Original Research

# ASSESSMENT OF EGFR AND p53 BIOMARKERS IN ORAL SQUAMOUS CELL CARCINOMA: A STUDY FROM A TERTIARY CARE CENTRE IN SOUTH INDIA

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## ABSTRACT

**Introduction**: In India, oral cancer ranks among the top three prevalent cancers, accounting for a huge proportion of head and neck cancer–related morbidity and mortality. TP53 mutations play a critical role in oral carcinogenesis and tumor progression. Overexpression or dysregulation of epidermal growth factor receptor (EGFR) is noted in the majority of head and neck squamous cell carcinomas and is associated with poor prognosis.

**Aim**: This study was conducted to understand the immunohistochemistry expression of p53 and epidermal growth factor receptor (EGFR) in oral squamous cell carcinoma and assess their correlation with clinicopathological characteristics.

**Materials and Methods**: Oral squamous cell carcinomas reported during the year 2024 were included in the study. Clinicodemographic data, including age, sex, and tumor site, were retrieved from pathology records. Immunohistochemical analysis for p53 and epidermal growth factor receptor (EGFR) was performed on representative sections. Results were subjected to the statistical analysis.

**Results:** Among the 52 cases studied, strong p53 expression was seen in 76.9%, and EGFR overexpression was noted in 86.5% of cases. p53 positivity and EGFR overexpression were significantly associated with histological grade ($p < 0.05$).

**Conclusion:** Oral squamous cell carcinoma frequently exhibits p53 and EGFR immunoexpression, which is strongly linked to tumor aggressiveness and advanced disease. Their combined assessment enhances prognostic evaluation and helps identify patients who may benefit from specific treatment approaches.

**Keywords:** Oral Squamous Cell Carcinoma, p53, Epidermal Growth Factor Receptor.

## INTRODUCTION

GLOBOCAN estimates indicate approximately 389,846 new cases[1] of oral squamous cell carcinoma (OSCC) worldwide, with around 188,438 deaths[1] attributed to the disease. In India, OSCC constitutes a major public health burden and ranks as the second most common cancer.[2] OSCC is strongly associated with risk factors such as tobacco use, betel quid chewing, alcohol consumption, and poor oral hygiene. The disease most commonly involves the buccal mucosa, [3] with a marked male predominance, typically presenting in the fifth to seventh decades of life.

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Histologically, OSCC is most frequently diagnosed as a moderately differentiated carcinoma, followed by well-differentiated and poorly differentiated variants.[4] Tumors with similar histomorphological features may demonstrate distinct biological behavior, suggesting the involvement of additional molecular markers. Immunohistochemistry plays a crucial role in elucidating the molecular alterations associated with the pathogenesis and progression of oral cancer.

p53 is a nuclear tumor suppressor phosphoprotein encoded by the *TP53* gene, located on chromosome 17p13. It binds to DNA and induces the synthesis of the p21 protein. p21 forms a complex with cyclin-dependent kinase 2 (CDK2), and the p21–CDK2 complex inhibits the cell from progressing to the next phase of the cell cycle. In addition, p53 can activate the transcription of various pro-apoptotic genes and thereby initiate apoptosis.

Mutations in *TP53* result in the overexpression and accumulation of mutant p53 protein that is unable to bind DNA and induce p21 synthesis. This loss of function leads to impaired cell cycle control and

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contributes to uncontrolled cellular proliferation.[5] Overexpression of p53, as detected by immunohistochemistry (IHC), can aid in distinguishing dysplastic or neoplastic changes from reactive (non-neoplastic) changes in tissue specimens.

Epidermal growth factor receptor 1 (EGFR) is a member of the type I receptor tyrosine kinase family and is a transmembrane glycoprotein normally expressed on the surface of various epithelial and non-epithelial cells. The EGFR molecule comprises an extracellular ligand-binding domain, a transmembrane lipophilic region, and an intracellular domain possessing tyrosine kinase activity. EGFR is activated by ligands such as epidermal growth factor (EGF) and transforming growth factor-α (TGF-α).

