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RESEARCH ARTICLE

A CLINICO-MORPHOLOGICAL STUDY OF ORAL SQUAMOUS CELL CARCINOMA IN PAKISTAN

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ABSTRACT

Objectives: To determine the clinicopathological features and histopathological grading of oral squamous cell carcinoma in local patients.
Material and Methods: A total of 127 patients presenting with various histological subtypes and grades of Oral Squamous Cell Carcinoma were recruited. Clinical and gross examination findings including age, gender, laterality, site of tumor and ulceration had been recorded. Microscopically tumour subtype and histological grading according to Anneroth's grading system was carried out.
Results: The mean age of patients was 51.46±12.286 years and male to female ratio was 1.5:1 with 76 (59.8%) males and 51 (40.2%) females. The most common presenting complaint was non healing ulcer which was present in n=84 (66.1%) patients. Out of 127 patients well differentiated and moderately differentiated tumours were seen in (n=57, 44.9%) in each grade respectively whereas only (n=13, 10.2%) were poorly differentiated. The predominant site of involvement was tongue (46%) followed by buccal mucosa (39%). The statistical relation between gender and site of involvement it was found to be significant (p=0.01).
Conclusion: The most common sites for OSCC are tongue and buccal mucosa. The most common histological subtype is conventional squamous cell carcinoma while well differentiated and moderately differentiated tumours form the largest number.

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INTRODUCTION

Oral cancers are malignant neoplasms that affect the structures or tissues of the mouth. These malignant neoplasms may start as primary lesion, a metastatic deposit from a distant site, or an extension of some adjacent tumoural area. Globally, oral cancer is the eighth most common cause of cancer-related deaths, of these oral cancers >90% are oral squamous cell carcinomas(OSCC) arising in the mucous membranes of the mouth and oropharynx (Lyer *et al*., 2004; Papadimitrakopoulou *et al*., 2009; Scully and Bagan, 2009). Oral cancer typically occurs after the fifth decade of life in men. In people from Asia, the average age of incidence is in the 5th and 6th decades. Globally, men are more prone to head and neck cancers than women (Feraly *et al*., 2010). In the developing countries, the use of betel nut and snuff, either alone or in combination, cause of the immense number of oral cancers and oral potentially malignant disorders (IARC, 2004). OSCC is manifested in various clinical forms. It may resemble leukoplakia, verrucous leukoplakia an erythro-leukoplakia, or erythroplakia either may eventually develop into a necrotic ulcer looking with irregular, raised edges indurated, or an exophytic mass of broad-based with a surface texture which can be warty gravel relatively soft (Neville *et al*., 2009; Bagan *et al*., 2010). OSCC can be subdivided into various histological subtypes. Most common histological subtypes of OSCC are conventional squamous cell carcinoma (CSCC), verrucous carcinoma (VC) and basaloid squamous cell carcinoma (BSCC). For decades, no change in mortality rate has been observed. Even with advancements in surgery and radiotherapy, mortality still is very high with a 5-year survival rate of only 50%. Five year survival rates in the advanced stages do not exceed 12% (Marsh *et al*., 2011). OSCC can be graded by different grading systems but the most reproducible is the Anneroth's system that has proven a significant association with patient's prognosis (Akhter *et al*., 2011).The present study was carried out to determine the clinicopathological features and histopathological grading of oral squamous cell carcinoma in local patients.

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MATERIALS AND METHODS

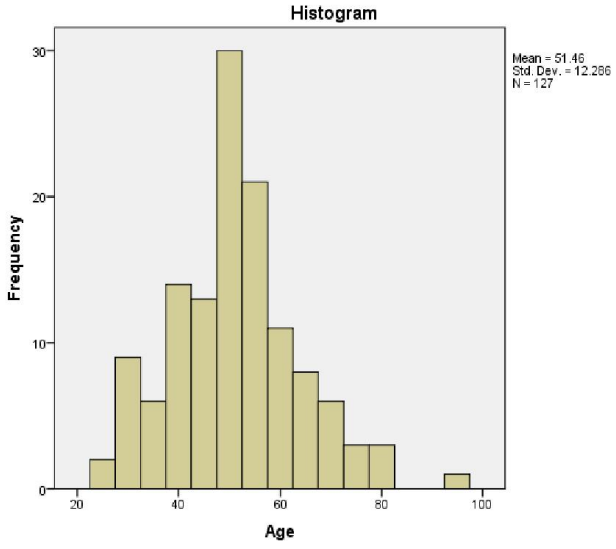
This was a descriptive type of study with convenient sampling technique. A total of 127 patients presenting with various

