

## Clinicopathological Profile of Head and Neck Squamous Cell Carcinoma

### Abstract

**Background:** Head and neck squamous cell carcinoma (HNSCC) constitutes one of the most common malignancies in the world. The geographic location influences the etiologic factors and site of tumor. **Aims and Objectives:** The present study was carried out to illustrate the clinicopathologic profiles of HNSCC patients since data regarding these tumors from eastern region of India are scarce. **Materials and Methods:** A prospective study was undertaken for 2 years in which patients with histologically proven HNSCC were included. The clinicopathologic features of each case were analyzed. **Results:** A total of 108 cases were included in the study, among which 79 (73.15%) were male and 29 (26.85%) were female. Mean age of the patients was 53.21 ( $\pm$ 12.17) years. The most common risk factor was smoking (63 cases, 58.33%) followed by tobacco or betel nut chewing (41 cases, 37.96%). The common patterns of presentation included ulcerated lesion (51 cases, 47.22%), whitish lesion (28 cases, 25.93%), and hoarseness of voice (11 cases, 10.19%). The most common sites involved were buccal mucosa (36 cases, 33.33%) and dorsal surface of the tongue (26 cases, 24.07%). The most common site for exophytic tumors was buccal mucosa (9 out of 23, 39.13%) and that for ulceroproliferative lesions was tongue (9 out of 17, 52.04%). Microscopically, well-differentiated (Grade I) tumors were most common (67 cases, 62.04%) followed by moderately differentiated (Grade II) tumors (38 cases, 35.19%). A statistically significant correlation was obtained between anatomic site and grade of the tumor. **Conclusion:** Patients of HNSCC from the eastern region of India have distinctive features with regard to macroscopic appearance and microscopic grade of their tumors.

**Keywords:** Anatomical distribution, demographic pattern, head and neck squamous cell carcinoma, histopathological grade, risk factors

### Introduction

Head and neck cancers (HNCs) are the sixth most common malignancy in the world. Majority of HNCs are squamous cell carcinoma (HNSCC), and among these, oral cancers account for up to 40% of all malignancies.<sup>[1]</sup> France, India, and Brazil have the highest age-adjusted rates of HNC and Indian females account for the highest age-adjusted rates of HNC in the world.<sup>[2,3]</sup> Anatomical sites affected by HNC varies worldwide. In India, the most common site is oral cavity, whereas pharynx accounts for majority of cases in France,<sup>[4]</sup> reflecting the influence of exposure to different risk factors in the population.<sup>[2,5]</sup> Because of indigenous practice of chewing pan and betel leaf with tobacco, cancers of tongue as well as buccal mucosa are frequent.<sup>[6]</sup> Prognosis of oral squamous cell carcinoma (OSCC) is influenced by tumor primary site, nodal involvement,

tumor thickness, and status of the surgical margins and is greatly influenced by the stage of the disease, especially pathological TNM (pTNM).<sup>[7]</sup>

A literature search revealed that data regarding distribution in different age groups and sex, anatomic distribution, and clinicopathologic profile of HNSCC are scarce in the eastern region of India. The present study aims to report these features from a series of HNSCC from a referral center in Kolkata, West Bengal.

### Materials and Methods

The duration of the present study was 2 years. All patients presented with HNC were screened for histologically proven SCC. These cases were evaluated for inclusion in the present study. Patients having other variants of malignancy, recurrence, metastatic carcinoma from unknown primary site, and lesions diagnosed only by cytological methods were excluded from the study group.

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Data regarding sex, age, duration of illness, risk factors, clinical presentation of the lesion, location, and size were obtained. Clinical presentation of the lesions was classified in three groups: ulcers (including plain ulcers, and exophytic ulcerated masses), leukoerythroplakias, and tumors presenting both ulcers and leukoerythroplakic areas.<sup>[8]</sup> Anatomic location of tumor in the oral cavity was subclassified based on the following sites: buccal mucosa (including buccal sulcus/mucobuccal fold), alveolar mucosa and gingiva (including retromolar area), border of tongue, floor of mouth (with extension to ventral tongue), upper and lower lips, soft palate, and tonsil areas. Histological slides were reviewed for the classification of tumors according to the following grade: well-differentiated (WD), moderately differentiated (MD), and poorly differentiated (PD) tumors according to the WHO criteria.<sup>[9]</sup> In cases where the tumor was excised by radical surgery, pTNM was performed. Standard statistical methods were applied to analyze these data.

## Results

A total of 123 cases were initially evaluated for inclusion in the study. After applying the exclusion criteria, 108 cases were selected as the study population. The anatomic distribution of cases is shown in Table 1. Buccal mucosa is the most common region (36 cases, 33.33%) followed by dorsal surface of tongue (26 cases, 24.07%) [Table 1].