Overexpression or aberrant expression of EGFR has been reported in a wide range of tumors of diverse origins. EGFR serves as a therapeutic target for specific monoclonal antibodies and is utilized in the treatment of EGFR-positive malignancies, including head and neck carcinomas.[6] Immunohistochemical evaluation of EGFR expression in tumor cells is essential for selecting patients for targeted immunotherapy and for predicting therapeutic response.

**Aim and Objective**:

The present study was conducted to assess the expression of the biomarkers p53 and EGFR by immunohistochemistry in cases of oral squamous cell carcinoma and to evaluate their correlation with clinicopathological parameters.

## MATERIALS AND METHODS:

This retrospective study was conducted in the Department of Pathology at a tertiary care centre in South India after obtaining ethical clearance from the Institutional Ethics Committee. A total of 52 cases of oral squamous cell carcinoma (OSCC) reported during the year 2024 were included in the study. Only primary cases diagnosed prior to the initiation of chemotherapy or radiotherapy were included. Other histological variants of oral cavity carcinoma were excluded. Clinicodemographic details, including age, sex, and tumor site, were retrieved from histopathology records.

All hematoxylin and eosin (H&E)–stained slides were independently reviewed by two histopathologists to confirm the histological diagnosis according to the World Health Organization (WHO) criteria[7]. Paraffin-embedded tissue blocks were subsequently utilized for immunohistochemical (IHC) analysis.

The primary antibodies used were p53 (clone BP53-12) and EGFR (clone EP22). Sections of normal skin served as positive controls, showing appropriate nuclear staining for p53 in basal keratinocytes and membranous staining for EGFR in epidermal keratinocytes, confirming the adequacy of the IHC technique. Immunohistochemical slides were evaluated independently by two experienced pathologists.

Immunostaining for p53 was interpreted as mutant overexpression when ≥10% of tumor cells exhibited strong and diffuse nuclear staining. Wild-type p53 expression was defined by weak and focal nuclear staining in <10% of tumor cells [8]. Null (complete absence) p53 expression was recorded when there was complete absence of nuclear staining in tumor cells with preserved staining in the internal positive controls.

EGFR immunostaining demonstrated membranous positivity and was evaluated based on staining intensity and extent. Staining intensity was scored on a scale of 0–3, where 0 = no staining, 1 = weak, 2 = moderate, and 3 = strong. The extent of staining was similarly scored on a scale of 0–3, where 0 = no stained cells, 1 = 1–10% of tumor cells, 2 = 11–50% of tumor cells, and 3 = >50% of tumor cells.

A final immunoreactivity score ranging from 0 to 9 was calculated by multiplying the intensity and extent scores. Scores of 0–2 were considered negative or low expression, scores of 3–4 indicated moderate expression, and scores ≥5 were interpreted as EGFR overexpression[9].

All data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) version 15.0. The Chi-square test was used to assess associations between variables. A *p* value <0.05 was considered statistically significant, while a *p* value ≥0.05 was considered not statistically significant.

## RESULTS

The clinicopathological characteristics of the 52 cases of oral squamous cell carcinoma (OSCC) analyzed in the present study are summarized in Table 1. The age of the patients ranged from 38 to 78 years, with a mean age of 58.3 years. The majority of cases (38/52; 73.1%) occurred in the 51–70-year age group. There was a male predominance, with 36 (69.2%) male and 16 (30.8%) female patients. The most common anatomical site involved was the tongue (24/52; 46.2%), followed by the buccal mucosa (12/52; 23.1%). Histologically, 28 cases (53.8%) were moderately differentiated, 15 (28.8%) were well differentiated, and 9 (17.3%) were poorly differentiated.

Strong p53 immunopositivity was observed in 40 cases (76.9%), while 12 cases (23.1%) showed focal p53 positivity. Strong p53 expression was predominantly noted in males (69.2%) and in patients older than 50 years (82.7%). It was most frequently observed in poorly differentiated tumors (9/9), followed by moderately differentiated tumors (25/28). In contrast, focal p53 positivity was more commonly seen in well-differentiated carcinomas (9/15) (Table 2).

