

EXPRESSION OF Ki67 IN ORAL SQUAMOUS CELL CARCINOMA

Histopathology

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ABSTRACT

Introduction : Oral squamous cell carcinoma (OSCC) is one of the most common malignancies of the head and neck region in India and continues to be associated with significant morbidity and mortality. Despite advances in treatment, prognosis remains variable due to biological heterogeneity of the tumor. Dysregulation of the cell cycle and increased cellular proliferation are key events in oral carcinogenesis. Immunohistochemical marker such as Ki-67, a proliferation marker, provide valuable insights into tumor biology and may aid in prognostication.

Aim : To study the expression of Ki-67 in oral squamous cell carcinoma and to evaluate their correlation. **Materials And Methods :** This study included histopathologically confirmed cases of oral squamous cell carcinoma. Formalin-fixed, paraffin-embedded tissue sections were subjected to immunohistochemical staining for Ki-67. The expression patterns of both markers were assessed and correlated with histological grades of OSCC. Statistical analysis was performed to determine the significance of associations between marker expression and tumor differentiation.

Results : Present study comprises of 38 cases, majority of cases were in 51-60 years of age group with equal sex distribution. Mandibulectomy (26.3%) and buccal mucosa (34.2%) were the most common received specimen. Majority were well differentiated squamous cell carcinoma accounting for almost 32 cases and Ki-67 showed moderate intensity with score of +2. **Conclusion :** The immunohistochemical evaluation of Ki-67 provides meaningful insight into the biological behaviour of oral squamous cell carcinoma. Ki-67 serves as a reliable indicator of proliferative activity and tumor aggressiveness. This assessment may be useful as an adjunct to routine histopathological evaluation in OSCC and may help in prognostication and risk stratification.

KEYWORDS

Oral squamous cell carcinoma, Ki-67.

INTRODUCTION:

Oral squamous cell carcinoma remains one of the most frequently encountered malignancies of the head and neck region, particularly in populations with high exposure to tobacco, areca nut, alcohol, and poor oral hygiene. According to national and GLOBOCAN data India had 143,759 cases of oral squamous cell carcinoma overall in 2023. Despite advances in surgical techniques, radiotherapy, and chemotherapy, the overall survival rates for oral squamous cell carcinoma have shown only modest improvement over the past few decades. This limited progress is largely attributable to late presentation, biological heterogeneity of the tumor, and the complex interplay of molecular events that drive malignant transformation and disease progression. In this context, understanding the molecular markers involved in cell cycle regulation and proliferation has become increasingly important, not only for prognostication but also for guiding treatment strategies and exploring targeted therapies.^{1,2}

Ki-67 is a well-established marker of cellular proliferation. It is a nuclear protein expressed during all active phases of the cell cycle, including G1, S, G2, and mitosis, but is absent in resting (G0) cells. Because of this unique expression pattern, Ki-67 labeling index serves as a reliable indicator of the growth fraction of a given cell population. In normal oral mucosa, Ki-67 expression is typically confined to the basal and parabasal layers, where cell division normally occurs. As epithelial dysplasia progresses and invasive carcinoma develops, the distribution and intensity of Ki-67 expression expand into the suprabasal layers, reflecting loss of normal growth control and increased proliferative activity.^{3,4}

AIM & OBJECTIVES

AIM:

- To study the role of Ki-67 in oral squamous cell carcinoma.

OBJECTIVES:

- To determine the expression of Ki-67 in oral squamous cell carcinoma.
- To correlate expression of Ki67 with age, sex, resected and biopsy specimen, histological grade, Ki67 grading.

MATERIALS AND METHODS:

The study was conducted in the Department of Pathology at Sri Siddhartha Medical College and Hospital (SSMCH), Agalakote, Tumkur, Karnataka. The hospital served as a tertiary care referral center for the region, managing a significant number of oral cancer cases. The pathology department maintained a well-organized archival

system of formalin-fixed paraffin-embedded (FFPE) tissue blocks and corresponding histopathological records, which formed the primary source of data. The immunohistochemistry laboratory within the department was equipped with necessary instruments for staining and analysis, ensuring all procedures could be performed on-site.

RESULTS:

Age-wise distribution of cases:

The age-wise distribution of cases shows that oral squamous cell carcinoma was most frequently observed in the 51–60 years age group, which accounted for the highest proportion of cases (26.3%). This was followed by patients aged 61–70 years (21%), indicating a clear predominance in the sixth and seventh decades of life. Lower frequencies were noted in the 41–50 years and 71–80 years age groups, each contributing 18.4% of cases, while the least number of cases were seen in the 30–40 years age group (15.7%).