histological subtypes and grades of Oral Squamous Cell Carcinoma were recruited from Maxillofacial Surgery Department of Nishtar Institute of Dentistry Multan and INMOL Hospital Lahore in accordance with inclusion and exclusion criteria during study period from January 2013 to September 2013. Adult patients of both genders which were known cases of OSCC were included in present study. While patients having chronic co-morbid conditions and severe debilitating immune diseases, were not included in present study. Patients who had received radiotherapy, chemotherapy or any other treatment before surgery and patients with recurrence and follow up were also excluded.

Socio-demographic information (name, age, gender, occupation, full address, history of smoking or using any form of smokeless tobacco, family history of any cancer and oral cancer) was obtained along with relevant clinical, laboratory and radiological information. Tissue sections of 4-6 µm thickness were cut by rotary microtome from each block which were then stained with haematoxylin and eosin to determine the diagnosis of squamous cell carcinoma and its histological grading/subtyping by three histopathologists. Anneroth's histological grading system had been used to grade OSCC cases on H&E staining (Akhter *et al*., 2010). The data was entered and analysed using SPSS 20.0. Data are expressed as mean ± SD. Comparisons between clinical and microscopic parameters were performed with the sample t-test. A difference of $P<0.05$ was considered to be significant. This study was certified by institutional ethical review committee and also from Advanced Studies and Research Board of University of Health Sciences Lahore, Pakistan.

RESULTS

The mean age of patients was 51.46 ±12.286 years and male to female ratio was 1.5:1 with 76 (59.8%) males and 51 (40.2%) females. The age range in males was 27 to 80 years while in females the age range was 25 to 95 years. This data shows that age of incidence was almost similar in both genders however most of the patients are in the range of 40 to 60 years of age (n=88) (Graph 1).



Graph 1. Age range of OSCC cases

The most common presenting complaint was non healing ulcer which was present in n=84 (66.1%) patients followed by fungating mass 9 (7.1%), combined ulcerating &fungating mass 30 (23.6), and plaque 4 (3.1%) (Figures 1& 2).

Figure 1. An exophytic and ulcerated lesion of OSCC on lateral border of tongue

Figure 2. An ulcerated lesion of OSCC on left buccal mucosa

Out of 127 patients well differentiated and moderately differentiated tumours were seen in (n=57, 44.9%) in each grade respectively whereas only (n=13, 10.2%) were poorly differentiated (Figures 3, 4, 5 & 6).

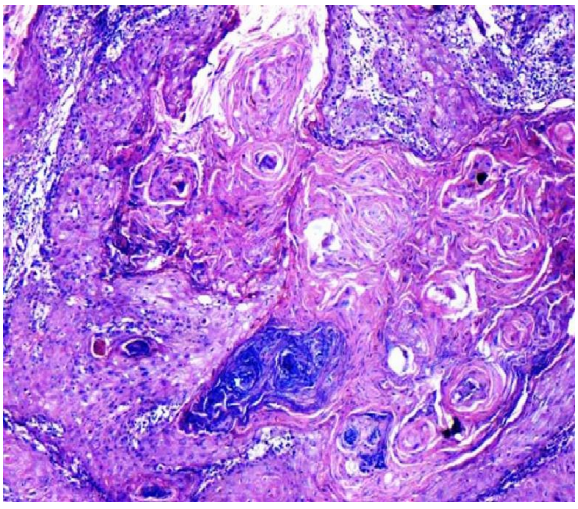


Figure 3. Photomicrograph of well differentiated OSCC with characteristic keratin pearls formation (H&E, 20x)

