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AN OBSERVATIONAL STUDY OF KI-67 ANTIGEN AND P53 PROTEIN EXPRESSION AT THE INVASIVE TUMOR FRONT OF ORAL SQUAMOUS CELL CARCINOMA

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ABSTRACT

Background: Oral Squamous Cell Carcinoma (OSCC) is one of the most common malignancies of the head and neck region, characterized by aggressive biological behavior and variable prognosis. The invasive tumor front (ITF) represents the most aggressive component of the tumor and is considered a critical area for prognostic evaluation. Cell proliferation marker Ki67 and tumor suppressor protein p53 are widely studied biomarkers implicated in tumor progression and carcinogenesis. The aim is to evaluate the expression of Ki67 antigen and p53 protein at the invasive tumor front of OSCC and to correlate their expression with histopathological grading systems and recurrence.

Materials and Methods: This Prospective study included 74 histopathologically confirmed cases of OSCC. Tumors were graded according to Broder's classification and Bryne's grading system at the invasive tumor front. Immunohistochemical analysis for Ki67 and p53 was performed in 57 available cases. Ki67 labeling index and p53 nuclear expression were assessed and correlated with clinicopathological parameters. Statistical analysis was performed using Chi-square test, and $p < 0.05$ was considered statistically significant.

Results: The mean age of patients was 53.66 ± 12.17 years, with female predominance (60.8%). Buccal mucosa was the most common site (48.6%). High Ki67 expression was observed in 55.4% of cases, while 44.6% showed strong (3+) p53 expression. Significant association was observed between Ki67 expression and Broder's grading ($p < 0.0001$) and recurrence ($p = 0.027$). Ki67 did not show significant association with Bryne's grade ($p = 0.161$). p53 expression showed significant association with Broder's grading ($p = 0.001$), Bryne's grading ($p = 0.009$), and recurrence ($p = 0.004$). A highly significant association was noted between Broder's and Bryne's grading systems ($p < 0.0001$).

Conclusion: Ki67 and p53 expression at the invasive tumor front correlate significantly with tumor differentiation and recurrence in OSCC. These markers may serve as valuable adjunct prognostic indicators in assessing tumor aggressiveness and biological behavior. Evaluation of proliferative and apoptotic markers at the invasive tumor front can enhance prognostic accuracy and aid in better risk stratification of OSCC patients.

Keywords: Oral Squamous Cell Carcinoma; Invasive Tumor Front; Ki67; p53; Immunohistochemistry; Tumor Proliferation; Histological Grading; Broders Classification; Bryne's Grading.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) is one of the most common malignancies affecting the oral cavity and represents a major global health burden. Oral cancers rank among the top six cancers worldwide in terms of incidence. India carries a disproportionately high burden, accounting for nearly one-third of the global incidence of oral carcinomas. More than 77,000 new cases and approximately 52,000 deaths are reported annually in India, contributing significantly to cancer-related morbidity and mortality.[1,2] The increasing incidence of oral cancer poses a serious public health concern in the Indian population.

OSCC develops through a multistep process involving accumulation of genetic alterations influenced by both intrinsic and extrinsic factors. Genetic predisposition combined with environmental exposures such as tobacco use (smoked and smokeless forms), alcohol consumption, betel quid chewing (with or without tobacco), chronic inflammation, viral infections, and other carcinogens play a crucial role in oral carcinogenesis.[3,4] Carcinogens interact with cellular DNA, resulting in mutations that disrupt normal cell cycle regulation, promote uncontrolled proliferation, and impair programmed cell death.

Tumor progression and prognosis in OSCC are closely related to the biological behavior of tumor cells at the advancing margin of invasion. The tumor invasive front (TIF), particularly the invasive tumor front (ITF), represents the deepest and most aggressive component of the tumor. At this region, small clusters of tumor cells or individual tumor buds detach from the main tumor mass and infiltrate the surrounding stroma. These tumor buds are considered highly aggressive and are believed to significantly influence local invasion, lymph node metastasis, and overall prognosis.[5,6]

Bryne (1998) proposed that molecular and morphological characteristics at the deeper invasive front provide more reliable prognostic information than evaluation of superficial tumor areas alone.[7] The grading system suggested by Bryne emphasizes parameters such as degree of keratinization, nuclear polymorphism, pattern of invasion, and host inflammatory response specifically at the invasive front, offering a more dynamic and prognostically relevant assessment of tumor aggressiveness.