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

Age in years	Number of cases (n)	Percentage (%)
30–40	6	15.7
41–50	7	18.4
51–60	10	26.3
61–70	8	21.0
71–80	7	18.4
Total	38	100

Gender-wise distribution of cases

The gender-wise distribution in the present study demonstrated an equal representation of male and female patients with oral squamous cell carcinoma. Out of the total 38 cases, 19 cases (50%) were males and 19 cases (50%) were females.

Table 2: Gender-wise distribution of patients with oral squamous cell carcinoma

Gender	Number of cases (n)	Percentage (%)
Male	19	50.0
Female	19	50.0
Total	38	100

Nature of resected specimens: The distribution of resected specimens shows that mandibulectomy was the most commonly performed surgical procedure, accounting for 10 cases (26.3%). This was followed by bite composite resection of the buccal mucosa in 7

cases (18.4%). Maxillectomy and glossectomy were less frequent, with 3 cases each, contributing 7.9% respectively. Overall, resected specimens constituted 23 out of 38 cases (60.5%), indicating that a majority of patients underwent definitive surgical management

Table 3: Distribution of cases according to nature of resected specimens

Nature of specimen (resected)	Number of cases (n)	Percentage (%)
Maxillectomy	3	7.9
Mandibulectomy	10	26.3
Glossectomy	3	7.9
Bite composite resection of buccal mucosa	7	18.4
Total (resected cases)	23 / 38	60.5

Nature of biopsy specimens The distribution of biopsy specimens shows that biopsies constituted 15 out of 38 cases (39.5%) in the present study. The majority of biopsy samples were obtained from the buccal mucosa, accounting for 13 cases (34.2%), indicating that this was the most common site requiring diagnostic biopsy. Biopsies from the tongue and hard palate were relatively uncommon, with 1 case each (2.6%).

Table 4: Distribution of cases according to nature of biopsy specimens

Nature of specimen (biopsy)	Number of cases (n)	Percentage (%)
Biopsy – buccal mucosa	13	34.2
Biopsy – tongue	1	2.6
Biopsy – hard palate	1	2.6
Total (biopsy cases)	15 / 38	39.5

Histological grading of oral squamous cell carcinoma

The distribution of histological grades revealed that the majority of cases were well differentiated oral squamous cell carcinoma, accounting for 32 out of 38 cases (84.2%). Moderately differentiated tumours constituted 5 cases (15.1%), while poorly differentiated carcinoma were only 1 case (1%).

Table 5: Distribution of cases according to histological differentiation.

Histological type	Number of cases (n)	Percentage (%)
Well differentiated	32 / 38	84.2
Moderately differentiated	5 / 38	15.1
Poorly differentiated	1 / 38	1.0
Total	38 / 38	100

Expression of Ki-67 expression with histological grade

Analysis of Ki-67 expression across histological grades revealed high proliferative activity in oral squamous cell carcinoma. Among well differentiated tumors, 29 out of 32 cases (90.6%) were Ki-67 positive, while 3 cases (9.4%) were negative. All moderately and poorly differentiated carcinomas showed 100% Ki-67 positivity. Overall, Ki-67 expression was present in 35 out of 38 cases (92.1%). The progressive increase and uniform positivity in higher grades indicate enhanced proliferative activity with loss of differentiation, highlighting Ki-67 as a reliable marker of tumor proliferation in oral squamous cell carcinoma.

Table 6: Expression of Ki-67 expression with histological grade in oral squamous cell carcinoma.

Histological grade	Total cases (n)	Ki-67 positive n (%)	Ki-67 negative n (%)
Grade 1 (Well differentiated)	32	29 (90.6)	3 (9.4)
Grade 2 (Moderately differentiated)	5	5 (100)	0 (0)
Grade 3 (Poorly differentiated)	1	1 (100)	0 (0)
Total	38	35 (92.1)	3 (7.9)

Ki-67 immunohistochemical scoring in positive cases

Among Ki-67 positive cases, moderate immunohistochemical expression was most common. A score of 2+ was observed in 17 cases (44.7%), indicating intermediate proliferative activity in nearly half of the tumors. Low positivity (1+) was seen in 12 cases (31.6%), while strong positivity (3+) was identified in 6 cases (15.8%).

Table 7: Distribution of Ki-67 immunohistochemical scores in positive cases.