EGFR overexpression was detected in 45 cases (86.5%), while 7 cases (13.5%) showed low EGFR expression. EGFR overexpression was more frequently observed in patients older than 50 years (41/43). With respect to histological grade, EGFR overexpression was seen in 10 of 15 well-differentiated cases, 26 of 28 moderately differentiated cases, and all poorly differentiated cases (9/9) (Table 3).

A strong association between p53 and EGFR expression was observed. EGFR overexpression was present in 38 of 40 cases (95%) with diffuse strong p53 positivity, whereas only 7 of 12 cases (58.3%) with focal p53 positivity demonstrated EGFR overexpression (Table 4).

**Table 1.** Clinicopathological Parameters of Oral Squamous Cell Carcinoma (OSCC, n = 52)

| **Parameters** | | **Total Number of Cases 52 N (%)** |
|---|---|---|
| AGE | <50 years | 9 (17.3%) |
| | >50 years | 43 (82.7%) |
| SEX | Male | 36 (69.2%) |
| | Female | 16 (30.8%) |
| SITE | Tongue | 24 (46.15%) |
| | Buccal mucosa | 12 (23.07%) |
| | Gingiva | 3 (5.7%) |
| | Floor of mouth | 3 (5.7%) |
| | Hard palate | 5 (9.6%) |
| | Retromolar trigone | 3 (5.7%) |
| | Lip | 2 (3.8%) |
| HISTOLOGICAL GRADE | Well | 15 (29%) |
| | Moderate | 28 (54%) |
| | Poor | 9 (17%) |

**Table 2.** Clinicopathological Parameters and p53 Expression in OSCC (n = 52)

| **Clinical Parameters** | | **Total Number of Cases (n)** | **p53 STRONG** | **p53 FOCAL** |
|---|---|---|---|---|
| AGE | <50 years | 9 | 4 | 5 |
| | >50 years | 43 | 34 | 9 |
| SEX | Male | 36 | 28 | 8 |
| | Female | 16 | 10 | 6 |
| SITE | Tongue | 24 | 17 | 7 |
| | Buccal mucosa | 12 | 8 | 4 |
| | Gingiva | 3 | 2 | 1 |
| | Floor of mouth | 3 | 3 | 0 |
| | Hard palate | 5 | 4 | 1 |
| | Retromolar trigone | 3 | 2 | 1 |
| | Lip | 2 | 2 | 0 |
| HISTOLOGICAL GRADE | Well | 15 | 6 | 9 |
| | Moderate | 28 | 25 | 3 |
| | Poor | 9 | 9 | 0 |

**Table 3.** Clinicopathological Parameters and EGFR Expression in OSCC (n = 52)

| Clinical Parameters | | Total Number of Cases (n) | EGFR Over Expression | EGFR Low Expression |
|---|---|---|---|---|
| AGE | <50 years | 9 | 6 | 3 |
| | >50 years | 43 | 41 | 2 |
| SEX | Male | 36 | 32 | 4 |
| | Female | 16 | 15 | 1 |
| SITE | Tongue | 24 | 23 | 1 |
| | Buccal mucosa | 12 | 10 | 2 |
| | Gingiva | 3 | 2 | 1 |
| | Floor of mouth | 3 | 3 | 0 |
| | Hard palate | 5 | 4 | 1 |
| | Retromolar trigone | 3 | 3 | 0 |
| | Lip | 2 | 2 | 0 |
| HISTOLOGICAL GRADE | Well | 15 | 10 | 5 |
| | Moderate | 28 | 26 | 2 |
| | Poor | 9 | 9 | 0 |

**Table 4:** Correlation between p53 and EGFR Expression in oral Squamous Cell Carcinoma

| p53 Expression | EGFR Over Expression | EGFR Low Expression | Total |
|---|---|---|---|
| DIFFUSE | 38 | 2 | 40 |
| FOCAL | 7 | 5 | 12 |
| TOTAL | 45 | 7 | 52 |

