Section: Pathology

Original Research Article

CLINICOPATHOLOGICAL CORRELATION AND PROGNOSTIC SIGNIFICANCE OF EGFR EXPRESSION IN ORAL SQUAMOUS CELL CARCINOMA AND SQUAMOUS DYSPLASIA

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ABSTRACT

Background: Oral squamous cell carcinoma (OSCC) is one of the most common malignancies of the oral cavity and is frequently preceded by potentially malignant disorders such as oral squamous dysplasia. Epidermal Growth Factor Receptor (EGFR) plays a pivotal role in tumor cell proliferation, survival, and invasion. Evaluating EGFR expression in oral epithelial lesions may provide valuable insights into disease progression and prognosis. The objective is to evaluate the clinicopathological correlation and prognostic significance of EGFR expression in oral squamous cell carcinoma and oral squamous dysplasia. **Materials and Methods:** This hospital-based observational study included 62 histopathologically confirmed cases comprising oral squamous dysplasia and OSCC. Immunohistochemical staining for EGFR was performed on formalin-fixed paraffin-embedded tissue sections. EGFR expression was assessed using a semi-quantitative scoring system based on staining intensity and proportion of positive cells. The expression pattern was correlated with clinicopathological parameters such as age, gender, site, histological grade, and disease severity. Statistical analysis was performed using appropriate tests, and a p-value of less than 0.05 was considered statistically significant. **Result:** The mean age of the study population was 54.6 ± 11.2 years, with a male predominance and significant association with tobacco chewing. High EGFR expression was observed in 83.9% of cases, with overall EGFR positivity in all samples. A statistically significant increase in EGFR expression was noted with increasing severity of dysplasia and higher tumor grade. However, no significant association was found between EGFR expression and demographic variables such as age, gender, and tumor site. **Conclusion:** EGFR is consistently overexpressed in oral squamous dysplasia and OSCC and shows significant association with disease severity, highlighting its potential role as a prognostic biomarker. Routine assessment of EGFR expression may aid in early identification of high-risk lesions and support the use of targeted therapeutic strategies in oral cancer management.

INTRODUCTION

Oral squamous cell carcinoma (OSCC) constitutes nearly 90% of all malignancies arising in the oral cavity and remains a major public health problem, particularly in developing countries where tobacco chewing, smoking, and alcohol consumption are highly prevalent. Despite advances in diagnostic techniques and therapeutic modalities, the overall five-year survival rate of OSCC has shown only modest improvement, largely due to late-stage diagnosis, high rates of loco-regional recurrence, and distant metastasis. Oral epithelial dysplasia represents a recognized precursor lesion in the multistep carcinogenesis of OSCC, characterized by progressive architectural and cytological alterations that predispose to malignant transformation. Identifying reliable molecular biomarkers that can predict malignant potential and patient prognosis is therefore of paramount importance.[1]

Epidermal Growth Factor Receptor (EGFR), a transmembrane tyrosine kinase receptor belonging to the ErbB family, plays a crucial role in regulating cell proliferation, differentiation, angiogenesis, invasion, and apoptosis. Aberrant activation and overexpression of EGFR have been reported in a wide spectrum of epithelial malignancies, including head and neck squamous cell carcinomas. In normal oral epithelium, EGFR expression is usually confined to the basal and parabasal layers; however, in

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dysplastic lesions and OSCC, it is often upregulated and distributed throughout the epithelial thickness and tumor cell nests. This altered expression pattern reflects increased proliferative activity and aggressive tumor behavior.[2]

Several studies have demonstrated that increased EGFR expression correlates with advanced tumor stage, higher histological grade, lymph node metastasis, and reduced overall survival in patients with OSCC. Moreover, EGFR overexpression in oral potentially malignant disorders has been associated with a higher risk of malignant transformation, suggesting its role in early carcinogenic events. The molecular mechanisms underlying EGFR-mediated oncogenesis involve activation of downstream signaling pathways such as PI3K/AKT, MAPK, and JAK/STAT, which promote tumor growth, invasion, and resistance to apoptosis.[3,4]

Aim: To evaluate the clinicopathological correlation and prognostic significance of EGFR expression in oral squamous cell carcinoma and squamous dysplasia.