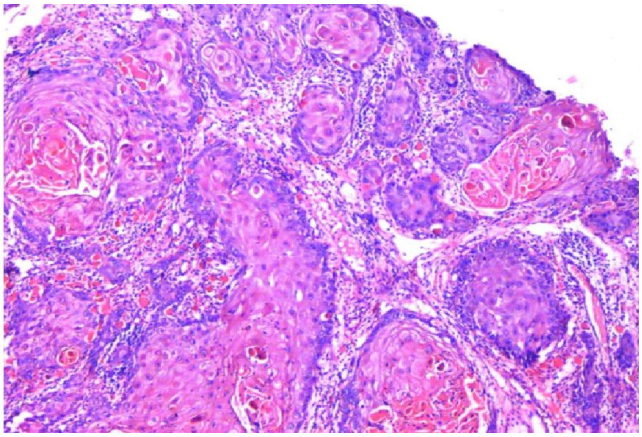


Figure 4. Well differentiated SCC with abundant keratinization, prominent intercellular bridges, nucleoli, atypical mitosis, marked pleomorphism and mild degree of lymphocytic infiltrate (H&E, 20x)

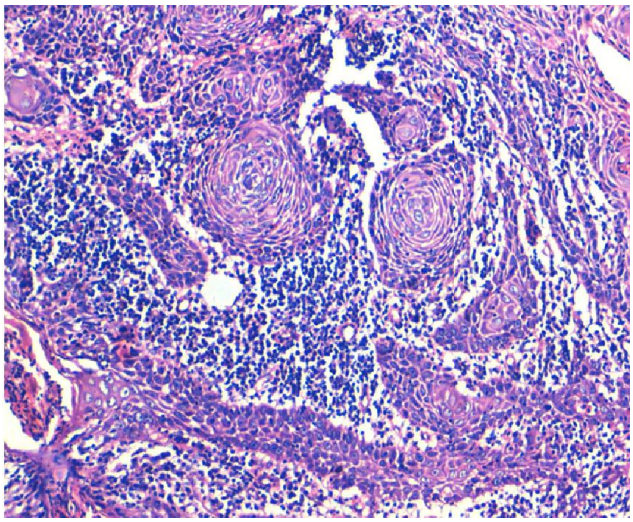


Figure 5. Poorly differentiated OSCC

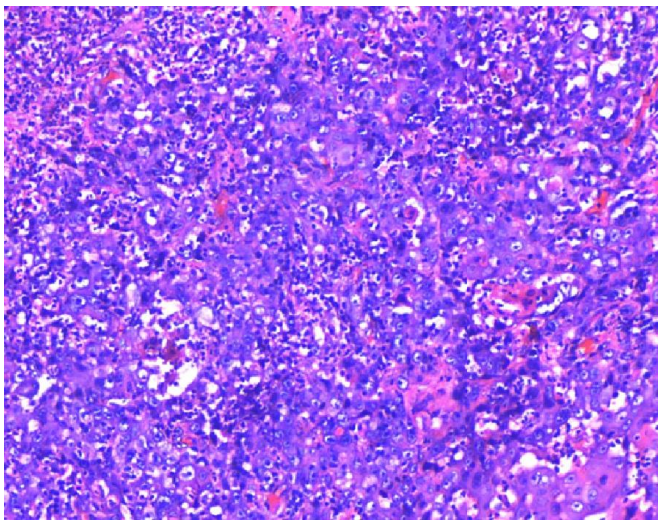
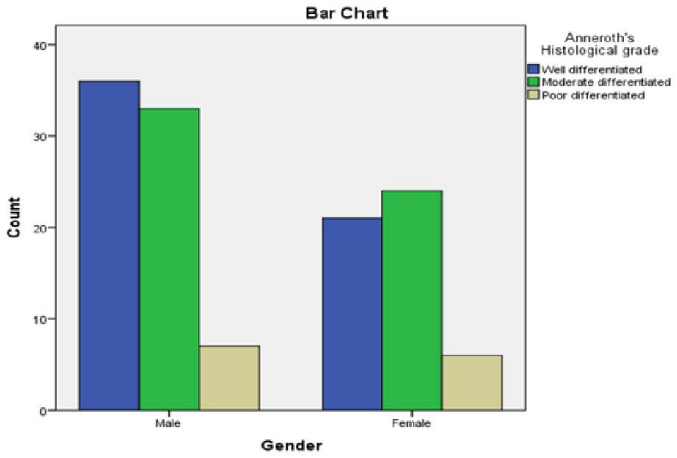


