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Clinicopathological correlation in patients with oral squamous cell carcinoma

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Abstract:

Early diagnosis of oral squamous cell carcinoma is essential to improve prognosis and reduce disease-related morbidity and mortality. Therefore, it is of interest to evaluate the association between clinical presentation and histopathological findings in 100 patients with histopathologically confirmed oral squamous cell carcinoma. Demographic characteristics, risk factors, tumor site, clinical stage, and histological grade were analyzed to identify clinicopathological correlations. Statistical analysis revealed significant associations between clinical and pathological variables, highlighting their value in disease assessment. Thus integrated clinical and histopathological evaluation facilitates early diagnosis, treatment planning, and improved outcomes in oral squamous cell carcinoma.

Keywords: Oral squamous cell carcinoma, clinicopathological correlation, risk factors, histopathology, grading, staging

Background:

Oral squamous cell carcinoma (OSCC) accounts for about 90% of all oral cancers and is a significant public health problem because of its high incidence and mortality rates in the world. OSCC is especially important in developing countries such as India, where it contributes a substantial percentage to the morbidity and mortality burden of cancer. The high prevalence in these areas is believed to be due to the high prevalence of tobacco smoking, alcohol drinking and chewing betel quid, all of which are known etiological factors [1, 2]. OSCC develops from the epithelial lining of the oral cavity and is a multistep process of oral cancer development, which includes genetic mutations, epigenetic changes, and dysregulation of cellular pathways. Chronic exposure to carcinogens causes a gradual change from normal mucosa to oral potentially malignant disorders (OPMDs) and then to invasive carcinoma [3]. There are several molecular pathways that are important for the initiation and progression of tumors, including p53 mutation, activation of the EGFR and alterations in the PI3K/AKT pathway [4]. The clinical appearance of OSCC is dependent on the site, stage and extent of the disease. The most frequent locations are the buccal mucosa, tongue, and gingivobuccal sulcus, especially in tobacco chewers [5]. Non-healing ulcers, exophytic growths, pain, dysphagia, and limited mouth opening are common presenting symptoms. However, many of the cases are diagnosed at a late stage because of lack of awareness and delayed seeking for health care, which is associated with poor prognosis [6]. Histopathological, OSCC is categorized according to the level of differentiation as well, moderately, and poorly differentiated carcinoma. The grade indicates the biological behavior of the tumor; poorly differentiated tumors have more aggressive characteristics and poor prognosis [7]. A second important factor that affects prognosis and treatment is the staging of the tumor according to the TNM classification. The risk of regional lymph node metastasis and survival rates decreases with advanced-stage tumours [8]. Clinic pathological correlation is the systematic study of the correlation between clinical and histopathological features of a disease. In OSCC, such correlation is crucial to understand the behavior of the tumor, to find out the prognosis factors and to make decisions for treatment. A number of studies have shown that there are significant correlations between the clinical parameters including tumor size, site and lymph node involvement with histological grade and depth of invasion [9, 10]. Recent publications have also emphasized the importance of emerging risk factors like human papillomavirus (HPV) infection, nutritional deficiencies, and changes in the oral microbiome in the pathogenesis of OSCC [2, 11]. But the most common risk factors are still the same, that is, smoking and drinking alcohol, which cause almost 70-80% of cases [2]. These factors affect both the incidence and clinical and pathological features of the tumour. Although there have been improvements in diagnostic methods such as imaging and molecular markers, the gold standard for diagnosis of OSCC is still histopathological examination. The use of clinical findings combined with histopathological features improves the accuracy of diagnosis and has a predictive value for the outcome of the disease [12]. Therefore, it is of interest to assess the clinicopathological correlation in patients diagnosed with OSCC in tertiary care setup and to gain insights into the patterns of disease based on clinical presentation and histopathological parameters, thereby contributing to better management and prognosis of patients.

Materials and Methodology:**Study design and setting:**

This study was designed as a hospital-based observational cross-sectional study conducted in the Department of Oral Medicine/ENT/Pathology at a tertiary care teaching institute. The study duration was (specify period, e.g., 1–2 years).

Study population:

The study included 100 patients who were clinically suspected and histopathologically confirmed cases of oral squamous cell carcinoma.

