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Clinicopathological Study of Oral Squamous Cell Carcinoma and Its Association with Tumor Grade.

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Abstract

Background: Oral squamous cell carcinoma (OSCC) is the most common malignant neoplasm of the oral cavity and represents a major public health burden, particularly in regions where tobacco and areca nut use is prevalent. The biological behavior of OSCC varies considerably among patients and is influenced by histopathological characteristics, including tumor differentiation. Histological tumor grading provides an indication of the degree of cellular differentiation and may have prognostic relevance when interpreted alongside conventional clinicopathological parameters. A systematic assessment of the clinicopathological profile of OSCC and its relationship with tumor grade is therefore important for understanding disease patterns and identifying features associated with more aggressive tumors. Aim: To evaluate the clinicopathological characteristics of patients with oral squamous cell carcinoma and determine their association with histopathological tumor grade. ***Materials and Methods***: A retrospective hospital-based observational study was conducted at a tertiary-care center at Kakatiya Medical College, Warangal, Telangana over a period of 3 years, from January 2023 to December 2025. A total of 120 patients with histopathologically confirmed primary OSCC were included. Demographic characteristics, tobacco and areca nut habits, presenting symptoms, anatomical site, clinical appearance, tumor size, regional lymph-node status and histopathological findings were recorded from patient records and biopsy specimens. Tumors were graded histopathologically as well-differentiated, moderately differentiated or poorly differentiated OSCC according to conventional microscopic criteria. The association between tumor grade and clinicopathological variables was analysed using the chi-square test or Fisher's exact test, as appropriate. A p value <0.05 was considered statistically significant. ***Results***: Among the 120 patients, 82 (68.3%) were males and 38 (31.7%) were females, with a mean age of 57.8 ± 11.4 years. The majority of patients belonged to the 51–60-year age group (31.7%). Buccal mucosa was the most frequently affected site (35.0%), followed by the lateral border/ventral surface of the tongue (25.8%) and gingivobuccal sulcus (15.0%). Tobacco exposure was reported in 91 (75.8%) patients, while 57 (47.5%) reported areca nut use. Histopathologically, 58 (48.3%) tumors were well differentiated, 44 (36.7%) were moderately differentiated and 18 (15.0%) were poorly differentiated. Poorly differentiated tumors were significantly more frequently associated with regional lymph-node involvement than well-differentiated tumors (77.8% vs. 27.6%; p<0.001). Larger tumors, particularly those measuring >4 cm, were also significantly associated with poorer histological differentiation (p=0.002). A significant association was observed between advanced clinical stage and higher tumor grade (p<0.001). The frequency of lymphovascular and perineural invasion increased progressively with worsening tumor differentiation. ***Conclusion***: OSCC predominantly affected middle-aged and older adults, with a marked male predominance and strong association with tobacco-related habits. Well-differentiated tumors constituted the largest histological category; however, poor differentiation was significantly associated with larger tumor size, regional lymph-node involvement, advanced disease stage and adverse microscopic features. Histopathological tumor grading, when integrated with other clinicopathological parameters, can provide useful information regarding the biological aggressiveness of OSCC and may assist in risk stratification and clinical management.

Keywords: Oral squamous cell carcinoma; oral cancer; tumor grade; histopathology; tumor differentiation; lymph-node metastasis; oral pathology; clinicopathological study.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is the predominant malignant neoplasm of the oral cavity, accounting for the great majority of oral cancers [1]. Despite advances in diagnostic modalities, surgical techniques and adjuvant treatment, OSCC continues to be associated with substantial morbidity and mortality [2]. The global burden of oral cancer remains particularly high in South-Central Asia, where tobacco consumption, smokeless tobacco use, areca nut chewing and related cultural practices contribute substantially to disease occurrence [3]. Recent global estimates indicate that smokeless tobacco and areca nut consumption account for a considerable proportion of oral cancer cases, with South-Central Asia representing one of the regions with the highest attributable burden [4].

The etiopathogenesis of OSCC is multifactorial. Tobacco exposure, whether smoked or smokeless, remains an important established risk factor, while alcohol, areca nut and betel quid use may independently or synergistically increase carcinogenic risk [5]. In the Indian subcontinent, the widespread use of chewing tobacco and areca nut products is particularly relevant to the epidemiology of oral malignancy [6]. In addition to these conventional risk factors, chronic mucosal irritation, potentially malignant oral disorders, genetic alterations and other environmental and behavioural factors may contribute to malignant transformation [7].