Among the various molecular markers studied in OSCC, Ki-67 antigen and p53 protein are of particular importance.

- Ki-67 is a nuclear proliferation-associated antigen expressed during active phases of the cell cycle (G1, S, G2, and M phases) but absent in resting cells (G0 phase). Its expression reflects the growth fraction of a tumor. Increased Ki-67 labeling index has been correlated with higher proliferative activity and aggressive biological behavior in OSCC.[8]
- p53 is a tumor suppressor protein that plays a central role in cell cycle regulation, DNA repair, and apoptosis. Mutation of the p53 gene leads to stabilization and accumulation of dysfunctional protein within tumor cells, which can be detected as overexpression by immunohistochemistry. Abnormal p53 expression has been associated with poor differentiation, increased invasiveness, and unfavorable prognosis in OSCC.[9,10]

Several studies have demonstrated overexpression of Ki-67 and p53 at the invasive tumor front of OSCC, suggesting that evaluation of these markers at the ITF may provide better insight into tumor aggressiveness compared to assessment of the entire tumor mass.[6,9] Therefore, correlating histopathological grading at the tumor front with the expression of Ki-67 and p53 may help in predicting biological behavior and prognosis of OSCC.

Aim of the Study

The present study aims:

- To perform histological grading of OSCC according to Broders' grading system (based on degree of differentiation) and Bryne's invasive front grading system (based on tumor morphology at the invasive front).
- To evaluate the expression of Ki-67 antigen and p53 protein at the invasive tumor front of OSCC using immunohistochemistry.
- To determine the association between histological grading at the tumor front and the expression of Ki-67 and p53 in OSCC.

MATERIALS AND METHODS

Study Design: This is a prospective observational study.

Place of Study and Study Period: This is a prospective and observational study conducted in the Department of Pathology, S.V.S. Medical College and Hospital, Yenugonda, Mahabubnagar, Telangana over a period of two years.

Study duration: January 2024 to December 2025.

All biopsy and surgical specimens received from the Departments of General Surgery, ENT, and Dental Surgery at SVS Medical College, Mahabubnagar and submitted to the Department of Pathology for histopathological examination were considered for inclusion.

Sample Size: A total of 74 cases of histopathologically confirmed Oral Squamous Cell Carcinoma (OSCC) were included in the study.

For immunohistochemical (IHC) analysis: Out of 74 cases, 17 paraffin blocks were unavailable (taken by patients for second opinion), and therefore 54 cases were subjected to IHC staining for Ki-67 and p53 markers.

Inclusion Criteria

- Biopsy and surgical specimens diagnosed as OSCC received from ENT, General Surgery, and Dental departments.

- Specimens containing adequate representation of the Invasive Tumor Front (ITF).

Exclusion Criteria

- Inadequate tissue sampling.
- Autolyzed or poorly preserved specimens.
- Cases with incomplete clinical history in the requisition form.

All received specimens were fixed in 10% neutral buffered formalin for approximately 24 hours.

Following fixation:

- Gross examination was performed according to standard surgical pathology protocol.
- Detailed gross descriptions were recorded.
- Extensive sampling was done, particularly from suspicious and infiltrative areas.
- Tissue bits were taken especially from the deep invasive tumor front (ITF).
- Routine manual tissue processing and paraffin embedding were carried out.
- Sections of 4–5 µm thickness were cut using a microtome.
- Sections were stained with Hematoxylin and Eosin (H&E) and mounted with DPX.
- Slides were examined under a light microscope.