Figure 6. Poorly differentiated OSCC

When Fisher's Exact Test was applied to observe the statistical relation between gender and histological grade of OSCC, it was found statistically insignificant (p=0.83). The statistical relation between histological grade and appearance of lesion was also insignificant (p=0.786) (Graph 2).

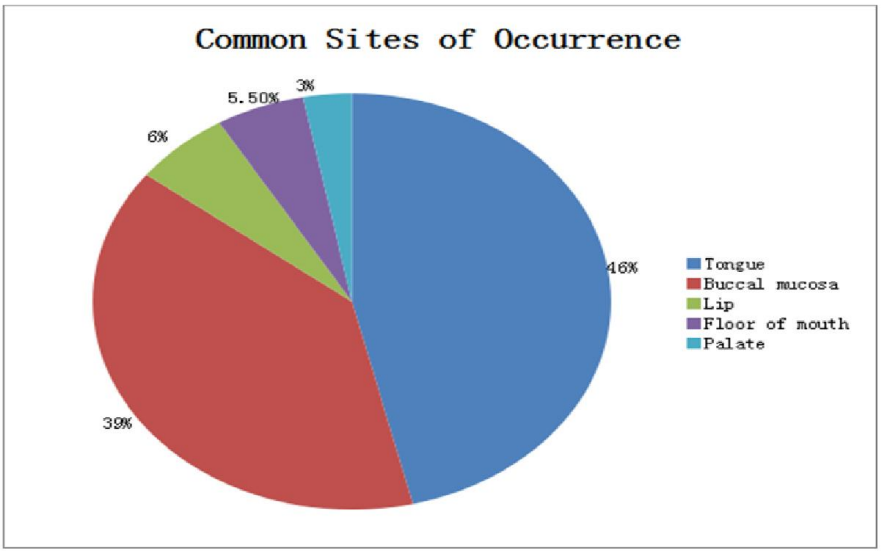


Graph 2. Comparison between Gender and Histological Grade of OSCC

Regarding the site of involvement of oral cavity, the predominant site of involvement of OSCC was tongue (mostly lateral border of tongue) which was seen in n=59 (46%) patients., then in descending order is as follow: n=50 (39%) patients present with tumour on buccal mucosa, other sites involved were lip n=8 (6%), n=7 (5.5%) cases of floor of mouth and only n=3 (2.3%) cases were seen on palate correspondingly. The involvement of buccal mucosa was significantly higher (66%) in males while in females tongue involvement was significantly seen in 60%. When we applied Fisher Exact Test to observe the statistical relation between gender and site of involvement it was found to be significant (p=0.01). While the statistical relation between site of involvement and grades of OSCC was insignificant (p= 0.223) (Graph 3).

DISCUSSION

The likelihood of developing oral SCC increases with the period of exposure to risk factors and increasing age adds to the dimension of the mutagenic and epigenetic changes associated with age. The age related findings of the present study are consistent with majority of local studies from Pakistan, also showed male predominance (Isaac *et al*., 2003; Alamgir *et al*., 2013). A morphological study of OSCC carried out in Pakistan by Ayaz*et al*. also reported 1.5:1 male to female ratio with 53 (SD ±15.16) years mean age of incidence (Ayaz *et al*., 2011). Similarly the study conducted in Mexico reported male to female ratio of 1.4:1 (Hernández-Guerrero *et al*., 2013). The exception, to age related findings of this present study, is a study from Lahore which reported female predominance with a ratio of 1.5:1 (Ali *et al*., 1998). Another study carried out in India on 80 cases of OSCC reported a prevalence of cancer in 61.25% of males (Khandekar and Bagdey, 2006) and Yazdi and Khalili in their study in Iran on 48 cases of OSCC of tongue reported male prevalence of 60.4% (Yazdi and Khalili, 2013). The present study is also positively co-related with both of these studies.