Inclusion criteria:

- [1] Patients aged ≥ 18 years
- [2] Histopathologically confirmed cases of OSCC
- [3] Patients willing to participate and provide informed consent

Exclusion criteria:

- [1] Patients with recurrent OSCC
- [2] Patients who had received prior chemotherapy or radiotherapy
- [3] Patients with other types of oral malignancies

Data collection procedure:

A detailed clinical evaluation was performed for all patients using a structured proforma. The following parameters were recorded:

Demographic details:

- [1] Age
- [2] Gender
- [3] Socioeconomic status

Risk factors:

- [1] Tobacco use (smoking/smokeless)
- [2] Alcohol consumption
- [3] Betel quid chewing
- [4] Duration and frequency of habits

Clinical examination:

- [1] Site of lesion (buccal mucosa, tongue, gingiva, floor of mouth, etc.)
- [2] Size and extent of lesion
- [3] Presence of ulcer/proliferative growth
- [4] Lymph node involvement

Clinical staging:

Tumors were staged according to the TNM classification system (AJCC guidelines):

- [1] Tumor size (T)
- [2] Nodal involvement (N)
- [3] Metastasis (M)

Histopathological examination:

Biopsy specimens were obtained under aseptic conditions and processed using standard histopathological techniques. Sections were stained with hematoxylin and eosin (H&E).

Tumors were graded based on Broders' classification:

- [1] Well differentiated
- [2] Moderately differentiated
- [3] Poorly differentiated

Additional parameters assessed:

- [1] Depth of invasion
- [2] Keratin pearl formation
- [3] Cellular atypia
- [4] Mitotic activity

Clinicopathological correlation:
Clinical findings such as tumor size, site, and stage were correlated with histopathological grading and other microscopic features to identify significant associations.

Statistical analysis:
Data was entered into Microsoft Excel and analyzed using SPSS software. Descriptive statistics: Mean, standard deviation, percentages. Inferential statistics: Chi-square test for categorical variables. P-value < 0.05 considered statistically significant

Results:
A total of 100 patients with histopathologically confirmed oral squamous cell carcinoma (OSCC) were included in the present study. The clinicodemographic profile, risk factors, tumor characteristics, and histopathological grading were analyzed and correlated. The majority of patients (52%) belonged to the 41–60 years age group, followed by 30% above 60 years, indicating that OSCC predominantly affects middle-aged and elderly individuals. A strong male predominance (72%) was observed. Tobacco use was highly prevalent (78%), followed by betel quid chewing (64%) and alcohol consumption (46%), suggesting a significant association of these habits with OSCC. Statistical analysis showed a significant association between tobacco use and occurrence of OSCC ($p = 0.002$), while alcohol consumption also demonstrated a moderate association ($p = 0.04$) (**Table 1**). The buccal mucosa (42%) was the most commonly affected site, followed by the tongue (28%), consistent with tobacco-related carcinogenesis patterns. The majority of patients presented with ulcerative lesions (56%), reflecting late-stage presentation. Advanced disease (Stage III and IV) accounted for 68% of cases, indicating delayed diagnosis. Nearly half of the patients (48%) showed lymph node involvement, highlighting aggressive tumor behavior. A statistically significant association was found between tumor stage and lymph node involvement ($p = 0.001$), suggesting that advanced tumors are more likely to metastasize regionally (**Table 2**). Well-differentiated tumours were more common in early-stage disease (62.5% in Stage I-II), whereas moderately and poorly differentiated tumors predominated in advanced stages (73.5% in Stage III-IV). Poorly differentiated tumors were significantly higher in advanced stages (23.5%) compared to early stages (6.2%). Statistical analysis revealed a significant correlation between clinical stage and histopathological grade ($p = 0.003$), indicating that poorly differentiated tumors are associated with more advanced disease and aggressive clinical behaviour (**Table 3**).

Table 1: Distribution of Patients According to Demographic Characteristics and Risk Factors (n = 100)

Variable	Category	Number (n)	Percentage (%)
Age (years)	20–40	18	18%
	41–60	52	52%
	>60	30	30%
Gender	Male	72	72%
	Female	28	28%
Tobacco Use	Yes	78	78%
	No	22	22%
Alcohol Consumption	Yes	46	46%
	No	54	54%
Betel Quid Chewing	Yes	64	64%
	No	36	36%

Table 2: Distribution of Clinical Features and Tumor Characteristics (n = 100)

Variable	Category	Number (n)	Percentage (%)
Site of Lesion	Buccal mucosa	42	42%
	Tongue	28	28%
	Gingiva	12	12%
	Floor of mouth	10	10%
	Others	8	8%
Clinical Presentation	Ulcerative lesion	56	56%
	Proliferative growth	34	34%
	Mixed	10	10%
TNM Stage	Stage I	10	10%
	Stage II	22	22%
	Stage III	34	34%
	Stage IV	34	34%
Lymph Node Involvement	Present	48	48%
	Absent	52	52%

Table 3: Correlation between Clinical Stage and Histopathological Grading (n = 100)