Objectives

1. To assess the immunohistochemical expression of EGFR in cases of oral squamous dysplasia and oral squamous cell carcinoma.
2. To correlate EGFR expression with clinicopathological parameters such as age, sex, site, histological grade, and tumor characteristics.
3. To analyze the prognostic significance of EGFR expression in relation to disease severity and progression.

MATERIALS AND METHODS

Source of Data: The study data were obtained from histopathologically diagnosed cases of oral squamous dysplasia and oral squamous cell carcinoma received in the Department of Pathology from surgical biopsy and resection specimens submitted by the Departments of Surgery, Surgical Oncology, and Otorhinolaryngology.

Study Design: This study was conducted as a hospital-based observational and analytical study.

Study Location: The study was carried out in the Department of Pathology of a tertiary care teaching hospital.

Study Duration: The study was conducted over a period of 12 months.

Sample Size: A total of 62 cases were included in the study, comprising histologically confirmed cases of oral squamous dysplasia and oral squamous cell carcinoma.

Inclusion Criteria

- Histopathologically confirmed cases of oral squamous cell carcinoma.
- Histologically proven cases of oral squamous dysplasia (mild, moderate, severe, and carcinoma in situ).
- Adequate formalin-fixed paraffin-embedded tissue blocks available for immunohistochemical analysis.
- Cases from all age groups and both sexes.

Exclusion Criteria

- Non-squamous malignancies of the oral cavity.
- Recurrent tumors and metastatic lesions involving the oral cavity.
- Poorly preserved tissue samples and inadequately fixed specimens.
- Cases with insufficient tissue for immunohistochemical evaluation.

Procedure and Methodology: Relevant clinical details including age, sex, site of lesion, clinical diagnosis, and risk factors were collected from hospital records. Hematoxylin and eosin stained slides were reviewed to confirm the diagnosis and histological grading. Representative paraffin blocks were selected for immunohistochemical analysis of EGFR expression.

Sample Processing: Formalin-fixed paraffin-embedded tissue blocks were sectioned at 4-micron thickness. Sections were mounted on poly-L-lysine coated slides. Antigen retrieval was performed using heat-induced epitope retrieval method. Immunohistochemical staining was carried out using monoclonal antibody against EGFR following standard protocols. Positive and negative controls were included in each batch.

Evaluation of Immunostaining: EGFR expression was assessed based on membrane staining pattern. Staining intensity and proportion of positive cells were evaluated semi-quantitatively. An immunoreactivity score was calculated by combining intensity score and percentage of positive tumor cells. Cases were categorized as low or high expression based on the final score.

Statistical Methods: The collected data were entered into Microsoft Excel and analyzed using statistical software. Descriptive statistics were used to summarize clinicopathological parameters. Chi-square test and Fisher's exact test were applied to assess associations between EGFR expression and categorical variables. A p-value of less than 0.05 was considered statistically significant.

Data Collection: All clinical, histopathological, and immunohistochemical findings were recorded in a pre-designed proforma. Data integrity and accuracy were ensured by cross-verification of laboratory records and pathology reports before final analysis.

RESULTS

[Table 1] depicts the baseline clinicopathological characteristics of the study population. The mean age of the participants was 54.6 ± 11.2 years, with a 95% confidence interval (CI) ranging from 51.8 to 57.4 years, which was significantly higher than the reference age of 50 years ($p < 0.001$), indicating a predominance of middle-aged and elderly individuals in the study cohort. Half of the study participants

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(50.0%) belonged to the 41–60 years age group, followed by 33.9% in the age group above 60 years, while only 16.1% were aged 40 years or below; however, this distribution across age groups did not show statistical significance (p = 0.212).

A clear male predominance was observed, with 39 patients (62.9%) being males compared to 23 patients (37.1%) females, and this gender difference was statistically significant (p = 0.018), highlighting the higher burden of oral lesions among males. Regarding disease category, 30 cases (48.4%) were premalignant and 32 cases (51.6%) were malignant, showing a nearly equal distribution between the two groups with no statistically significant difference (p = 0.624). Tobacco chewing was reported in 39 patients (62.9%), which was significantly higher than non-users (p = 0.011), emphasizing the strong association between tobacco exposure and oral epithelial pathology in the study population.