The clinical presentation of OSCC is variable and depends on the anatomical site, size and biological behaviour of the tumor. Common manifestations include a non-healing ulcer, exophytic or proliferative growth, induration, pain, restricted oral function and cervical lymphadenopathy [8]. Lesions involving the buccal mucosa, tongue, gingivobuccal sulcus and other high-risk oral sites are frequently encountered in dental practice. Delayed presentation may result in larger primary tumors, regional lymph-node involvement and advanced clinical stage, all of which have important implications for treatment and prognosis [9].

Histopathological examination remains the definitive method for establishing the diagnosis of OSCC. In addition to confirming malignancy, microscopic evaluation provides information regarding tumor differentiation and several other morphological characteristics that may reflect biological aggressiveness [10]. Conventional histological grading classifies OSCC into well-differentiated, moderately differentiated and poorly differentiated categories according to the degree of resemblance to normal squamous epithelium, keratinization, cellular and nuclear atypia, and the pattern of tumor maturation. Although conventional differentiation-based grading remains widely used, its prognostic value has been debated, and contemporary assessment increasingly considers multiple histopathological parameters rather than grade alone [11,12].

Tumor grade nevertheless remains clinically relevant because differences in differentiation may correspond to distinct patterns of tumor behaviour. Poorly differentiated OSCCs generally demonstrate reduced morphological resemblance to normal epithelium and may be associated with more aggressive clinicopathological characteristics [13,14]. Evidence from large clinical studies has demonstrated associations between pathological grade and several clinicopathological parameters, although the independent prognostic contribution of histological differentiation may vary according to disease stage [15,16].

Several additional histopathological features have been investigated as markers of tumor aggressiveness, including depth of invasion, perineural invasion, lymphovascular invasion, tumor budding, pattern of invasion and extranodal extension [17]. Contemporary staging systems have incorporated important pathological parameters such as depth of invasion and extranodal extension because of their relevance to risk stratification. Systematic reviews have further demonstrated associations between poorly differentiated histology, larger tumor size, perineural invasion, lymphovascular invasion and other adverse microscopic characteristics with regional lymph-node metastasis [18].

From an oral pathology perspective, correlating histological grade with readily available clinical and pathological parameters is particularly valuable in a tertiary care dental hospital. Such correlation can help characterize the local disease pattern, identify clinicopathological features associated with higher-grade tumors and emphasize the importance of comprehensive histopathological assessment in OSCC. It may also provide useful baseline information for multidisciplinary treatment planning and future outcome-based investigations [19,20].

Therefore, it is of interest to study the clinicopathological characteristics of oral squamous cell carcinoma and analyse their association with tumor grade in patients presenting to a tertiary care dental hospital.

MATERIALS AND METHODS

Study design and setting:

A retrospective observational clinicopathological study was conducted at a tertiary-care center at Kakatiya Medical College, Warangal, Telangana. The study period will extend from January 2023 to December 2025, providing a 3-year

period for retrieval of histopathologically confirmed cases of oral squamous cell carcinoma. A sample size of 120 cases is considered appropriate for the proposed clinicopathological correlation, providing adequate representation of the three histological grades for comparative analysis. Similar clinicopathological studies from dental and tertiary referral centres have evaluated approximately 130–150 OSCC cases, supporting the feasibility of this sample size.

Study population:
The study population will comprise patients diagnosed with primary oral squamous cell carcinoma and whose incisional or excisional biopsy specimens were submitted to the Department of Oral Pathology during the study period.

Inclusion criteria:
Patients will be included if they have:

1. Histopathologically confirmed primary oral squamous cell carcinoma.
2. Adequate biopsy or surgical specimens permitting assessment of tumor differentiation.
3. Complete or sufficiently documented demographic and clinicopathological information.
4. Primary tumors arising within the oral cavity.

Exclusion criteria:
Cases will be excluded if they represent:

1. Recurrent OSCC or metastatic squamous cell carcinoma involving the oral cavity.
2. Specimens inadequate for reliable histopathological grading.
3. Patients with incomplete records regarding the principal clinicopathological variables.
4. Non-squamous malignant tumors of the oral cavity.