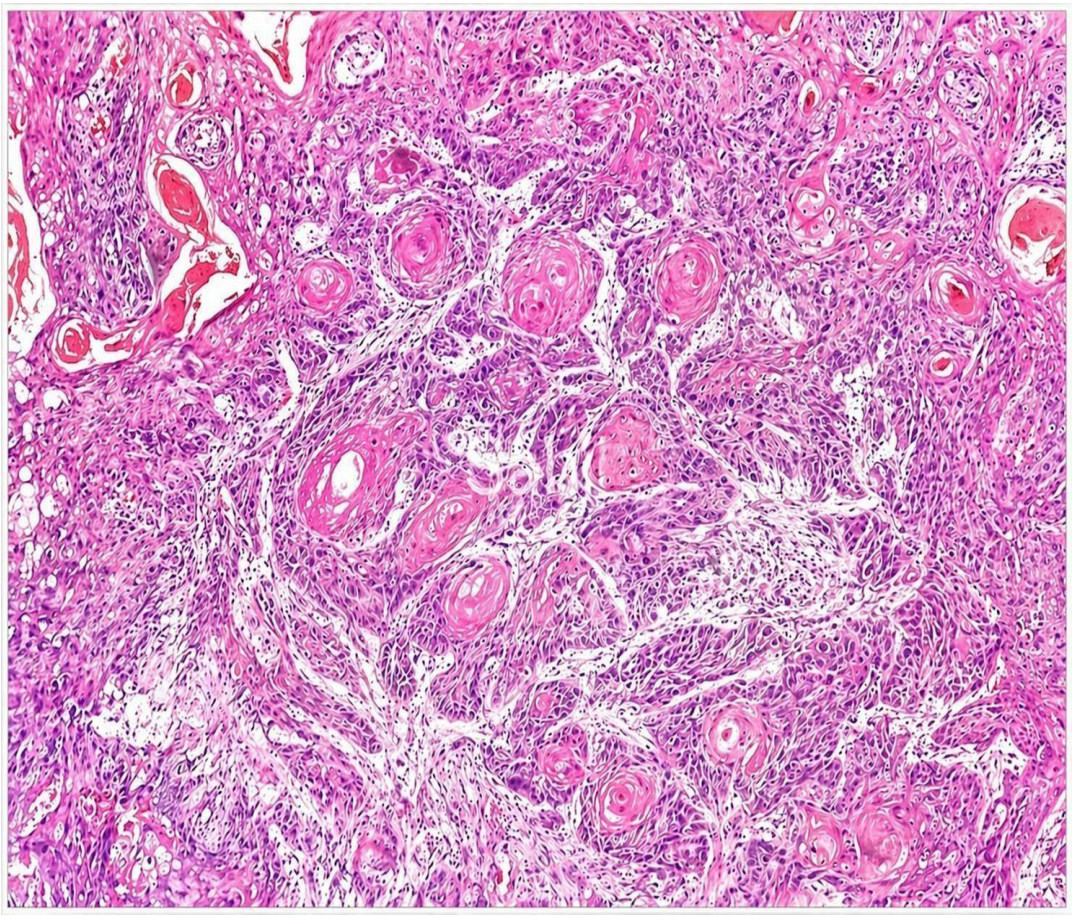

**Figure 1.** Well-Differentiated Squamous Cell Carcinoma Showing Characteristic Keratin Pearls. (Hematoxylin & Eosin Stain, ×100)

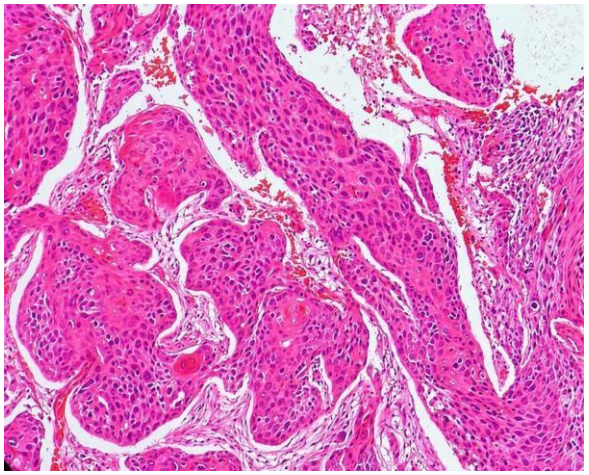

**Figure 2.** Moderately Differentiated Squamous Cell Carcinoma Showing Intracytoplasmic Keratinization and Nuclear Pleomorphism. (Hematoxylin & Eosin Stain, ×100).