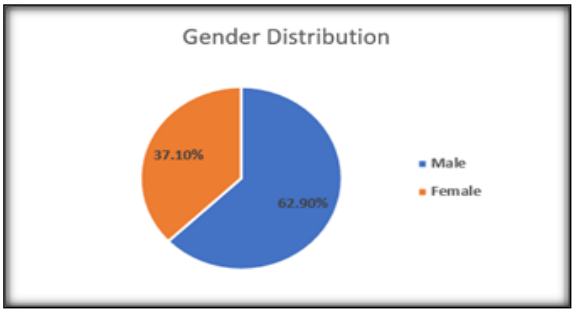

Chart 1: Gender Distribution

Table 1: Clinicopathological Profile of Study Population (N = 62)

Parameter	Category	n (%) / Mean ± SD	95% CI	Test of Significance	p value
Age (years)	—	54.6 ± 11.2	51.8 – 57.4	One-sample t-test vs 50 yrs	<0.001
Age group	≤40 yrs	10 (16.1%)	7.9–28.1	χ^2 test	0.212
	41–60 yrs	31 (50.0%)	37.9–62.1		
	>60 yrs	21 (33.9%)	22.6–47.0		
Gender	Male	39 (62.9%)	49.7–74.5	χ^2 test	0.018
	Female	23 (37.1%)	25.5–50.3		
Study group	Premalignant	30 (48.4%)	36.1–60.9	χ^2 test	0.624
	Malignant	32 (51.6%)	39.1–63.9		
Tobacco chewing	Yes	39 (62.9%)	49.7–74.5	χ^2 test	0.011
	No	23 (37.1%)	25.5–50.3		

Table 2: Immunohistochemical Expression of EGFR in Oral Squamous Dysplasia and OSCC (N = 62)

EGFR Immunoreactivity	Score (IS×PS)	n (%)	95% CI	Test of Significance	p value
Negative	0	0 (0%)	—	—	—
Low expression	1–4	10 (16.1%)	7.9–28.1	One-sample proportion Z-test vs 50%	<0.001
High expression	5–12	52 (83.9%)	71.9–92.1		
Overall EGFR positivity	—	62 (100%)	94.2–100	Exact binomial test	<0.001

[Table 2] summarizes the immunohistochemical expression pattern of EGFR in the study cohort. None of the cases showed negative EGFR expression. Low EGFR expression (score 1–4) was observed in 10 cases (16.1%), whereas high EGFR expression (score 5–12) was seen in a substantial majority of 52 cases (83.9%), with the proportion of high expressers being statistically significant when compared to the expected distribution (p < 0.001). Furthermore, all 62 cases (100%) demonstrated overall EGFR positivity, with a 95% CI of 94.2% to 100%, which was highly significant on exact binomial testing (p < 0.001).

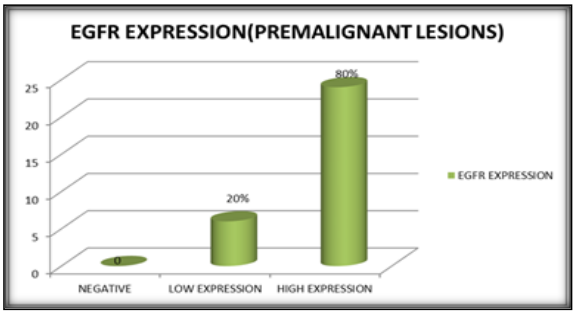

Chart 2: Bar Chart showing immunoreactivity of EGFR in oral premalignant lesions in study group

Table 3: Correlation of EGFR Expression with Clinicopathological Parameters (N = 62)

Parameter	Category	High EGFR n (%)	Low EGFR n (%)	Test of Significance	p value
Age group	≤40 yrs (n=10)	6 (60.0%)	4 (40.0%)	χ^2 test	0.071
	41–60 yrs (n=31)	27 (87.1%)	4 (12.9%)		
	>60 yrs (n=21)	20 (95.2%)	1 (4.8%)		
Gender	Male (n=39)	33 (84.6%)	6 (15.4%)	χ^2 test	0.55
	Female (n=23)	19 (82.6%)	4 (17.4%)		
Site	Buccal mucosa (n=29)	23 (79.3%)	6 (20.7%)	χ^2 test	0.788
	Tongue (n=10)	9 (90.0%)	1 (10.0%)		
	Other sites (n=23)	20 (87.0%)	3 (13.0%)		

[Table 3] illustrates the association between EGFR expression and selected clinicopathological parameters. With increasing age, a rising trend in high EGFR expression was noted. High EGFR expression was observed in 60.0% of patients aged ≤40 years, 87.1% in the 41–60 years age group, and 95.2% among patients older than 60 years. Although this trend suggested an age-related increase in EGFR

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expression, it did not reach statistical significance (p = 0.071).