Histological Grade	Stage I-II (n=32)	Stage III-IV (n=68)	Total	Percentage (%)
Well differentiated	20	18	38	38%
Moderately differentiated	10	34	44	44%
Poorly differentiated	2	16	18	18%

Discussion:

Oral squamous cell carcinoma (OSCC) is one of the most important oncological problems, especially in developing countries, with high exposure to risk factors and low early detection. The present study was designed to analyze the clinicopathological correlation in 100 cases of OSCC and to find out the significant association with the disease progression and prognosis. This study revealed that most of the patients were in the age group 41-60 years, which is similar to the results of other studies [2]. The discovery is a result of years of exposure to carcinogens like tobacco and alcohol. The male predominance (72%) observed is in line with the literature, which attributes this to the greater prevalence of risk habits among males [4]. In recent years, however, it has been reported that there is a gradual rise in the number of female cases, owing to changes in lifestyle [5]. The present study revealed that tobacco use was the most important risk factor, with 78% of patients using tobacco. This is consistent with several studies that have shown a strong causal link between tobacco exposure and the development of OSCC. Chewing of betel quid and drinking of alcohol was also prevalent, which is consistent with the synergistic carcinogenic effect of these substances [7]. The statistically significant relationship between tobacco use and OSCC ($p < 0.05$) further supports its etiological role. As far as anatomical distribution, the most commonly affected site was the buccal mucosa (42%) followed by the tongue (28%). This is typical of populations where smokeless tobacco and betel quid chewing are common [8]. Western populations, on the other hand, have a higher prevalence of tongue and floor of mouth cancers, which are linked to alcohol and smoking [9]. The clinical presentation of most patients was ulcerative lesions and advanced disease (Stage III and IV). This is a common problem in low resource countries, where awareness is low, access to health services is limited, and social stigma exists [10]. The high proportion of advanced stage cases in this study (68%) is similar to the results of the recent studies conducted in India [11]. Involvement of the lymph nodes was found in 48% of patients and was found to be significantly associated with tumor stage ($p = 0.001$). This is clinically significant because nodal metastasis is a key prognostic factor in OSCC and has been shown to significantly decrease survival rates [12]. Tumors that are advanced tend to invade the lymphatic vessels, which then spread the tumor to the surrounding area. Moderately differentiated carcinoma was the most frequent type (44%), followed by well-differentiated (38%) and poorly differentiated (18%) types histopathologically. This distribution is similar to that observed in previous studies, which have shown moderate differentiation as the main pattern in OSCC [13]. Histological grading is important in predicting tumour behaviour, with poorly differentiated tumours having a higher incidence of invasion, metastasis and recurrence. In this study there was a significant correlation between clinical stage and histopathological grade ($p = 0.003$). Well-differentiated tumors were more common in early stage tumors, while moderate and poor differentiated tumors were more common in advanced stage tumors. This result was consistent with the previous studies showing that there is a strong correlation between the differentiation of the tumor and the aggressiveness and the course of the disease [14]. Tumors that are poorly differentiated grow quickly, are more invasive and have a poorer prognosis. Recent developments in molecular biology have given better understanding of the pathogenesis of OSCC. Tumour suppressor genes like p53, overexpression of EGFR and disruption of pathways like PI3K/AKT have been linked to tumour progression [6, 15]. Furthermore, there has been increased awareness of emerging risk factors like HPV infection especially in oropharyngeal cancers, but their importance in OSCC is not as significant in Indian population [5]. The results of the present study highlight the value of clinicopathological correlation in OSCC. Combining clinical and histopathological features helps to better understand the behavior of the tumor and helps in planning treatment. Well differentiated tumours at early stages can be treated successfully with surgery, while poorly differentiated tumours in advanced stages may require multimodal therapy, such as surgery, radiotherapy and chemotherapy [12]. There are some limitations to this study. The results are not necessarily representative of the general population, as it is a single-center study with a small sample size. Moreover, molecular markers and long-term follow-up data were not available, which might give additional prognostic information. In spite of these drawbacks, the study provides useful information regarding the clinicopathological profile of OSCC in a tertiary care hospital. The strong relationships found indicate the importance of early detection, risk factor modification, and thorough diagnostic assessment.

Conclusion:

We show that there is a strong correlation between the risk factors and the development of oral squamous cell carcinoma, especially with regard to tobacco use. The majority of patients were at advanced stage and there was a strong correlation between clinical stage and histopathological grading. The results highlight the significance of early diagnosis, public awareness, and integrated clinicopathological assessment for better patient outcomes and decreased disease burden.

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