Histopathological Grading

A. Conventional Grading (Broders' System)

Cases were graded based on histomorphology into:

- • Well differentiated
- • Moderately differentiated
- • Poorly differentiated

B. Invasive Tumor Front Grading (Byrne's Classification)

Cases were graded based on morphological parameters at the ITF (keratinization, nuclear polymorphism, pattern of invasion, host inflammatory response).

Total score ranges from 4–16:

- Grade 1: 4–8
- Grade 2: 9–12
- Grade 3: 13–16

Immunohistochemistry (IHC) Procedure

IHC staining was performed on selected paraffin sections from the deep invasive front of tumor.

- Sections were deparaffinized and rehydrated.
- Antigen retrieval was performed.
- Primary antibodies for Ki-67 and p53 were applied.
- Detection was performed using DAB chromogen.
- Development of brown nuclear staining was considered positive expression.

Scoring of Ki-67 and p53 Markers

Ki-67 Scoring

Counting was performed in three randomly selected high-power fields (×400 magnification).

Ki67 Index= Number of stained tumor cells/Total number of tumor cells ×100

Classification based on Ki-67 index:

- 6%–13% → Well differentiated
- 13%–30% → Moderately differentiated
- >30% → Poorly differentiated

p53 Expression Scoring

The number of p53-positive nuclei per 100 tumor cells was recorded.

- <10% → Negative (−)
- 10–30% → Mild positive (+)
- 31–50% → Moderate positive (++)
- >50% → Strong positive (+++)

Statistical Analysis

- Data were entered into Microsoft Excel and analyzed using SPSS software.
- Descriptive statistics were expressed as mean ± SD and percentages.
- Association between histological grade and marker expression was analyzed using Chi-square test.
- Correlation between Ki-67 and p53 expression was assessed using Pearson/Spearman correlation.
- A p-value < 0.05 was considered statistically significant.

RESULTS

Table 1: Clinicopathological and Immunohistochemical Profile of OSCC Cases (n = 74)

Variable	Category	Frequency (n)	Percentage (%)
Sex	Male	29	39.2
	Female	45	60.8
Recurrent Cases	Yes	14	18.9
	No	60	81.1
Gross Appearance	Exophytic	4	5.4
	Fungating	7	9.5
	Ulceroproliferative	63	85.1
Site of OSCC	Lt Buccal Mucosa	18	24.3
	Rt Buccal Mucosa	18	24.3
	Lt Lower Alveolus	10	13.5
	Lt BM + Alveolus	4	5.4
	Lt Lo GB Sulcus	4	5.4
	Lt RMT	3	4.1
	Rt RMT	3	4.1
	Rt Lower Alveolus	3	4.1
	Lt Cheek	2	2.7
	Lt BM + Submandibular Mass	2	2.7
	Rt Lo Alveolus + RMT	2	2.7

	BM + Tonsil	1	1.4
	Lower Lip	1	1.4
	Lt BM + Ulcer Lower Lip	1	1.4
	Lt Lateral Tongue	1	1.4
	Upper Lip + GB Sulcus	1	1.4
Broders Grading	Well differentiated SCC	22	29.7
	Verrucous variant WD SCC	3	4.1
	Moderately differentiated SCC	42	56.8
	Poorly differentiated SCC	5	6.8
	Poorly differentiated Sarcomatoid SCC	2	2.7
Byrne Score (Raw)	7	3	4.1
	8	4	5.4
	9	10	13.5
	10	17	23.0
	11	9	12.2
	12	14	18.9
	13	8	10.8
	14	4	5.4
	15	3	4.1
	16	2	2.7
Byrne Grade (ITF)	Grade I	7	9.5
	Grade II	50	67.6
	Grade III	17	23.0
PTNM Staging	NA	8	10.8
	PT1N0Mx	2	2.7
	PT2N0Mx	11	14.9
	PT2N2Mx	2	2.7
	PT3N0Mx	25	33.8
	PT3N1Mx	5	6.8
	PT3N2Mx	11	14.9
	PT3N3Mx	2	2.7
	PT4N0Mx	6	8.1
	PT4N2Mx	2	2.7
Ki-67 Expression	Blocks NA	17	23.0
	Low	5	6.8
	Intermediate	11	14.9
	High	41	55.4
p53 Expression	Blocks NA	17	23.0
	Negative	17	23.0
	1+	2	2.7
	2+	5	6.8
	3+	33	44.6
Habitual Risk Factors	Tobacco chewing	56	75.7
	Gutka	6	8.1
	Betelnut/Leaf	4	5.4
	Smoking	10	13.5
	Alcohol	13	17.6