Gender-wise analysis revealed comparable EGFR expression patterns between males and females. High EGFR expression was noted in 84.6% of males and 82.6% of females, with no statistically significant association (p = 0.55). Site-wise evaluation showed high EGFR expression in 79.3% of buccal mucosa lesions, 90.0% of tongue lesions, and 87.0% of lesions from other oral subsites, with no significant difference among sites (p = 0.788).

Table 4: Prognostic Significance of EGFR Expression in Disease Severity and Progression (N = 62)

Pathological Parameter	Category	High EGFR n (%)	Low EGFR n (%)	Test of Significance	p value
Degree of dysplasia (n=30)	Mild (n=16)	11 (68.8%)	5 (31.2%)	χ^2 test	0.004
	Moderate (n=2)	1 (50.0%)	1 (50.0%)		
	Severe/CIS (n=12)	12 (100%)	0		
Carcinoma grade (n=32)	Grade I (n=17)	16 (94.1%)	1 (5.9%)	Fisher's exact test	0.032
	Grade II (n=15)	12 (80.0%)	3 (20.0%)		
Overall disease severity	Premalignant (n=30)	24 (80.0%)	6 (20.0%)	χ^2 test	0.324
	Malignant (n=32)	28 (87.5%)	4 (12.5%)		

[Table 4] highlights the prognostic relevance of EGFR expression in relation to disease severity and progression. Among premalignant lesions, high EGFR expression was observed in 68.8% of mild dysplasia cases, 50.0% of moderate dysplasia cases, and 100% of severe dysplasia and carcinoma in situ cases, demonstrating a statistically significant association between increasing severity of dysplasia and EGFR overexpression (p = 0.004). This finding suggests a progressive increase in EGFR expression with worsening epithelial atypia.

In malignant cases, high EGFR expression was detected in 94.1% of Grade I tumors and 80.0% of Grade II tumors, with a statistically significant association between tumor grade and EGFR expression (p = 0.032), indicating higher EGFR expression in well-differentiated carcinomas. However, when overall disease severity was considered, high EGFR expression was present in 80.0% of premalignant cases and 87.5% of malignant cases, and this difference was not statistically significant (p = 0.324).

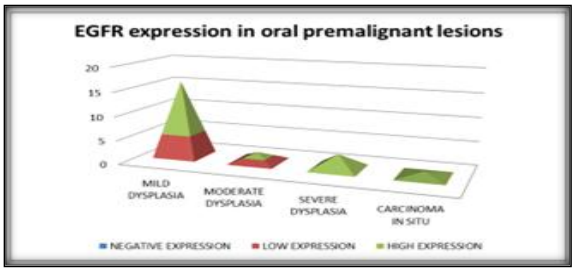

Chart 3: Immunoreactivity of EGFR in patients with oral premalignant lesions according to degree of dysplasia

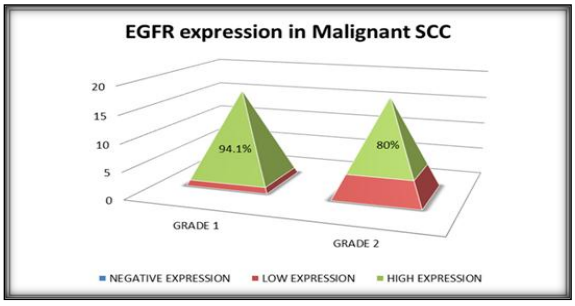

Chart 4: Bar chart showing expression of EGFR in patients with oral squamous cell carcinoma in correlation with histopathological grade of tumor.