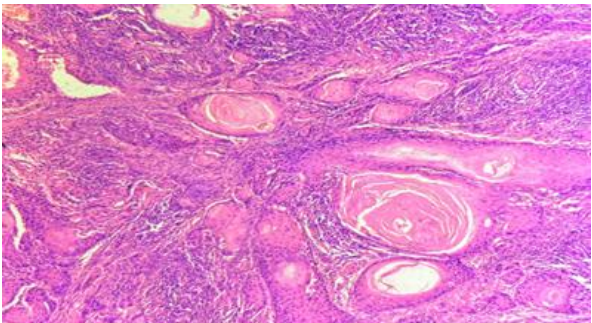
Ki-67 score	+1	+2	+3	Total
Number of cases	12	17	06	35
Percentage	31.6%	44.7%	15.8%	100%

PHOTOMICROGRAPHS:

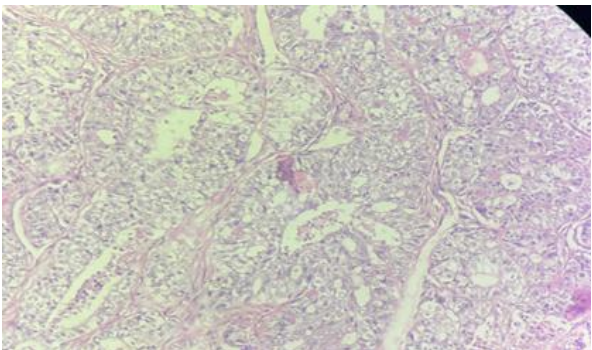


Figure 1-Showing gross picture of buccal mucosa

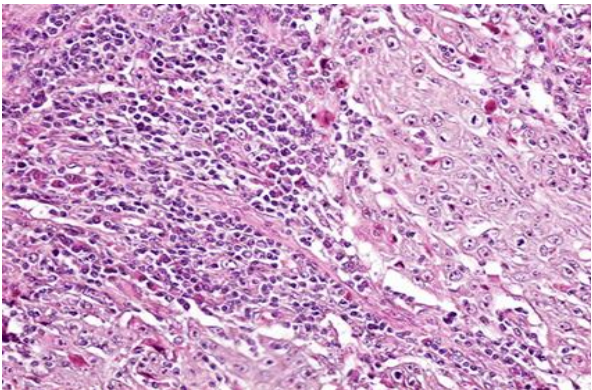
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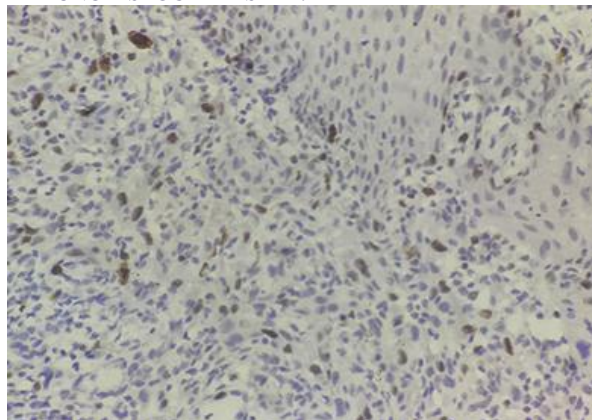
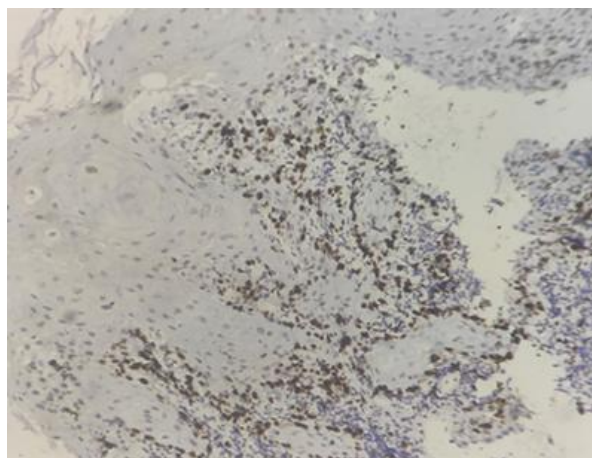
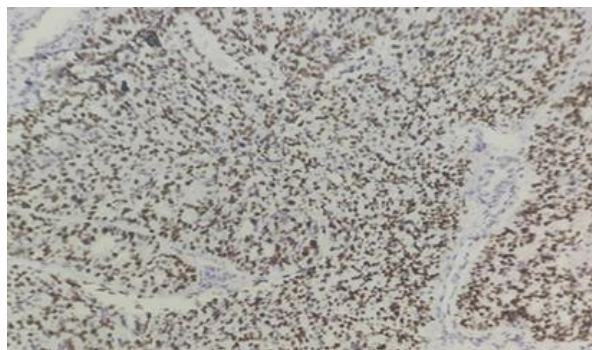
WELL DIFFERENTIATED SQUAMOUS CELL CARCINOMA FIGURE:2