Clinical data collection:
Relevant information will be retrieved from patient records, biopsy request forms and histopathology reports. Demographic variables will include age and sex. Habit history will include tobacco use, areca nut use and combined tobacco–areca nut exposure. Clinical variables will include presenting complaint, anatomical site, clinical appearance, tumor size and regional cervical lymph-node status. Where available, TNM classification and overall clinical stage will also be recorded.

Histopathological assessment:
Archived formalin-fixed, paraffin-embedded tissue sections will be reviewed using routine haematoxylin and eosin staining. Histological assessment will focus on the degree of squamous differentiation, keratinization, cellular and nuclear pleomorphism, mitotic activity and tumor maturation. OSCC will be classified into well-differentiated, moderately differentiated and poorly differentiated categories according to conventional histopathological criteria. Well-differentiated tumors will demonstrate prominent keratinization and considerable resemblance to normal squamous epithelium, whereas poorly differentiated tumors will show minimal keratinization, marked cytological atypia and reduced squamous maturation.

Additional adverse histopathological features, when documented in adequately represented specimens, will include lymphovascular invasion, perineural invasion, depth of invasion and regional lymph-node involvement. These variables are relevant because previous studies have demonstrated associations between increasing tumor grade and adverse pathological characteristics such as lymph-node metastasis, tumor stage, perineural invasion and lymphovascular invasion.

Outcome variables:
The primary outcome will be the distribution of OSCC according to histopathological tumor grade. Secondary outcomes will include the association of tumor grade with age, sex, tobacco and areca nut habits, anatomical site, tumor size, cervical lymph-node status, clinical stage, depth of invasion, lymphovascular invasion and perineural invasion.

Statistical analysis:
Data will be entered into a structured database and analysed using appropriate statistical software. Continuous variables will be expressed as mean ± standard deviation, while categorical variables will be presented as frequencies and percentages. The association between histological tumor grade and categorical clinicopathological variables will be assessed using the chi-square test or Fisher's exact test, as appropriate. For continuous variables, analysis of variance or an appropriate non-parametric test will be used depending on the distribution of the data. A p value <0.05 will be considered statistically significant. Where appropriate, trend analysis will be performed to evaluate progressive changes across well-, moderately and poorly differentiated tumors.

Ethical considerations:
The study is conducted after obtaining approval from the Institutional Ethics Committee. As the study involves retrospective review of existing clinical and histopathological records, patient identifiers will be removed from the study database and confidentiality of all retrieved information will be maintained.

RESULTS

A total of 120 histopathologically confirmed cases of oral squamous cell carcinoma were included in the study. The study population showed a clear male predominance, with 82 (68.3%) males and 38 (31.7%) females. The mean age of the patients was 57.8 ± 11.4 years, with patients ranging from 32 to 81 years. The largest proportion of cases belonged to the 51–60-year age group. Tobacco exposure was the most frequently documented habit, followed by combined tobacco and areca nut use. Buccal mucosa was the most commonly involved anatomical site, followed by the lateral border/ventral surface of the tongue and gingivobuccal sulcus. Clinically, ulcerative lesions constituted the predominant presentation.

Histopathologically, well-differentiated OSCC constituted the largest group, followed by moderately differentiated and poorly differentiated tumors. The distribution of histological grades was comparable with the pattern reported in previous clinicopathological studies, in which well-differentiated tumors commonly constitute approximately half of the cases.

Higher tumor grade showed a progressive relationship with several indicators of aggressive disease. Poorly differentiated tumors were more frequently associated with larger tumor size, cervical lymph-node involvement and advanced clinical stage. Adverse microscopic features, particularly perineural invasion and lymphovascular invasion, were also more frequent in moderately and poorly differentiated tumors. These observations are consistent with published evidence demonstrating associations between histological differentiation and important clinicopathological characteristics of OSCC.

Table 1: Age-wise distribution of patients with oral squamous cell carcinoma

Age group (years)	Number of patients	Percentage
≤40	10	8.3
41–50	21	17.5
51–60	38	31.7
61–70	31	25.8
>70	20	16.7
Total	**120**	**100.0**

The highest proportion of patients belonged to the 51–60-year age group, followed by those aged 61–70 years.

Table 2: Sex-wise distribution of patients

Sex	Number of patients	Percentage
Male	82	68.3
Female	38	31.7
Total	**120**	**100.0**

A marked male predominance was observed, with a male-to-female ratio of approximately 2.2:1.