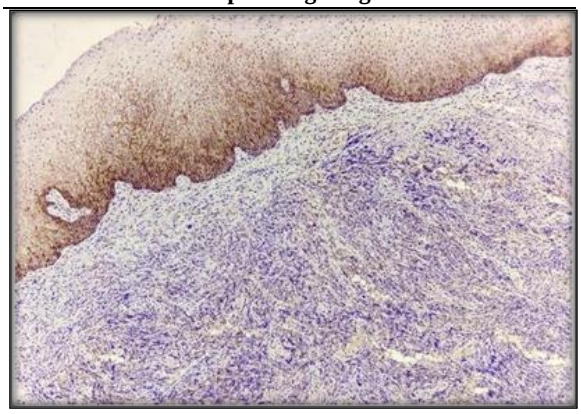

Figure 1: EGFR control only basal layer of epidermis show high EGFR expression

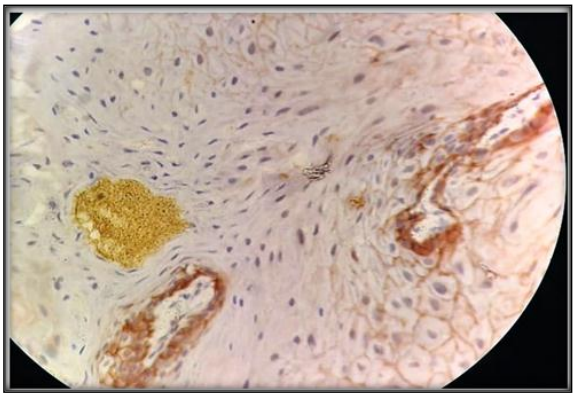

Figure 2: Low EGFR Expression (2x2) 10X

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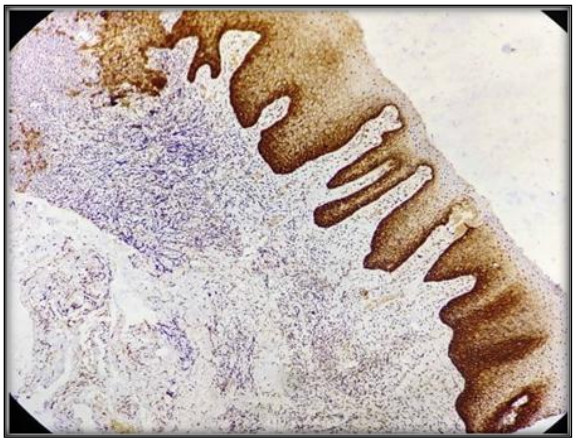

Figure 3: Dysplasia Showing High EGFR Expression (3x4) 10X

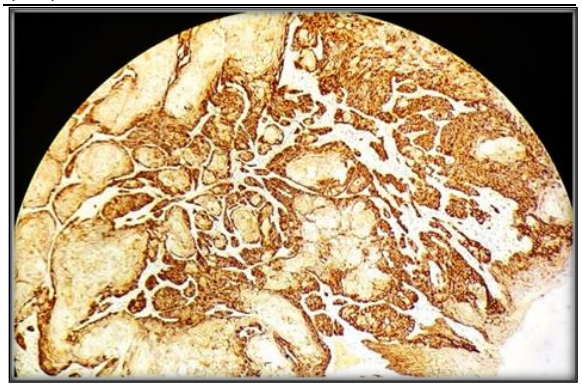

Figure 4: Squamous Cell Carcinoma Showing High EGFR Expression (3x4) 10X

DISCUSSION

With respect to age distribution (Table 1), the mean age of presentation in the current study was 54.6 ± 11.2 years, which is comparable to observations reported by Tarle M et al. (2023),[5] who documented peak incidence of OSCC in the fifth and sixth decades of life. The predominance of cases in the 41–60 years age group (50.0%) reflects the cumulative effect of long-term exposure to carcinogens such as tobacco and alcohol. Similar age trends have been described by Mandal M et al. (2020),[6] reinforcing the role of chronic risk factor exposure in oral carcinogenesis. Although a progressive increase in EGFR expression was observed with advancing age in the present study, this trend did not reach statistical significance, which is consistent with the findings of Okubo S et al. (2025),[7] who also reported no strong age-dependent association with EGFR overexpression.