Male accounted for 79 cases (73.15%) while 29 cases (26.85%) occurred in female (M:F - 2.7:1) [Table 2]. Majority of anatomic locations had a sex ratio in favor of males, the highest being buccal mucosa (M:F - 8:1). Exceptionally, cases of neoplasms arising from alveolar mucosa/gingiva/retromolar area had a sex ratio in favor of females (M:F - 0.45:1). The age range of cases in the study group noted was between 31 and 81 years. Most cases occurred in the age group of 40–59 years (58 cases, 53.70%) [Chart 1]. Mean age of all cases was 53.21 ( $\pm 12.17$ ) years [Table 2]. However, cases of SCC arising from pharynx had a mean age of 63.22 ( $\pm 7.40$ ) years.

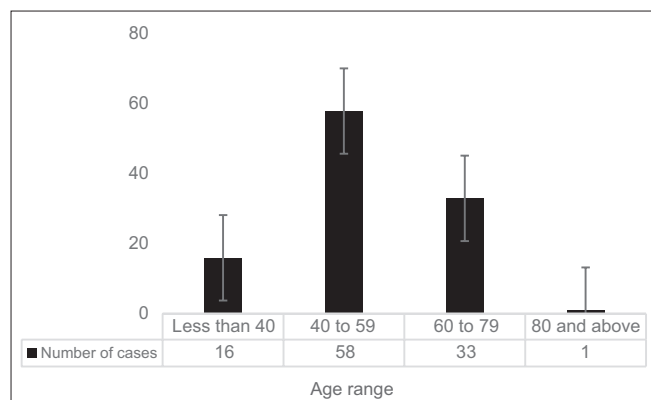


Chart 1: Distribution of cases according to age range

History of smoking was obtained in 63 (58.33%) cases and tobacco/beetle nut chewing in 41 (37.96%) cases. Consumption of alcohol was noted in 45 (41.67%) cases. No addition of these substances was noted in 21 cases (19.44%). Clinically, the most common presentation was ulcerated lesion (51 cases, 47.22%) followed by whitish lesion or mass (28 cases, 25.93%) and hoarseness of voice (11 cases, 10.19%). On examination, anemia was noted in 29 (26.85%) cases and palpable regional lymph node was detected in 18 (16.67%) cases.

Clinically, duration of symptoms in most cases (60.19%) was <6 months and only 10.19% cases had duration of >1 year [Table 3]. Most common clinical appearance

**Table 1: Distribution of cases according to anatomic location**

Location	Number of cases (%)
Buccal mucosa	36 (33.33)
Dorsal surface of tongue	26 (24.07)
Alveolar mucosa/gingiva/retromolar area	16 (14.81)
Larynx	13 (12.04)
Pharynx	9 (8.33)
Floor of mouth	3 (2.78)
Ventral surface of tongue	1 (0.93)
Palate	1 (0.93)
Nasal cavity	2 (1.85)
Lower lip	1 (0.93)
Total	108 (100.00)

**Table 2: Demographic data of the study group according to anatomical site**

Site	Average age	Male:female
Buccal mucosa	50.08 $\pm$ 11.39	8:1
Dorsal surface of tongue	50.62 $\pm$ 13.20	1.6:1
Alveolar mucosa/gingiva/retromolar area	54.31 $\pm$ 11.97	0.45:1
Larynx	53.69 $\pm$ 12.76	All male
Pharynx	63.22 $\pm$ 7.40	3.5:1
Others	61.75 $\pm$ 7.40	2:1
Total	53.23 $\pm$ 12.17	2.7:1

**Table 3: Clinical characteristics of cases in the study group (n=108)**

Parameters	Number of cases (%)
Duration of symptoms	
<6 months	65 (60.19)
6-12 months	32 (29.63)
>12 months	11 (10.19)
Predominant clinical appearance of tumors	
Ulcer	30 (27.78)
Ulcer with leukoerythroplakia	43 (39.81)
Exophytic mass	28 (25.93)
Leukoerythroplakia	7 (6.51)

of tumors was ulcer with leukoerythroplakia (39.81%) followed by ulcerated lesions (27.78%).

Specimen of radical surgery was obtained in 45 cases (41.67%) and biopsy of the tumor was available in 63 cases (58.33%) for pathological study [Table 4]. Microscopically, Grade I (WD) were the most common (67 cases, 62.04%) followed by Grade II (MD) tumors (38 cases, 35.19%), while Grade III (PD) tumors were the least common.