Graph 3. Distribution of OSCC cases at different sites of oral cavity

High proportion of cases among men may be due to the high prevalence of their habits (smoking, snuff pan chewing and gutka etc.) which varies according to the geographical area whereas females in our society is less exposed to such habits as compared to foreign countries but now recent studies shows almost equal incidence of OSCC in both males and females because of almost same habits in females as that in males. Regarding the site of involvement of oral cavity the tongue was involved most commonly in the present study. The involvement of buccal mucosa was significantly higher (66%) in males while in females tongue was significantly (60%) involved. The study carried out in Brazil also reported that tongue was predominantly involved in OSCC patients (Gervásio *et al*., 2001). Similarly many international studies reported the tongue predominance in OSCC patients which is also the same as narrated in the present study (Jerjes *et al*., 2010; Halboub *et al*., 2012). Whereas the study conducted in Pakistan by Tahir and his colleagues is in contrast with the present study which reported that buccal mucosa was the most common site of involvement which was seen predominantly in (32.4%) cases (Tahir *et al*., 2013). Many studies carried out in USA and Europe has reported quite similar findings. In Western countries oral SCC involves the tongue in 20% - 40% of cases and the floor of the mouth in 15% - 20% of the cases, and together these sites represent approximately 50% of all cases of oral SCC. The gums, palate, retromolar area and the buccal and labial mucosa are oral sites affected less frequently (Warnakulasuriya, 2009; Bello *et al*., 2010). The study conducted in Hungary reported that floor of mouth was the most common site of involvement in OSCC patients (Nemes *et al*., 2008). As narrated in the present study that the most common site of involvement is tongue and also most of the patients with OSCC are habitual smokers, this might be due to carcinogens released from the cigarettes which mostly effect the tongue, whereas habits of naswar and pan chewing are mostly associated with tumours on buccal mucosa which is the 2nd most common site of involvement in present study. Many international studies also reported a significant association between site of tumour and addictive habits of the patients. As the present study reported a slight high incidence of buccal mucosa tumours in males as compared to females and this slight difference is due to their habits and consumptions of carcinogenic agents like pan, betel quid, naswar, whereas in our society females are less commonly indulge in tobacco smoking pan and other habits but this difference is decreasing gradually because of consumption of these carcinogenic agents by females.

As considering the histological grading of OSCC, the study conducted by Jerjes and his associates stated that half of the patients were presented with MDSCC (Jerjes *et al*., 2010).The study carried out in Iran narrated that more than 70% of the cases were presented with WDSCC (Al-RawiandTalabani, 2008). Whereas the study conducted in Pakistan, Lahore reported that mostly pateints were presented with PDSCC which is in contrast with the present study (Haq *et al*., 2010). Tumours can grow to a size that exceeds its blood supply, leading to tumour necrosis and ulceration. In the present study the most frequent presenting symptom was ulceration alone or combined ulcerated and fungating mass (89.7%) which was significantly higher on tongue and buccal mucosa (p=0.049). This is comparable to another study carried out in Pakistan in the recent past in which the most common clinical presentation of OSCC was as non-healing indurated ulcer (51.4%) and it was also significantly common on the buccal mucosa (P= 0.001) (Ali *et al*., 2013). Another study reported in Canada by Mirbod *et al.* also reported that ulceration was the most common finding in OSCC patients; this finding is consistent with the present study (Mirbod and Ahing, 2000).

Conclusion

OSCC is a growing malignancy in Pakistan which predominantly affects older age males. The most common sites for OSCC are tongue and buccal mucosa. The most common histological subtype is conventional squamous cell carcinoma while well differentiated and moderately differentiated tumours form the largest number. This study will surely be a significant contribution in epidemiological and morphological data about patients with oral squamous cell carcinoma in our region and it will also be helpful in educating both medical community and

general public about common clinical and histopathological features of OSCC.

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