	897 (51.2)
Ulceroproliferative	596 (34)
Ulcerative	179 (10.2)
Verrucous	81 (4.6)
Tumour grade	
Grade I	1529 (87.2)
Grade II	203 (11.6)
Grade III	21 (1.2)
Maximum tumour size (cm)	2.91±1.25 || 2.80 (2.00-3.60) || 0.20-10.50
Depth of invasion (mm)	8.67±4.50 || 8.00 (6.00-11.00) || 0-48
Stromal involvement	
Deep and infiltrating	1022 (58.3)
Deep and pushing	504 (28.7)
Superficial and pushing	151 (8.6)
Superficial and infiltrating	70 (4)
Deep	3 (0.2)
Superficial	3 (0.2)
Skin involvement (Present)	65 (3.7)
LVSI (Present)	123 (7)
PNI (Present)	565 (32.2)
Margin (Positive)	203 (11.6)
Number of nodes retrieved	20.76±11.98 || 19.00 (12.00-27.00) || 0-86
Lymph node (Positive)	691 (39.4)
Extra capsular extension (Present)	28 (1.6)

[Table/Fig-2]: The histopathology characteristics of patients of OSCC.
LVSI: Lymphovascular space invasion; PNI: Perineural invasion

Lymphovascular space invasion was present in 123 (7%) patients, PNI was observed in 565 (32.2%) patients. In this study, 203 (11.6%) patients had margin positive. Skin involvement was observed in 65 (3.7%) patients. Mean number of cervical lymph nodes retrieved was 20.76±11.98. Lymph node was positive in 691 (39.4%) patients while extracapsular extension was seen in 28 (1.6%) patients.

In the present study, on analysis of T category, maximum patients i.e., 985 (56.2%) had T_2 lesion while only 97 (5.6%) had T_4 lesion as is shown in [Table/Fig-3]. Highest number of patients i.e., 1057 (60.3%)

Parameters	Mean±SD || Median (IQR) || Min-Max || Frequency (%)
pT	
T_1	415 (23.6%)
T_2	985 (56.2%)
T_3	256 (14.6%)
T_4	97 (5.6%)
pN	
N_0	1057 (60.3%)
N_1	252 (14.4%)
N_2	416 (23.7%)
N_3	28 (1.6%)
cM	
M_0	1751 (99.9%)
M_1	2 (0.1%)
Stage	
Grade I	308 (17.5%)
Grade II	559 (31.9%)
Grade III	380 (21.7%)
Grade IV	506 (28.9%)

[Table/Fig-3]: The TNM grouping and stage of patients of OSCC.

had N_0 status while lowest number of patients i.e., 28 (1.6%) had N_3 disease. Most of the patients were in stage III and stage IV with 380 (21.7%) and 506 (28.9%) patients, respectively.

DISCUSSION

Mean age of presentation of squamous cell carcinoma of oral cavity was 50.55±12.56 years with majority of patients presented at age group 40-49 years (28.1%) followed by 25.3% patients at the age group 50-59 years. Various authors have highlighted that OSCC are mostly diagnosed in adult at a mean age of 50-70 years [5-8]. Most of OSCC patients present at a median age of 62 years are at international level [9]. But in the present study, the mean age of presentation was 10 years earlier than Western population. Possible explanation for this presentation is due to lifestyle of consumption of tobacco at young age.

On analysis of sex distribution, OSCC was predominant among male having male:female ratio ranging from 6.1:2.1 [10-13]. However, in the present study, male:female ratio was 3.69:1 which was due to the habit of chewing tobacco more commonly among male than female population.

With respect to site of distribution of OSCC, buccal mucosa was the most common site of presentation comprising 41.7% of patients followed by carcinoma of tongue i.e., 20.5% in this study. In Western literature, carcinoma of tongue was the most common site of OSCC, however, in Asian population, buccal mucosa is the most common site of involvement [14-16]. This finding may be explained by the habit of consumption of tobacco and areca nut in chewable form.

In the current study, 57.5% patients presented with lesion at left side and 41.9% at right side of oral cavity. The predominance of OSCC in left side of oral cavity is due to habit of retaining chewing form of tobacco in left quid bed by the right handed persons.