MODERATELY DIFFERENTIATED SQUAMOUS CELL CARCINOMA FIGURE:3



POORLY DIFFERENTIATED SQUAMOUS CELL

CARCINOMA FIGURE:4**IMMUNOHISTOCHEMISTRY:****Ki67 GRADE -1 FIGURE:5****Ki67 GRADE 2 FIGURE:6****Ki67 GRADE-3 FIGURE 7****DISCUSSION:**

The findings of the present study are in concordance with existing literature, confirming that oral squamous cell carcinoma predominantly affects individuals in the later decades of life. This emphasizes the importance of targeted screening, early detection strategies, and public health interventions focused on middle-aged populations who are at the highest risk for developing oral malignancies.

Table 8: Comparison of age distribution with previous studies

Study	Age range (years)	Mean age (years)
Present study	31–80	55.5
Richter et al. ⁵	27–96	61.5
Agarwal et al. ⁶	17–92	51.3
Rashid et al. ⁷	33–89	54.2

Gender Distribution and Its Clinical Relevance

The present study demonstrated an equal gender distribution of oral squamous cell carcinoma, with males and females contributing equally

to the total number of cases. This finding contrasts with the traditionally reported male predominance in oral squamous cell carcinoma and suggests a changing epidemiological trend.

Table 9: Comparison of gender distribution with previous studies

Study	Gender distribution
Present study	M = F
Richter et al. ⁵	M > F
Agarwal et al. ⁶	M > F
Rashid et al. ⁷	M > F

Site-wise Distribution of Oral Squamous Cell Carcinoma

In the present study, the buccal mucosa emerged as the most commonly involved site, accounting for nearly two-thirds of all oral squamous cell carcinoma cases. This was followed by the tongue, while other sites such as the gingivobuccal sulcus, retromolar trigone, hard palate, lip, and floor of the mouth contributed comparatively fewer cases.

Table 10: Comparison of site distribution with previous studies

Site	Present (%)	Tyagi et al. ⁸ (%)	Rashid et al. ⁷ (%)
Buccal mucosa	63.2	56	42
Tongue	15.8	14	18
Gingivobuccal sulcus	5.3	16	6
Retromolar trigone	5.3	6	4
Lip	2.6	4	26
Hard palate	5.3	2	4
Floor of mouth	2.6	2	0
Total	100	100	100

Histopathological Grading of Oral Squamous Cell Carcinoma

In the present study, the majority of cases were diagnosed as well differentiated oral squamous cell carcinoma, with moderately differentiated tumors forming a smaller proportion and few poorly differentiated carcinoma. This predominance of well differentiated tumors suggests that a significant number of cases retained morphological features of squamous maturation at the time of diagnosis.

Table 11: Comparison of histopathological grading with previous studies

Histopathological type	Present	Agarwal et al. ⁵	Tyagi et al. ⁸	Rashid et al. ⁵
Well differentiated	84.2%	70%	32%	40%
Moderately differentiated	13.2%	27.5%	54%	54%
Poorly differentiated	2.6%	2.5%	14%	6%

Table 12: Comparison of histopathological grading with previous studies

Histopathological type	Present	Agarwal et al. ⁵	Tyagi et al. ⁸	Rashid et al. ⁷
Well differentiated	84.2%	70%	32%	40%
Moderately differentiated	13.2%	27.5%	54%	54%
Poorly differentiated	2.6%	2.5%	14%	6%

Overall Expression Pattern of Ki-67 in Oral Squamous Cell Carcinoma

In the present study, Ki-67 immunohistochemical expression was observed in a high proportion of oral squamous cell carcinoma cases, indicating increased proliferative activity within tumor tissue. The majority of tumors showed Ki-67 positivity, with only a small subset of cases being negative. Among positive cases, most demonstrated low to moderate labeling indices, while fewer cases exhibited strong positivity. This overall high expression of Ki-67 reflects the active proliferative nature of oral squamous cell carcinoma and underscores its utility as a marker of tumor growth dynamics.

Table 13: Comparison of Ki-67 immunohistochemical expression with previous studies

Study	+1 (%)	+2 (%)	+3 (%)	Negative (%)	Total cases
Present study	31.6	44.7	15.8	7.9	38
Tyagi et al. ⁸	24	42	34	0	50
Rashid et al. ⁷	32	46	16	6	50

CONCLUSION:

Expressions of Ki67 is indicative of rapid tumor cell proliferation and

poor tumor differentiation and it indicates how fast the tumor is growing.

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