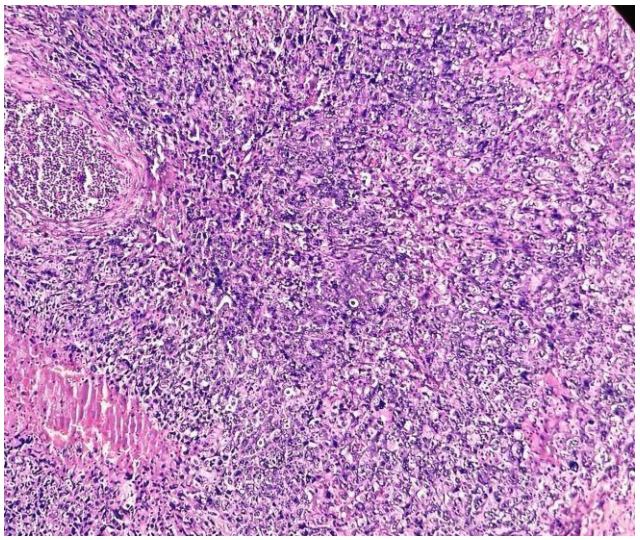

**Figure 3.** Poorly Differentiated Squamous Cell Carcinoma Showing Highly Pleomorphic Tumor Cells. (Hematoxylin & Eosin Stain, ×100).

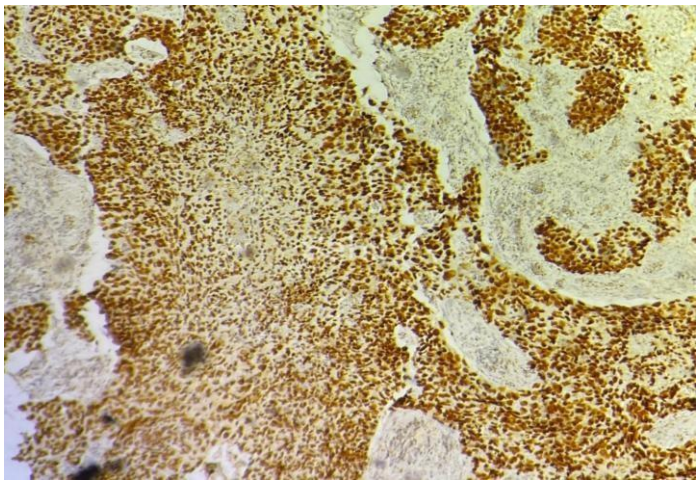

**Figure 4:** Immunohistochemical Staining of p53 Showing Diffuse Strong Nuclear Positivity In >10% of Tumor Cells (×100).