Clinical and biological behaviour of OSCC is predicted by the histological grading. World Health Organisation (WHO) classified grades of OSCC into well-differentiated (grade I), moderately differentiated (grade II) and poorly differentiated (grade III). This grading system is based upon pleomorphism, mitosis, and degree of keratinisation [9]. Majority of OSCC present at grade II disease are followed by grade I disease [13,15]. In the present study, 1529 (87.2%) patients were presented with grade I disease, 203 (11.6%) grade with II and 21 (1.2%) patients with grade III disease. As per the available literature, the most common grade of the tumour varies in different anatomical subsites of OSCC i.e. buccal mucosa, oral tongue, gingivobuccal sulcus, floor of mouth and hard palate. Usually buccal mucosa lesions are grade I and tongue lesions are grade II [17,18]. In the present study, most of the anatomical subsites were buccal mucosa and tongue, hence grade II and grade I lesions were common.

The DOI has been incorporated into American Joint Committee on Cancer (AJCC) Tumour, Node, Metastasis (TNM) classification which redefines the staging system [19]. This parameter explores the risk of occult cervical node metastasis as well as the recurrence at primary sites. This guides the clinician to undergo Elective Neck Dissection (END) or prophylactic neck node irradiation. Mean DOI in present study was 8.67±4.5 mm which is in agreement with other published literature [20]. However, in present series, DOI was higher than that of published literature i.e., in United Kingdom 5.7 mm and in Finland 6.3 mm [21].

Positive surgical margin is a negative prognostic factor with increased chances of local recurrences. In histopathology, if the distance of the invasive front to the resected margin is >5 mm, it is considered as negative margin, <5 mm as close margin and presence of carcinoma in situ or invasive carcinoma at resected margin as positive margin [22]. The factors like site of primary, T category, availability of frozen section and the surgical skills determines the incidence of negative margin. According to study by Maxwell JH et al., 10.6% patients had positive margin, 37.5% had negative margin and 7.50% had close margin [23]. But in the present study, margin positivity was 11.6% which was mostly due to non availability of frozen section facility in the institution.

Positive Lympho-Vascular Space Invasion (LVSI) is one of the adverse prognostic factor which is responsible for locoregional failure and poor survival in OSCC and associated with cervical node metastasis. Cassidy RJ et al., highlighted in their study that the incidence of LVSI is 20% in patients of OSCC which is responsible for poor locoregional control and Overall Survival (OS) and such patients were in need of adjuvant radiotherapy [24]. In contrast to above literature, the incidence of LVSI was 7% in present study.

The PNI in OSCC is due to high expression of nerve growth factor and tyrosine kinase. The PNI is associated with advanced stage of disease and poor disease specific survival and poor disease free five years' survival [25]. The incidence of PNI in OSCC ranges from 2.5-71%. This is commonly observed in carcinoma tongue and floor of mouth [26]. Involvement of PNI depends on tumour size, DOI and grade of disease [27]. In present study, PNI was present in 565 (32.2%) patients.

Pathological staging is one of the important prognostic factors that predict the recurrence as well as survival. Suresh GM et al., reveal that in their study, when they did survival analysis of OSCC, patients with T_1 lesion had better Disease Free Survival (DFS) of 55.7 months and Overall Survival (OS) of 58.1 months compared to T_2 and other lesions, who were having DFS of 22.7 months and OS of 3.7 months which was statistically significant ($p<0.001$) [28]. Incidence of pT and pN category varies from country to country which depends upon the economic status, education and also the health system like screening, early detection and early referral. Authors from developed countries reported the disease in early pT which ranges from 66-76% [17,20]. In the present study, 23.7% of patients presented with pT1, pT2 56.2%, pT3 14.6%, pT4 5.6%. Similarly, 60.6% patients had N_0 disease, 14.4% patients N_1, 23.7% N_2 and 1.6% N_3 disease. On stage wise analysis, 17.6% patients presented in stage I, 31.9% stage II, 21.7% stage III, and 28.9% in stage IV disease. On comparison to developed countries, majority of patients in this series presented in advanced stage of the disease. This is due to consumption of smokeless tobacco in early age, poor socio-economic status, lack of awareness of the disease and delay in diagnosis.

Limitation(s)

This study population may not reflect the whole population.

CONCLUSION(S)

The present study showed that patients of OSCC presented comparatively at an early age, having most commonly left sided buccal mucosal lesion with advanced stage of disease. This presentation is due to tobacco habit at an early age, poor socioeconomic status, lack of awareness, lack of screening facility as well as delayed diagnosis and poor referral system. Emphasis should be given to avoid tobacco use, active screening and early diagnosis so that the mortality of OSCC can be reduced.

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