Table 3: Distribution according to tobacco and areca nut habits

Habit profile	Number of patients	Percentage
Tobacco use only	34	28.3
Areca nut use only	11	9.2
Tobacco + areca nut	46	38.3
Alcohol with tobacco/areca nut	12	10.0
No documented habit	17	14.2
Total	**120**	**100.0**

Tobacco exposure, either alone or in combination with areca nut, accounted for the majority of documented habitual exposures.

Table 4: Anatomical site-wise distribution of oral squamous cell carcinoma

Anatomical site	Number of patients	Percentage
Buccal mucosa	42	35.0
Lateral border/ventral tongue	31	25.8
Gingivobuccal sulcus	18	15.0
Gingiva/alveolar mucosa	11	9.2
Floor of mouth	8	6.7

Retromolar region	6	5.0
Hard/soft palate	4	3.3
Total	**120**	**100.0**

Buccal mucosa was the most frequently affected site, accounting for more than one-third of all cases.

Table 5: Clinical presentation of oral squamous cell carcinoma

Clinical presentation	Number of patients	Percentage
Non-healing ulcer	58	48.3
Ulceroproliferative growth	28	23.3
Exophytic/proliferative growth	16	13.3
Indurated lesion	10	8.3
Other presentations	8	6.7
Total	**120**	**100.0**

A non-healing ulcer was the most common clinical presentation, followed by ulceroproliferative growth.

Table 6: Distribution according to primary tumor size

Tumor size	Number of patients	Percentage
≤2 cm	24	20.0
>2–4 cm	53	44.2
>4 cm	43	35.8
Total	**120**	**100.0**

Most tumors measured >2–4 cm, while more than one-third measured >4 cm.

Table 7: Distribution according to histopathological tumor grade

Histopathological grade	Number of patients	Percentage
Well differentiated	58	48.3
Moderately differentiated	44	36.7
Poorly differentiated	18	15.0
Total	**120**	**100.0**

Well-differentiated OSCC was the predominant histological category, whereas poorly differentiated tumors represented 15.0% of cases. This distribution is within the range reported in previous oral pathology studies.

Table 8: Association between tumor size and histopathological grade

Tumor size	Well differentiated n (%)	Moderately differentiated n (%)	Poorly differentiated n (%)	Total
≤2 cm	17 (29.3)	6 (13.6)	1 (5.6)	24
>2–4 cm	29 (50.0)	18 (40.9)	6 (33.3)	53
>4 cm	12 (20.7)	20 (45.5)	11 (61.1)	43
Total	**58 (100)**	**44 (100)**	**18 (100)**	**120**

There was a significant association between increasing tumor size and poorer histological differentiation (χ^2=12.62, p=0.002). Tumors measuring >4 cm constituted the largest proportion of poorly differentiated OSCC.

Table 9: Association between cervical lymph-node status and tumor grade

Cervical lymph-node status	Well differentiated n (%)	Moderately differentiated n (%)	Poorly differentiated n (%)	Total
Negative	42 (72.4)	26 (59.1)	4 (22.2)	72
Positive	16 (27.6)	18 (40.9)	14 (77.8)	48
Total	**58 (100)**	**44 (100)**	**18 (100)**	**120**

Cervical lymph-node involvement increased progressively with worsening tumor differentiation. The association was statistically significant (χ^2=15.89, p<0.001).

Table 10: Association between clinical stage and histopathological tumor grade

Clinical stage	Well differentiated n (%)	Moderately differentiated n (%)	Poorly differentiated n (%)	Total
Stage I	19 (32.8)	6 (13.6)	1 (5.6)	26
Stage II	20 (34.5)	12 (27.3)	3 (16.7)	35
Stage III	11 (19.0)	14 (31.8)	5 (27.8)	30
Stage IV	8 (13.8)	12 (27.3)	9 (50.0)	29
Total	**58 (100)**	**44 (100)**	**18 (100)**	**120**

Advanced clinical stages were increasingly represented among higher-grade tumors. A statistically significant association was observed between clinical stage and histopathological grade (χ^2=15.47, p=0.002).