Additional pathological observation was documented in specimens of radical surgeries ( $n = 45$ ). Most tumors had the greatest dimension between 2 and 4 cm (18 cases, 40.00%). Mean tumor thickness was 0.98 ( $\pm 69$ ) cm. Tumor depth was <1 cm in 17 cases (37.78%) and 1–2 cm in

16 cases (35.56%). Surgical resection margin was involved by the tumor in 16 (35.56%) cases, while metastatic deposit in the lymph nodes was seen in 10 (22.22%) patients. Other notable findings were lymphovascular invasion (7 cases, 15.56%), perineurial invasion (5 cases, 11.11%), and bone or cartilage invasion (2 cases, 4.44%).

In 62 cases (57.41%) documented, macroscopic appearance of tumors was available (as noted either in resected specimens or by imaging) [Table 5]. While exophytic lesions were most common in the buccal mucosa (9 out of 23, 39.13%), ulceroproliferative lesions were most common in the tongue (9 out of 17, 52.04%). However, microscopic examination revealed that Grade I SCC is the most common histological grade in both locations (72.22% and 65.38%).

Chi-square test was used to find a correlation between sets of two variables, i.e., microscopic grade of tumor to age of patient, site of tumor, duration in months, and macroscopic appearance of lesion. The correlation between microscopic grade and anatomic site of tumor was found to be statistically significant [Table 6].

**Table 4: Histological characteristics of tumors**

	Number of cases (%)
Tumor differentiation ( $n=108$ )	
Grade I well differentiated	67 (62.04)
Grade II moderately differentiated	38 (35.19)
Grade III poorly differentiated	3 (2.78)
Specimens of radical surgery ( $n=45$ )	
Greatest dimension of tumor	
2 cm or less	12 (26.67)
2-4 cm	18 (40.00)
>2 cm	15 (33.33)
Tumor depth	
<1 cm	17 (37.78)
1-2 cm	16 (35.56)
>2 cm	12 (26.67)
Status of surgical resection margins	
Involved	16 (35.56)
Uninvolved	29 (64.44)
Lymph node metastasis	
Involved	10 (22.22)
Not involved	35 (77.78)
Lymphovascular invasion	7 (15.56)
Perineurial invasion	5 (11.11)
Bone/cartilage invasion	2 (4.44)
Dysplasia at margin	12 (26.67)

## Discussion

OSCC is the major bulk of tumor constituting HNSCC as well as oral cancers. There is a wide variation in the incidence of OSCC in different regions of the world. However, high proportion of occurrence of OSCC among these groups represents the exposure to different carcinogenic substances and their genetic predisposition.

Among the known risk factors, smoking, chewing tobacco, betel quid, areca nuts, and drinking alcohols are significant. In a case–control study conducted in the US involving 1114 patients of oral and pharyngeal cancer, it was observed that risks of cancer increased in a multiplicative manner in persons who are both smokers and drinkers. There were similar relative risk patterns among different races and sexes.<sup>[10]</sup> Similarly, in a large study involving 5458 cases of HNC in Andhra Pradesh, India, only 21.22% cases were free from such risk factors.<sup>[11]</sup> In the present study, only 19.44% cases had no addiction of these

**Table 5: Macroscopic appearance and microscopic grade of tumors according to site of the lesion**

Tumor features	Buccal mucosa	Dorsal surface of Tongue	Alveolar mucosa/gingiva/retromolar area/lower lip	Larynx	Pharynx	Others	Total
Macroscopic appearance ( $n=62$ )	23	17	10	7	3	2	62
Ulcer	6	3	5	1	1	2	18
Ulceroproliferative	7	9	0	6	2	0	24
Exophytic	9	3	4	0	0	0	16
Infiltrative	1	2	1	0	0	0	4
Total							
Microscopic grade ( $n=108$ )	36	26	16	13	9	8	108
Grade I	26	17	11	3	5	5	67
Grade II	10	9	5	9	3	2	38
Grade III	0	0	1	1	1	0	3

**Table 6: Correlation between histopathological grade with clinical features. Chi-square test is significant in the correlation of grade and anatomic site ( $P < 0.05$ )**

Parameter	Microscopic grade			P
	Grade I (n=67)	Grade II (n=38)	Grade III (n=3)	
Age (years)				
<50	27	13	1	0.814778
50 or more	40	25	2	
Anatomic site				
Oral cavity	56	25	1	0.026487
Other sites	11	13	2	
Duration (months)				
<6	41	23	1	0.627198.
>6	26	15	2	
Macroscopic appearance				
Ulcer/ulcer with leukoerythroplakia	46	25	2	0.954941
Other lesions	21	13	1	

causative substances. Other risk factors include ultraviolet radiation and poor oral hygiene.<sup>[12]</sup> Human papillomavirus is now emerging as a significant risk factor in nonsmokers and in cancers involving tonsil, oropharyngeal region, and tongue.<sup>[13]</sup>