A total of 74 histopathologically confirmed cases of Oral Squamous Cell Carcinoma (OSCC) were included in the present observational study. The clinicopathological parameters, histological grading at the invasive tumor front (ITF), and immunohistochemical expression of Ki-67 antigen and p53 protein were analyzed and correlated.

Demographic Distribution: Out of 74 cases, 45 (60.8%) were females and 29 (39.2%) were males, showing a female predominance in the present study.

Site Distribution of OSCC: The most common anatomical site involved was the buccal mucosa, accounting for 36 cases (48.6%) when both right and left sides were combined. The left buccal mucosa (24.3%) and right buccal mucosa (24.3%) were equally affected.

The next most common site was the left lower alveolus (13.5%), followed by involvement of retromolar trigone (RMT), gingivobuccal sulcus, lip, tongue, and other combined sites. The distribution reflects the pattern of tobacco-related carcinogenesis commonly seen in the Indian population.

Recurrence Status: Among the 74 cases, 14 cases (18.9%) were recurrent tumors, while 60 cases (81.1%) were primary tumors.

Gross Appearance of Tumor: Most tumors presented as ulceroproliferative growth (85.1%), followed by fungating growth (9.5%) and exophytic growth (5.4%).

Histopathological Grading

Broders Grading

Based on Broders classification:

- Moderately differentiated SCC was the most common type (56.8%).
- Well differentiated SCC accounted for 29.7%.
- Poorly differentiated SCC constituted 6.8%.
- Rare variants such as poorly differentiated sarcomatoid SCC (2.7%) and verrucous variant (4.1%) were also observed.

Thus, the majority of tumors showed moderate differentiation.

Byrne's Grading at Invasive Tumor Front

According to Byrne's invasive front grading:

- Grade II tumors were predominant (67.6%)
- Grade III tumors constituted 23.0%
- Grade I tumors were least common (9.5%)

The Byrne's score ranged from 7 to 16, with the majority clustering between scores 10–12.

A statistically significant association was observed between Broders grading and Byrne's grading (χ^2 = 53.762, p < 0.0001) indicating strong correlation between conventional grading and invasive front morphology.

TNM Staging (PTNM)

The most frequent stage was PT3N0Mx (33.8%), followed by:

- PT2N0Mx (14.9%)
- PT3N2Mx (14.9%)
- PT4N0Mx (8.1%)

Advanced stages (PT3 and PT4) constituted a significant proportion of cases, indicating late clinical presentation.

Immunohistochemical Expression

Ki-67 Expression

Ki-67 expression was evaluated at the invasive tumor front:

- High expression was observed in 41 cases (55.4%).
- Intermediate expression in 14.9%.
- Low expression in 6.8%.
- 23% of blocks were not available for analysis.

A statistically significant association was found between:

- Ki-67 expression and Broders grading (χ^2 = 37.951, p < 0.0001)
- Ki-67 expression and recurrence (χ^2 = 7.242, p = 0.027)

Higher Ki-67 expression was associated with poorer differentiation and recurrent tumors.

p53 Expression

p53 immunoreactivity showed:

- Strong positivity (3+) in 44.6% of cases.
- Negative expression in 23.0%.
- 2+ in 6.8%.
- 1+ in 2.7%.
- 23% blocks unavailable.

Statistical analysis revealed:

- Significant association between p53 expression and Broders grading (χ^2 = 34.472, p = 0.001).
- Significant association between p53 expression and recurrence (χ^2 = 13.497, p = 0.004).

Strong p53 expression correlated with higher histological grade and recurrent tumors.