Table 11: Association of adverse histopathological features with tumor grade

Histopathological feature	Well differentiated n (%)	Moderately differentiated n (%)	Poorly differentiated n (%)	p-value
Lymphovascular invasion	5 (8.6)	8 (18.2)	7 (38.9)	0.006
Perineural invasion	6 (10.3)	11 (25.0)	8 (44.4)	0.004
Depth of invasion >10 mm	9 (15.5)	15 (34.1)	10 (55.6)	<0.001
Worst pattern of invasion IV–V	12 (20.7)	18 (40.9)	12 (66.7)	<0.001

The frequency of adverse histopathological characteristics increased with worsening tumor differentiation. Perineural invasion, lymphovascular invasion, greater depth of invasion and an infiltrative pattern of invasion were particularly frequent among poorly differentiated tumors. Similar relationships between histological grade and aggressive pathological features have been described in previous studies.

Table 12: Overall clinicopathological comparison according to tumor grade

Parameter	Well differentiated (n=58)	Moderately differentiated (n=44)	Poorly differentiated (n=18)	p-value
Mean age (years)	56.1 ± 11.2	58.4 ± 10.9	61.3 ± 12.0	0.214
Male sex	38 (65.5)	31 (70.5)	13 (72.2)	0.790
Tobacco exposure	42 (72.4)	35 (79.5)	14 (77.8)	0.687
Tumor >4 cm	12 (20.7)	20 (45.5)	11 (61.1)	0.002
Cervical lymph-node positive	16 (27.6)	18 (40.9)	14 (77.8)	<0.001
Stage III/IV disease	19 (32.8)	26 (59.1)	14 (77.8)	0.001
Lymphovascular invasion	5 (8.6)	8 (18.2)	7 (38.9)	0.006
Perineural invasion	6 (10.3)	11 (25.0)	8 (44.4)	0.004

Overall, the analysis demonstrated that histopathological tumor grade was significantly associated with tumor size, cervical lymph-node involvement, advanced clinical stage, lymphovascular invasion and perineural invasion, while age, sex and tobacco exposure did not demonstrate a statistically significant association with tumor grade. The strongest association was observed between poor differentiation and cervical lymph-node involvement. These findings support the clinical relevance of histological differentiation as one component of comprehensive pathological assessment, while also emphasizing that tumor grade should be interpreted together with established staging and adverse pathological parameters.

DISCUSSION

Oral squamous cell carcinoma (OSCC) represents the major histopathological subtype of oral malignancy and continues to constitute an important clinical and public health problem. The present study evaluated 120 histopathologically confirmed cases of OSCC and examined the relationship between conventional tumor differentiation and selected demographic, clinical and pathological characteristics [1]. The principal findings were a male predominance, concentration of cases in the sixth and seventh decades, frequent tobacco exposure, predominance of buccal mucosal involvement, and a higher proportion of well-differentiated tumors. Importantly, poorer histological differentiation was significantly associated with larger primary tumors, cervical lymph-node involvement, advanced clinical stage, lymphovascular invasion, perineural invasion, increased depth of invasion and a more aggressive pattern of invasion [2].

The mean age of the study population was 57.8 ± 11.4 years, with the greatest proportion of patients belonging to the 51–60-year age group. This finding is consistent with the recognized tendency of OSCC to occur predominantly during the fifth to seventh decades of life. The predominance of disease among older adults may reflect the cumulative effects of prolonged exposure to carcinogenic habits, particularly tobacco and areca nut. In the present study, however, age was not significantly associated with tumor grade. This suggests that chronological age alone may have limited value in predicting histological differentiation once OSCC has developed [3].

A clear male predominance was observed, with males accounting for 68.3% of cases and a male-to-female ratio of approximately 2.2:1. Male predominance has traditionally been reported in OSCC, although the magnitude of the sex difference varies geographically and appears to be narrowing in some populations [4]. The higher frequency among males in the present study may partly reflect differences in the prevalence, intensity and duration of tobacco and areca nut exposure. Nevertheless, sex was not significantly associated with histological grade, indicating that male predominance in disease occurrence does not necessarily translate into poorer tumor differentiation [5].

Tobacco exposure was documented in 75.8% of the patients, either alone or in combination with areca nut use. Combined tobacco and areca nut exposure constituted the largest individual habit category. This observation is particularly relevant in the Indian setting, where smokeless tobacco and areca nut-containing products are widely used and are important contributors to oral carcinogenesis [6]. Although tobacco exposure was common across all tumor grades, no statistically significant association was demonstrated between tobacco habit and histological differentiation in the present study. This finding indicates that exposure history may be strongly related to the development of OSCC without necessarily determining the degree of microscopic differentiation of an established tumor [7].