Gender distribution revealed a significant male predominance (62.9%) in the current study [Table 1]. This observation is in agreement with studies by Mohanapure NS et al. (2022),[4] which reported higher OSCC incidence among males, attributed mainly to higher prevalence of tobacco and alcohol consumption. The strong association between tobacco chewing and disease burden in the present study (62.9%, p = 0.011) further supports the etiological role of tobacco, as emphasized by Tyagi D et al. (2023),[8] who identified tobacco use as a major contributor to EGFR pathway activation and tumor progression.

Immunohistochemical analysis [Table 2] demonstrated high EGFR expression in 83.9% of cases, with universal EGFR positivity across all samples. These findings are comparable to earlier reports by Wongpattaraworakul W et al. (2022),[9] who reported EGFR overexpression in 70–90% of OSCC cases. The high prevalence of EGFR positivity in premalignant lesions observed in the current study further supports the concept that EGFR upregulation is an early molecular event in oral carcinogenesis, as proposed by Kappler M et al. (2020).[3]

Correlation analysis [Table 3] revealed no statistically significant association between EGFR expression and gender or tumor site. Similar findings were reported by Jadhav T et al. (2024),[10] suggesting that EGFR overexpression is a generalized molecular alteration in oral epithelial tumors, rather than being site-specific or gender-dependent. However, the observed trend of increasing EGFR expression with age supports the hypothesis of cumulative molecular damage leading to enhanced receptor activation over time.

The prognostic significance of EGFR expression [Table 4] was particularly evident in relation to the severity of dysplasia and carcinoma grade. High EGFR expression was noted in 100% of severe dysplasia and carcinoma in situ cases, indicating a strong association between increasing epithelial atypia and EGFR upregulation. Similar progressive increases in EGFR expression across dysplasia grades have been documented by El Hanbuli HM et al. (2022),[11] supporting the role of EGFR as a marker of malignant potential. Additionally, the significantly higher EGFR expression observed in well-differentiated carcinomas compared to moderately differentiated tumors aligns with findings by Tashiro K et al (2020),[12] who suggested that EGFR overexpression is associated with tumor proliferation and differentiation status.

CONCLUSION

The present study demonstrates that Epidermal Growth Factor Receptor (EGFR) is widely expressed in both oral squamous dysplasia and oral squamous cell carcinoma (OSCC), highlighting its crucial role in oral epithelial carcinogenesis. A significantly high proportion of cases showed strong EGFR immunoreactivity, indicating that EGFR overexpression is an early molecular event that persists throughout disease progression. The clinicopathological analysis revealed a higher prevalence of oral lesions among middle-aged and elderly individuals, with a male predominance and a strong association with tobacco chewing, emphasizing the influence of lifestyle-related risk factors in oral cancer development.

Importantly, EGFR expression showed a significant correlation with increasing severity of dysplasia and tumor grade, supporting its prognostic relevance. The

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progressive rise in EGFR expression from mild dysplasia to severe dysplasia and carcinoma in situ suggests that EGFR may serve as a useful biomarker for identifying high-risk premalignant lesions with a greater potential for malignant transformation. Furthermore, the high expression of EGFR in well and moderately differentiated carcinomas indicates its involvement in tumor proliferation and differentiation dynamics. Although no statistically significant association was observed between EGFR expression and demographic parameters such as age, gender, and tumor site, the consistently elevated expression across different subgroups underscores the universal role of EGFR in oral tumor biology.

Overall, the findings of this study reinforce the clinicopathological and prognostic significance of EGFR expression in oral squamous neoplasia. Assessment of EGFR status may aid in risk stratification, prognostication, and selection of patients who could potentially benefit from targeted anti-EGFR therapies. Incorporating EGFR evaluation into routine histopathological assessment may contribute to improved early detection, better therapeutic decision-making, and enhanced patient outcomes in oral cancer management.

Limitations of the Study

1. The study was conducted at a single tertiary care center, which may limit the generalizability of the results to a broader population.
2. The sample size was relatively small, which could have influenced the statistical power of certain subgroup analyses.
3. The retrospective nature of data collection limited the availability of detailed follow-up information for long-term survival and recurrence analysis.
4. Survival outcomes such as overall survival and disease-free survival were not evaluated, restricting the assessment of the true prognostic impact of EGFR expression.
5. Molecular analysis of EGFR gene amplification or mutation status was not performed, and the study relied solely on immunohistochemical expression.
6. Inter-observer variability in immunohistochemical scoring could not be completely eliminated despite standardized scoring methods.
7. The influence of treatment modalities on EGFR expression and patient outcomes was not assessed.