Habitual Risk Factors

The most common risk factor identified was tobacco chewing (75.7%), followed by:

- Alcohol consumption (17.6%)
- Smoking (13.5%)
- Gutka use (8.1%)
- Betel nut/leaf chewing (5.4%)

Table 2: Association between Ki-67, p53 Expression, Histological Grading Systems, and Recurrence in OSCC

S. No	Association Studied	Key Distribution Findings	Chi-Square (χ^2)	P-Value	Significance
1	Ki-67 vs Byrne Grade	High Ki-67 predominantly in Grade II (61.0%) and Grade III (26.8%)	6.568	0.161	Not Significant
2	Ki-67 vs Broders Grade	73.2% of High Ki-67 cases were Moderately Differentiated SCC	37.951	<0.0001	Very Highly Significant
3	Ki-67 vs Recurrence	34.1% recurrence in High Ki-67 group; none in Low/Intermediate	7.242	0.027	Significant
4	p53 vs Byrne Grade	63.6% of 3+ p53 cases in Grade II; 30.3% in Grade III	17.042	0.009	Significant
5	p53 vs Broders Grade	75.8% of 3+ p53 cases in Moderately Differentiated SCC	34.472	0.001	Significant
6	p53 vs Recurrence	100% of recurrent cases showed 3+ p53 expression	13.497	0.004	Significant
7	Broders vs Byrne Grade	Grade III Byrne strongly associated with Moderately & Poorly Differentiated SCC	53.762	<0.0001	Very Highly Significant

The present study demonstrates that proliferative and tumor suppressor markers show meaningful associations with histopathological grading systems and recurrence in Oral Squamous Cell Carcinoma (OSCC). Although Ki-67 expression increased with higher Byrne invasive tumor front grades, the association was not statistically significant (p = 0.161). However, Ki-67 showed a very highly significant association with Broders histological grading (p < 0.0001), with the majority of high Ki-67 cases occurring in moderately differentiated SCC. Importantly, recurrence was observed exclusively in the high Ki-67 group, establishing a significant association (p = 0.027), suggesting its prognostic relevance.

Similarly, p53 overexpression (3+ grade) showed statistically significant associations with both Byrne grading (p = 0.009) and Broders grading (p = 0.001), indicating that higher p53 expression correlates with poorer differentiation and higher invasive potential. Notably, all recurrent cases demonstrated strong (3+) p53 expression, revealing a significant association with recurrence (p = 0.004). Furthermore, a very highly significant correlation was observed between Broders grading and Byrne invasive front grading (p < 0.0001), reinforcing the prognostic importance of evaluating the invasive tumor front.

Overall, these findings suggest that Ki-67 and p53 expression at the invasive tumor front may serve as

important prognostic indicators in OSCC, particularly in predicting tumor aggressiveness and recurrence.