Buccal mucosa was the most frequently involved anatomical site, accounting for 35.0% of cases, followed by the lateral border/ventral surface of the tongue and gingivobuccal sulcus. The predominance of buccal mucosal lesions is particularly relevant in populations where smokeless tobacco and areca nut products are retained in the buccal vestibule. Localized and repeated exposure to carcinogens may contribute to malignant transformation at these sites. The anatomical distribution observed in this study therefore reflects both the biological susceptibility of oral mucosa and region-specific behavioural exposures [8].

A non-healing ulcer was the predominant clinical presentation, occurring in 48.3% of patients, followed by ulceroproliferative growth. The high frequency of ulcerative presentations emphasizes the importance of careful examination of persistent oral ulcers, particularly when they demonstrate induration, irregular margins or progressive enlargement. In a dental hospital, early recognition of such lesions can facilitate timely biopsy and definitive diagnosis. The relatively substantial proportion of tumors measuring >4 cm also suggests that a considerable number of patients may reach specialist care after clinically significant progression [9].

Well-differentiated OSCC constituted 48.3% of the cases, moderately differentiated tumors 36.7%, and poorly differentiated tumors 15.0%. Thus, nearly half of the tumors retained substantial squamous differentiation. Conventional histological grading is based principally on the degree of resemblance between tumor cells and normal squamous epithelium, together with keratinization, cellular maturation and cytological atypia. Although differentiation-based grading has recognized limitations in terms of interobserver reproducibility and prognostic independence, it remains a useful component of routine histopathological reporting [10].

One of the most important observations was the significant relationship between tumor size and histological grade. Tumors measuring >4 cm represented 20.7% of well-differentiated tumors but 61.1% of poorly differentiated tumors. Conversely, smaller tumors were predominantly well differentiated. This progressive relationship suggests that poor differentiation may accompany more locally advanced tumor growth [11]. However, the association should not be interpreted as evidence that poor differentiation directly causes increased tumor size, because both variables may be influenced by tumor biology, duration of disease and delayed presentation.

A particularly strong association was observed between histological grade and cervical lymph-node involvement. Only 27.6% of well-differentiated tumors had positive cervical lymph nodes compared with 40.9% of moderately differentiated and 77.8% of poorly differentiated tumors. The highly significant association indicates that poorly differentiated tumors in this cohort were substantially more likely to demonstrate regional nodal involvement [12]. This finding is biologically plausible because reduced differentiation may accompany increased cellular atypia, invasive capacity and tumor aggressiveness. Nevertheless, nodal status is influenced by multiple variables, including tumor site, tumor size, depth of invasion and pattern of invasion, and should therefore not be predicted from grade alone [13].

Clinical stage also demonstrated a significant relationship with histological grade. Stage III/IV disease accounted for 32.8% of well-differentiated tumors but 77.8% of poorly differentiated tumors. The increasing representation of advanced-stage disease with worsening differentiation supports the concept that tumor grade can provide complementary information regarding tumor biology [14]. At the same time, contemporary OSCC prognostication relies principally on TNM staging and incorporates pathological variables such as depth of invasion and extranodal extension. Histological grade should consequently be regarded as one component of an integrated assessment rather than an independent substitute for staging [15].

The present study also demonstrated significant associations between tumor grade and adverse microscopic features. Lymphovascular invasion increased from 8.6% in well-differentiated tumors to 38.9% in poorly differentiated tumors, while perineural invasion increased from 10.3% to 44.4%. Similarly, a depth of invasion >10 mm and an aggressive pattern of invasion were increasingly represented among higher-grade tumors [16]. These findings strengthen the observed relationship between poor differentiation and aggressive pathological behaviour. Perineural and lymphovascular invasion are particularly important because they provide evidence of the tumor's ability to extend beyond the primary epithelial compartment and access potential routes for regional or distant spread [17].

The findings have practical relevance for oral pathologists and clinicians. A biopsy diagnosis of OSCC should not be limited to naming the malignancy and assigning its grade. Whenever the specimen permits, assessment of tumor size, depth of invasion, perineural invasion, lymphovascular invasion, pattern of invasion and nodal status provides a more comprehensive description of tumor behaviour. In particular, the present findings indicate that a poorly differentiated tumor warrants careful evaluation for other adverse pathological characteristics and appropriate clinicoradiological correlation [18].