REFERENCES

1. Civico-Ortega JL, Gonzalez-Ruiz I, Ramos-Garcia P, Cruz-Granados D, Samayoa-Descamps V, González-Moles MÁ. Prognostic and clinicopathological significance of epidermal growth factor receptor (EGFR) expression in oral squamous cell carcinoma: systematic review and meta-analysis. International Journal of Molecular Sciences. 2023 Jul 25;24(15):11888.
2. Aamir R, Rauf F, Iqbal F, Yousuf S, Rehman A, Sheikh AK, Muhammad S. Immunohistochemical expression of epidermal growth factor receptor (EGFR) in oral squamous cell carcinoma and oral potentially malignant disorders. Applied Immunohistochemistry & Molecular Morphology. 2024 Mar 1;32(3):157-62.
3. Kappler M, Dauter K, Reich W, Bethmann D, Schwabe M, Rot S, Wickenhauser C, Al-Nawas B, Eckert AW. Prognostic impact of cytoplasmatic EGFR upregulation in patients with oral squamous cell carcinoma: A pilot study. Molecular and Clinical Oncology. 2020 Dec;13(6):88.
4. Mohanapure NS, Khandeparkar SG, Saragade PB, Gogate BP, Joshi AR, Mehta SR. Immunohistochemical study of epidermal growth factor receptor, human epidermal growth factor receptor 2/neu, p53, and Ki67 in oral squamous cell carcinoma. Journal of Oral and Maxillofacial Pathology. 2022 Jan 1;26(1):127-8.
5. Tarle M, Raguž M, Muller D, Lukšić I. Nuclear epidermal growth factor receptor overexpression as a survival predictor in oral squamous cell carcinoma. International journal of molecular sciences. 2023 Mar 18;24(6):5816.
6. Mandal M, Saha R, Chakraborty J. Expression of EGFR and HER2 in Oral Dysplastic Epithelium and Squamous Cell Carcinoma. Indian J Pathol. 2020 Jan;9(1):49-56.
7. Okubo S, Miyabe S, Fukumura M, Sasaki J, Fujii H, Terasawa F, Watanabe S, Okada S, Miyabe M, Miyabe K, Sugita Y. Molecular Characterization of Oral Epithelial Dysplasia and Oral Squamous Cell Carcinoma Using EGFR, CDKN2A, and HRAS Alterations. Cancers. 2025 Dec 10;17(24):3949.
8. Tyagi D, Singhal M, Gulati N, Jain A, Shetty DC. Evaluation of EGFR in prognostic characterization in histopathological variants of oral squamous cell carcinoma. Journal of Cancer Research and Therapeutics. 2023 Jan 1;19(Suppl 2):S743-6.
9. Wongpattaraworakul W, Gibson-Corley KN, Choi A, Buchakjian MR, Lanzel EA, Kd AR, Simons AL. Prognostic role of combined EGFR and tumor-infiltrating lymphocytes in oral squamous cell carcinoma. Frontiers in oncology. 2022 Jul 25;12:885236.
10. Jadhav T, Malik A, Kashif AW, Shelly D, Mishra PS, Baranwal AK, Sahu R. Study of the association of the known prognostic variables with EGFR expression in head and neck squamous cell carcinomas. Indian Journal of Pathology and Microbiology. 2024 Jan 1;67(1):36-45.
11. El Hanbuli HM, Abou Sarie MA. KRAS protein expression in oral squamous cell carcinoma: a potential marker for progression and prognosis. Iranian Journal of Pathology. 2022 Sep 10;17(4):469.
12. Tashiro K, Oikawa M, Miki Y, Takahashi T, Kumamoto H. Immunohistochemical assessment of growth factor signaling molecules: MAPK, Akt, and STAT3 pathways in oral epithelial precursor lesions and squamous cell carcinoma. Odontology. 2020 Jan;108(1):91-101.

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