In worldwide, most studies had documented that HNSCC mostly occurred in males.<sup>[8,10,11]</sup> The male predominance is also apparent in all age groups and in all anatomic sites.<sup>[8,11]</sup> A similar trend has been observed in the present study where M:F ratio was 2.7:1 with the highest ratio in buccal mucosa (M:F - 8:1). These patterns of sex ratio may be explained by the fact that males are more commonly addicted to risk factors such as alcohol, smoking, and chewing tobacco which are consumed concurrently.<sup>[8,14]</sup>

Age groups that have been affected most commonly in the present study are 40–59 years (58 cases, 53.70%) followed by 60–79 years (33 cases, 30.56%). No case has been detected in persons below 30 years in the present study. The preponderance of such age distribution may be explained by the fact that these persons are usually exposed to risk factors for a sufficient duration, resulting in neoplastic changes. The occurrence of OSCC below 40 years of age is uncommon and ranges from 0.4% to 6%.<sup>[8,15]</sup>

In the present study, the most common site affected was buccal mucosa (33.33%) followed by dorsal surface of tongue (24.07%). Addala *et al.* reported similar sites of affection among patients of HNC in Andhra Pradesh, India.<sup>[11]</sup> The predilection for buccal mucosa in patients from Southeast Asia has been attributed to areca nut- and tobacco-chewing habits of people in this region.<sup>[16]</sup> In fact, the variations in the commonly affected sites in different geographic locations are guided by the etiologic factors which are prominent in that particular zone. In American and European countries, the most common site affected is the border of the tongue, while the lower and upper gingiva have been reported to be commonly affected in Nigeria.<sup>[8]</sup>

It was found in the current study that duration of symptoms in most cases (60.19%) was <6 months. In only 10.19% of cases, the duration exceeded 1 year. A comparable time span has been reported by Shenoi *et al.* in their study. They attributed the delay in diagnosis to low literacy rate, poor financial status, and tendency of Indian patients to resort to home remedies before seeking medical help.<sup>[17]</sup> Interestingly, Pires *et al.* observed that the mean time of complaint before diagnosis was longer in females than in males.<sup>[8]</sup>

Many studies report that the site of predilection in HNC is apparently influenced by gender though exact reasons justifying such distribution remain obscure. The palate, alveolar mucosa, buccal mucosa, and gingiva are more commonly affected in females, whereas in males, border of tongue, ventral surface of tongue, and floor of mouth are the more common sites.<sup>[8,14]</sup> In the present study, alveolar mucosa, gingiva, and retromolar area were found to be the common sites of affection in females as compared to buccal mucosa and dorsal surface of tongue, which showed a predilection for males.

Varied clinical appearances of tumors were appreciated in the present study, the most common being ulcer with leukoerythroplakia (39.81%), followed by ulcerated lesions (27.78%). Pires *et al.* however noted in their study that ulcers were the most common presentation (62%). They reported ulcers with leukoerythroplakia in 21% cases only.<sup>[8]</sup>

In the present study, microscopically, Grade I (WD) tumors were the most common (67 cases, 62.04%) followed by Grade II (MD) tumors (38 cases, 35.19%). Most studies report HNC to be histologically WD or MD tumors.<sup>[8]</sup> However, Effiom *et al.* in their study reported PD tumors to be the most common.<sup>[18]</sup> Pires *et al.* found a relationship between the grade of tumor and gender of the patients. Males were mostly diagnosed with MD and PD tumors while females with WD and MD tumors. They

also suggested an association of grade of tumor with site. According to their observations, WD tumors are more common in buccal mucosa, buccal sulcus, and lower lip, whereas borders of tongue, ventral tongue, floor of mouth, and gingiva are the common sites for MD tumors.<sup>[8]</sup> In the present study, Grade I SCC was most common in both buccal mucosa and tongue (72.22% and 65.38%, respectively).

The correlation between microscopic grade and anatomic site of the tumor was found to be statistically significant in the present study. An attempt was made by Shenoï *et al.* to correlate sets of two variables, i.e., site and habits, staging and anatomic site, stage and duration of illness, stage and habits, and stage and age of patient. However, none of these correlations was reported to be statistically significant by them.<sup>[17]</sup>

### Conclusion

The present study has revealed that males having an age range of 40–59 years were the most common population affected by HNSCC. Such tumors are strongly associated with addiction and only 19.44% cases were not addicted to any substances. Buccal mucosa is the most common anatomic location of HNSCC in the present study followed by dorsal surface of tongue. Ulceroproliferative and exophytic lesions were the most common macroscopic appearances while Grade I (WD) SCC was the predominant microscopic pattern in most sites. The histologic grading was statistically significant when correlated with anatomic site. Although these features have similarities with other studies conducted in India and abroad, some distinctive observations noted in this study were the macroscopic appearance and microscopic grade.

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### Conflicts of interest

There are no conflicts of interest.

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