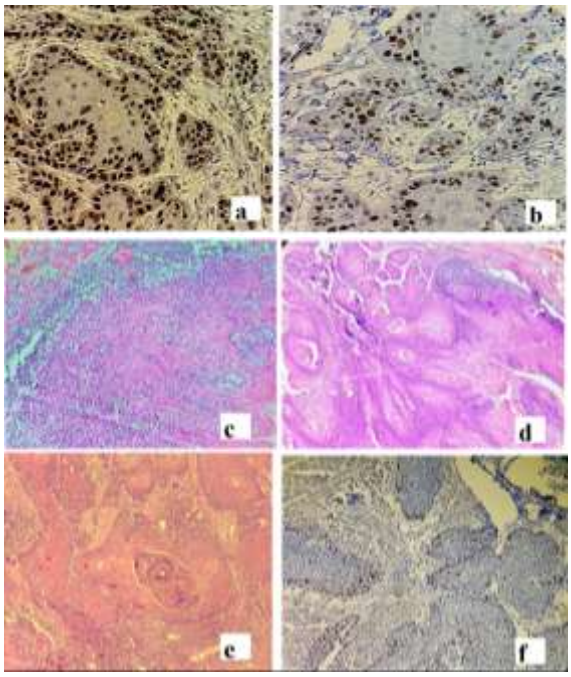

Figure 1: a.P53 IN OSCC 400X: Positive nuclear expression at ITF . b. KI67 in OSCC 400X: positive nuclear expression in actively proliferating tumor cells .c.100X shows infiltrating tumor cells in to muscle bundles and lymphoplasmacytic infiltration. d.100X: Well differentiated verrucous variant of OSCC showing invasion into adjacent stroma along with lymphoplasmacytic infiltrate. e. H&E sections under 100X shows moderately differentiated OSCC. f. KI67 expression in well differentiated SCC in 100X.

DISCUSSION

In the present study, the buccal mucosa (48.60%) was identified as the most commonly affected site in oral squamous cell carcinoma (OSCC). This finding is consistent with epidemiological patterns observed in South Asian populations, where buccal mucosa involvement is strongly associated with smokeless tobacco and betel quid placement habits.[11]

The development of oral cancer is closely linked to lifestyle-related risk factors, particularly tobacco use (both smoked and smokeless forms), alcohol consumption, betel quid chewing, and poor oral hygiene. Histologically, the majority of oral malignancies are squamous cell carcinomas (SCCs). OSCC is believed to arise from precancerous dysplastic lesions through a multistep carcinogenic process involving cumulative genetic and molecular alterations. Clinically and histopathologically, SCC often coexists with epithelial dysplasia or leukoplakia. The malignant transformation rate of oral potentially malignant disorders has been reported to reach up to 17.5%, underscoring the importance of early detection and molecular evaluation.[11]

In the present study, smokeless tobacco chewing was the most common predisposing habit, contributing to 75.70% of OSCC cases. This observation correlates with Pandey et al,[11] who reported that 78% of OSCC cases were associated with dried smokeless tobacco use. These findings reinforce the strong etiological link between smokeless tobacco and oral carcinogenesis.

The invasive tumor front (ITF) represents the deepest and most biologically aggressive region of the tumor. Cells at the ITF exhibit enhanced proliferative activity, invasiveness, and molecular alterations. In this study, tumors were graded using both Broder's and Bryne's histological grading systems, with Bryne's classification focusing specifically on morphological characteristics at the invasive tumor front.[12-16]

Interestingly, the present study showed a female predominance (60.81%), which contrasts with studies such as Durga & Shanthi et al. (2019), where males (66.67%) were more frequently affected.[17] This variation may reflect regional differences in tobacco usage patterns.

A highly significant association was observed between Broder's and Bryne's grading systems ($P < 0.0001$), which is consistent with findings reported by Bryne et al. (1989), Dissanayake et al. (2017), and Durga & Shanthi et al. (2019). This strong correlation supports the reliability of invasive front grading in reflecting tumor differentiation and aggressiveness.

Immunohistochemical analysis for p53 and Ki-67 was performed in 57 cases (77% of total samples). The findings demonstrated that tumor aggressiveness is closely related to tumor stage, histological grade, and molecular alterations. Among the 57 cases evaluated for p53 expression, 29.82% were negative, while 3.50%, 8.77%, and 57.89% showed 1+, 2+, and 3+ expression respectively. Overall, 70.16% of cases were positive for p53, which is slightly higher than the 65% positivity reported by Swaminathan et al.[18]

The tumor suppressor protein p53 plays a central role in genomic stability by regulating cell cycle arrest, apoptosis, DNA repair, and senescence. Mutation of the TP53 gene results in loss of cell cycle control and accumulation of genetically unstable cells. In the present study, significant associations were observed between p53 expression and Broder's grading ($P = 0.001$), Bryne's grading ($P = 0.009$), and recurrence ($P = 0.004$). These findings align with Verma et al. (2014) and support the role of p53 overexpression as an indicator of tumor aggressiveness and recurrence risk.[19]

Sequential mutation analyses have shown that p53 alterations occur early in oral carcinogenesis and are maintained during progression from dysplasia to carcinoma. Although p53 immunostaining does not always confirm gene mutation, increased immunoreactivity correlates with tumor progression and invasive behavior.