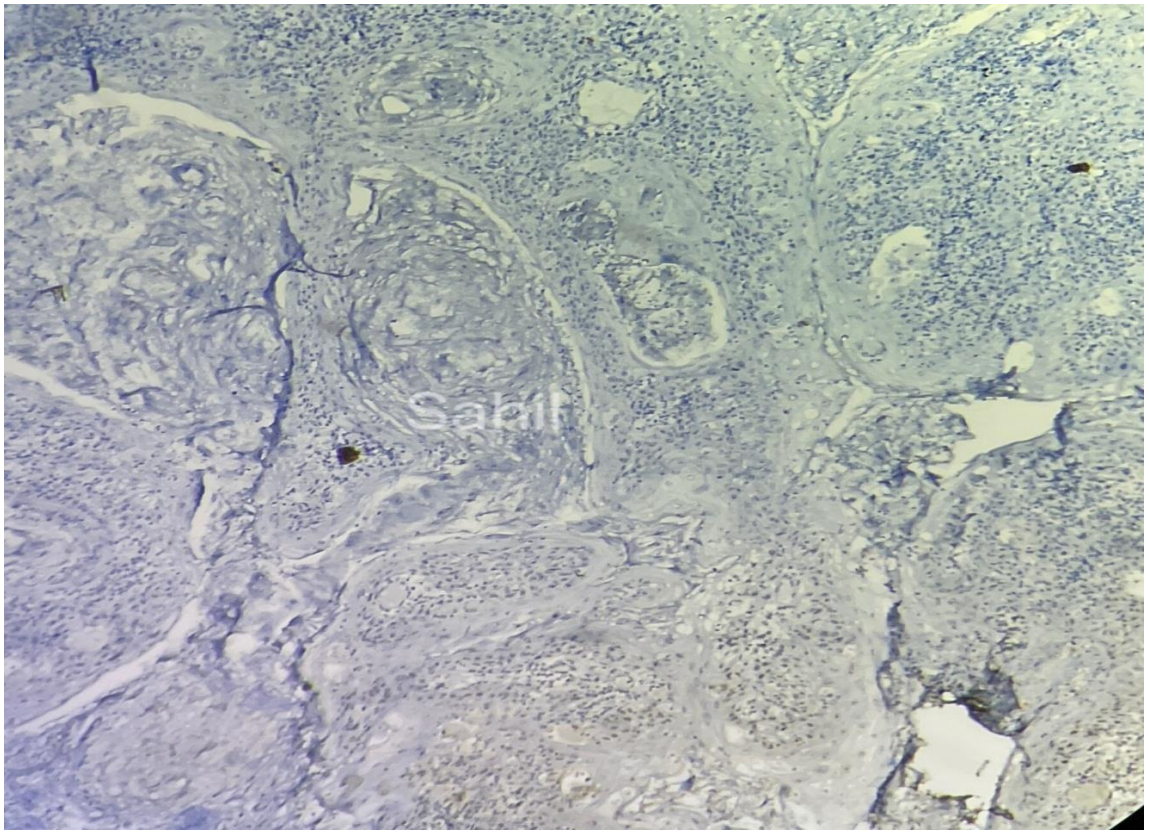

**Figure 5:** Immunohistochemical Staining of p53 Showing Focal Weak Nuclear Positivity in <10% of Tumor Cells (×100)

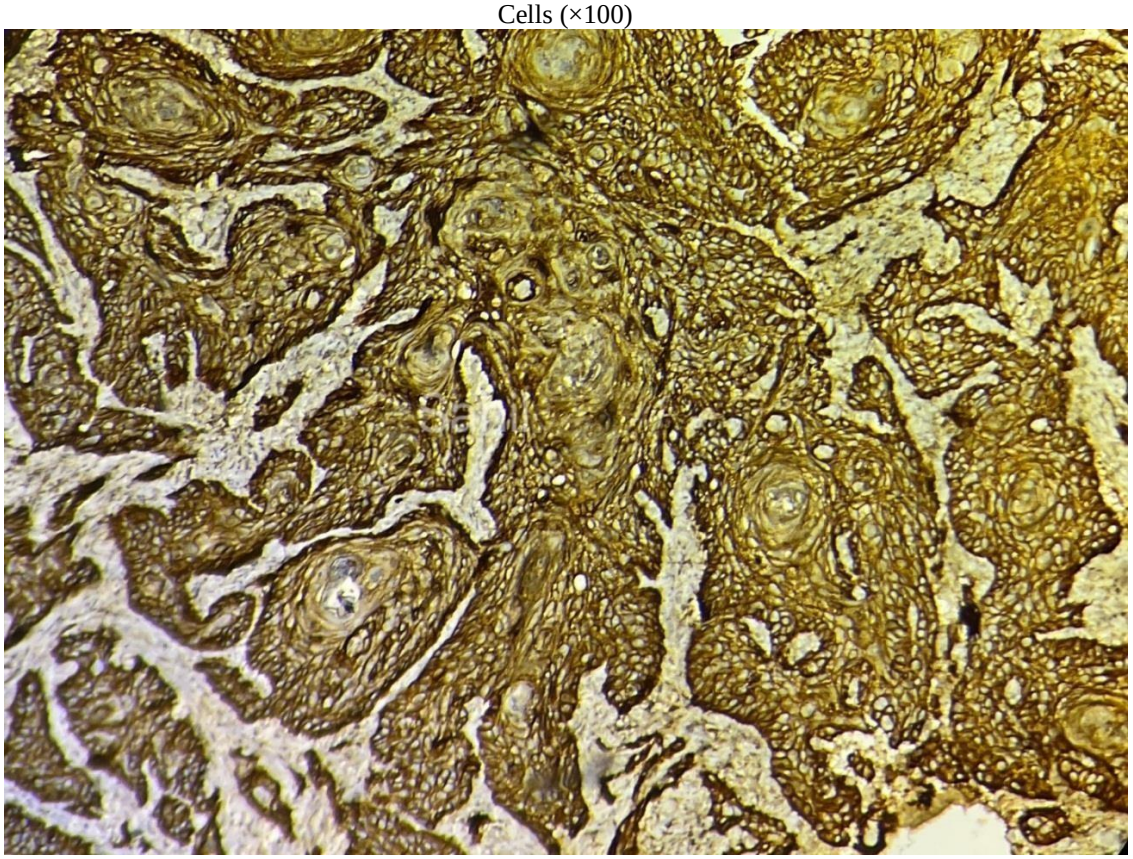

**Figure 6:** Immunohistochemical Staining of EGFR Showing Strong Membranous Positivity with a Total Score of 9 (×100)

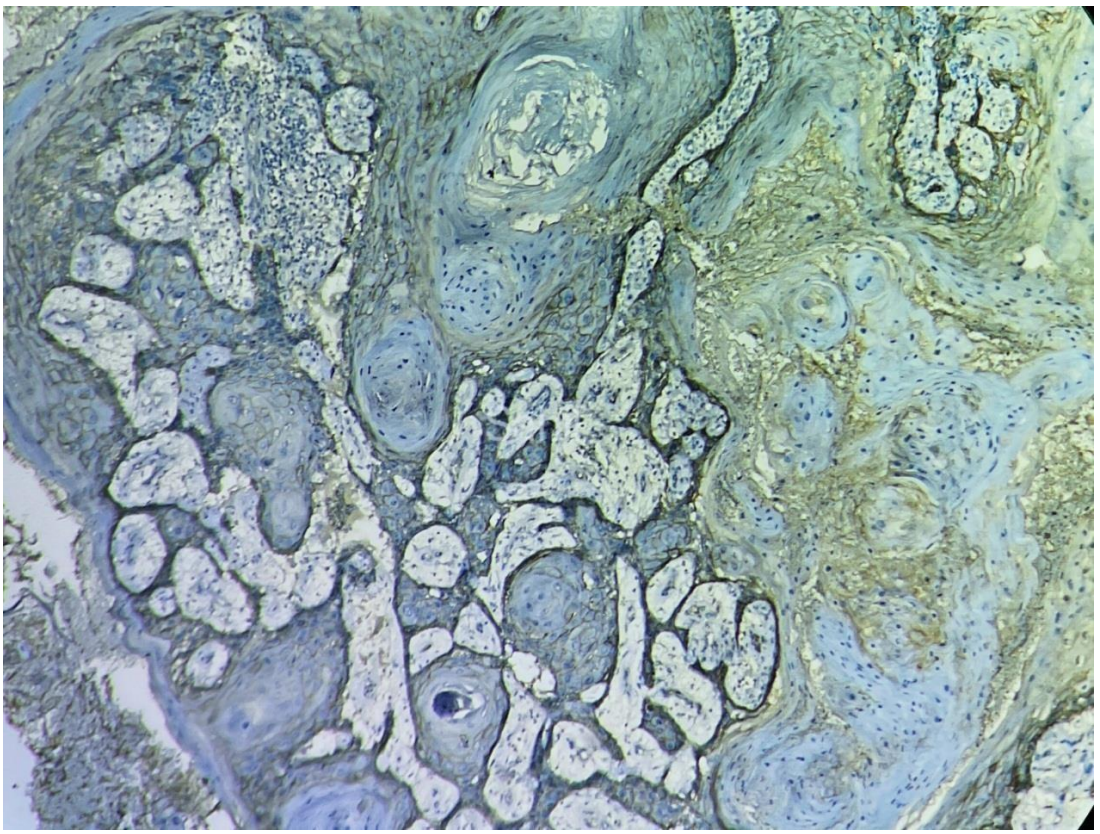

**Figure 7:** Immunohistochemical Staining of EGFR Showing Low Membranous Positivity with a Total Score of 2(x100)

## DISCUSSION

In developing nations, cancer is among the ten leading causes of mortality, with oral cancer being the sixth most common cancer globally.[10] Oral squamous cell carcinoma (OSCC) represents a major public health concern in the Indian subcontinent.[11]