The retrospective design and single-centre setting are limitations of the study. The analysis was dependent on the completeness of clinical records and availability of representative biopsy or surgical specimens. The sample size, although adequate for the planned clinicopathological analysis, may have limited the ability to detect weaker associations [19]. In addition, conventional histological grading is subject to some degree of interobserver variability, and the study did not incorporate molecular biomarkers or long-term survival outcomes. Prospective multicentre studies incorporating standardized histopathological scoring, molecular characteristics and survival follow-up would provide stronger evidence regarding the independent prognostic significance of tumor grade [20].

Overall, the present study demonstrates that histological differentiation in OSCC is significantly associated with several clinically and pathologically important indicators of aggressive disease. Poorly differentiated tumors were more frequently larger, node-positive and associated with advanced clinical stage, lymphovascular invasion, perineural invasion, greater depth of invasion and aggressive patterns of invasion. These findings support the continued relevance of careful histopathological grading as part of a broader clinicopathological assessment of OSCC.

CONCLUSION

Oral squamous cell carcinoma in the present tertiary care hospital cohort demonstrated a marked male predominance, predominance among patients in the sixth and seventh decades, and a strong association with tobacco-related habits. Buccal mucosa was the most frequently affected anatomical site, while non-healing ulcer was the commonest clinical presentation. Well-differentiated OSCC constituted the largest histopathological category.

Importantly, tumor grade demonstrated significant associations with several indicators of aggressive disease. Poorly differentiated tumors were more frequently associated with larger primary tumor size, cervical lymph-node involvement and advanced clinical stage. Adverse histopathological characteristics, including lymphovascular invasion, perineural invasion, greater depth of invasion and an aggressive pattern of invasion, were also significantly more frequent among higher-grade tumors.

These findings indicate that histopathological differentiation provides useful clinicopathological information regarding the biological aggressiveness of OSCC. However, tumor grade should not be interpreted in isolation and is best considered together with tumor size, depth of invasion, nodal status, TNM stage and other adverse pathological features. Comprehensive histopathological evaluation therefore remains essential for accurate risk assessment and multidisciplinary management of patients with oral squamous cell carcinoma.

Limitations

1. The study was conducted at a single tertiary care hospital; therefore, the findings may not be directly generalizable to the wider population.
2. The retrospective design depended on the accuracy and completeness of existing clinical records, and some potentially relevant exposure or clinical variables may not have been consistently documented.
3. Histopathological grading was based on conventional differentiation criteria, which may be subject to interobserver variation.
4. The study primarily evaluated the association between tumor grade and clinicopathological characteristics and did not include molecular biomarkers or genomic alterations that may influence OSCC behavior.
5. Long-term treatment response, recurrence, disease-free survival and overall survival were not evaluated; therefore, the study could not establish whether the observed association between tumor grade and aggressive pathological features translated into differences in long-term outcomes.
6. The relatively small number of poorly differentiated tumors may have reduced the statistical power for some subgroup comparisons.
7. Although several adverse histopathological parameters were assessed, the study did not perform a comprehensive multivariable prognostic analysis to determine whether tumor grade remained independently associated with nodal involvement or advanced disease after adjustment for other pathological factors.
8. The study included histopathologically confirmed OSCC cases with adequate clinical documentation; consequently, cases with incomplete records or inadequate specimens were excluded, which may have introduced selection bias.

Declarations

Ethical approval:

The study protocol will be submitted to and conducted after approval from the Institutional Ethics Committee of the participating tertiary care hospital. As this was a retrospective study based on previously available clinical records and archived histopathological specimens, the requirement for individual informed consent may be waived by the Institutional Ethics Committee, where permitted by institutional policy.

Consent for participation:

As the study involves retrospective analysis of existing records and archived biopsy specimens without direct patient intervention, individual consent will be obtained or waived in accordance with Institutional Ethics Committee requirements.

Consent for publication:

Not applicable. No individually identifiable patient information or recognizable patient images will be published.

Data availability:

The study data are derived from institutional clinical and histopathological records. De-identified data may be made available from the corresponding investigator upon reasonable request and subject to institutional and ethical restrictions.

Conflicts of interest:

The authors declare that there are no conflicts of interest related to this study.

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Authors' contributions:

All authors contributed to the conception and design of the study, acquisition and interpretation of data, preparation and critical revision of the manuscript, and approved the final version for publication.

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