In this study, 18.19% of cases were recurrent. Notably, 100% of recurrent cases demonstrated 3+ p53 expression, reinforcing its prognostic significance. Disruption of p53-mediated pathways results in uncontrolled proliferation and accumulation of additional genetic damage, thereby promoting malignant progression.

Ki-67, a well-established proliferation marker, was positive in all 57 evaluated cases. Histologic grading revealed 8.77% low, 19.29% intermediate, and 71.94% high Ki-67 expression. A highly significant association was found between Ki-67 expression and Broder's grading ($P < 0.0001$), indicating that proliferative activity increases with decreasing differentiation. However, the association between Ki-67 and Bryne's grading was not statistically significant ($P = 0.161$). A significant association was observed between Ki-67 expression and recurrence ($P = 0.027$).

Ki-67 is expressed during all active phases of the cell cycle (G1, S, G2, and M) but is absent in quiescent (G0) cells. Its short half-life (approximately 60–90 minutes) makes it a reliable marker of active proliferation. Increased Ki-67 expression has been associated with aggressive behavior, poor differentiation, and reduced survival in several malignancies.

Histologically, well-differentiated OSCC showed Ki-67 positivity predominantly at the peripheral layers of tumor islands, whereas moderately and poorly differentiated tumors exhibited more diffuse and intense staining. This pattern suggests that proliferative activity is greater in less differentiated and more aggressive tumor components, particularly at the invasive front.

The present study also evaluated associations between molecular markers and risk factors. Tobacco use showed higher Ki-67 and p53 positivity, although not all associations were statistically significant. Alcohol consumption demonstrated significant associations with both Ki-67 ($P = 0.037$) and p53 expression ($P = 0.041$), supporting its role as a synergistic carcinogenic factor. Betel nut usage showed statistically significant associations with both Ki-67 ($P = 0.009$) and p53 ($P = 0.02$). Smoking and gutka intake did not demonstrate statistically significant associations in this cohort.

The strong association between p53 overexpression and higher histological grades suggests that disruption of tumor suppressor pathways contributes substantially to tumor progression. Mutant p53 protein has an increased half-life, leading to its accumulation and detection by immunohistochemistry. Loss of normal p53 function impairs G1 checkpoint control, enabling proliferation of genetically damaged cells.[20-23]

Ki-67 overexpression further confirms increased proliferative activity in aggressive OSCC. Abnormal cell proliferation is considered a hallmark of tumorigenesis, and Ki-67 serves as a reliable biomarker for growth fraction assessment. Its elevated expression at the invasive tumor front highlights the biological aggressiveness of this region.

Overall, the findings of the present study emphasize that evaluation of molecular markers specifically at the invasive tumor front provides valuable prognostic information. Both p53 and Ki-67 expression patterns correlate with histological grading and recurrence, indicating their potential utility as adjunct prognostic biomarkers in OSCC.

These results support the hypothesis that combined histopathological and molecular evaluation enhances understanding of tumor behavior and may contribute to improved prognostic stratification and therapeutic decision-making in oral squamous cell carcinoma.

CONCLUSION

This study highlights the significant role of p53 and Ki67 in the progression of Oral Squamous Cell Carcinoma (OSCC), particularly at the invasive tumor front, the most biologically aggressive region of the tumor. Increased Ki67 expression correlated with poorer differentiation and higher tumor grades, indicating enhanced proliferative activity in aggressive lesions. Similarly, p53 overexpression showed significant association with histological grade and recurrence, supporting its involvement in malignant transformation and tumor progression.

The findings suggest that the invasive tumor front is the most appropriate site for evaluating proliferative and apoptotic markers. Both p53 and Ki67 demonstrated statistically significant relationships with tumor behavior, underscoring their potential as adjunct prognostic biomarkers.

Integration of immunohistochemical assessment of p53 and Ki67 with conventional histopathology may improve grading accuracy, prognostic evaluation, and therapeutic planning in OSCC, thereby aiding in better risk stratification and individualized patient management.

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