Of the 52 cases analyzed, the majority of patients were aged between 51 and 70 years. Several studies worldwide, including those by Alshami et al., Thanikachlam et al., and Ferreira e Costa et al., have reported a similar predominance of OSCC in individuals older than 50 years.[12,13] Advancing age has been recognized as an important contributing risk factor in the development of oral squamous cell carcinoma.

A marked male predominance was observed in the present study, with 69.2% of cases occurring in men, indicating a higher disease burden among males, likely attributable to greater exposure to tobacco- and alcohol-related habits. This finding is in agreement with a study by Sharma et al. from Northern India, which reported that 68.7% of OSCC cases occurred in male patients.[14]

In the present study, the tongue was the most commonly affected site, accounting for 46.2% of cases. Similar findings have been reported by Saghravanian et al. and Hulke et al., who also identified the tongue as the predominant site of involvement in OSCC.[15,16] The higher incidence of tongue involvement may be attributed to its proximity to areas frequently exposed to carcinogens such as tobacco and alcohol, thereby increasing the risk of OSCC development, as suggested by Ferreira e Costa et al.[13]

Moderately differentiated squamous cell carcinoma was the most prevalent histological grade in the present study, comprising 54% of cases, followed by well-differentiated and poorly differentiated carcinomas. This observation is in concordance with studies by Jadhav et al. and Liu et al., who reported a predominance of moderately differentiated OSCC in their respective cohorts.[17,18]

In the present study, strong p53 positivity was observed in 76.9% of cases, consistent with previous reports by Watling et al. and Nylander et al.[19,20] A higher frequency of p53 positivity was noted in males over 50 years of age, in agreement with findings reported by Nylander et al.[20] Moreover, p53 immunopositivity was more frequently observed in poorly and moderately differentiated squamous cell carcinomas compared to well-differentiated tumors, indicating a positive association between p53 overexpression and increasing histological grade. This observation aligns with earlier studies by Watling et al., who demonstrated increased accumulation of p53 protein in poorly differentiated OSCC, suggesting loss of normal cell cycle control during tumor progression. Similarly, Boyle et al., Chiang et al., and Nylander et al. reported a strong correlation between p53 overexpression and poor histological differentiation, highlighting its role in tumor progression and adverse prognosis.[21,22] The findings of the present study reinforce existing

evidence that elevated p53 expression is associated with higher histological grade in OSCC, supporting its utility as a biomarker of tumor aggressiveness.

In the present study of 52 OSCC cases, EGFR overexpression was observed in 86.5% of cases, consistent with findings reported by Sarkis et al [23]. Kalyankrishna and Grandis have also noted that EGFR overexpression is more common in patients over 50 years of age, in agreement with our results.[9] Our study demonstrated a statistically significant association between EGFR overexpression and higher histological grade of OSCC, with increased positivity observed in moderately and poorly differentiated carcinomas. Similar findings have been reported by Rikimaru et al. and Shintani et al., who observed enhanced EGFR expression in poorly differentiated tumors, suggesting a role for EGFR in tumor progression and aggressive biological behavior.[24 25]

Furthermore, diffuse p53 positivity in the present cohort showed a statistically significant association with EGFR expression (OR = 13.57, $p$ = 0.0049), indicating coordinated dysregulation of cell cycle control and growth factor signalling. These results are in accordance with observations by Singla et al., who reported significant p53-EGFR co-expression in oral squamous cell carcinoma.[26]

## CONCLUSION

Oral squamous cell carcinoma demonstrated significant EGFR overexpression and frequent diffuse p53 positivity, both indicative of aggressive tumor behavior. Combined assessment of p53 and EGFR provides a valuable prognostic biomarker panel in OSCC.

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Conflicts of Interest: The authors declare no conflicts of interest.

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