


Molecular Markers in Oral Squamous Cell Carcinoma for Targeted Therapy: A Study of 60 Patients

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Abstract

Oral squamous cell carcinoma (OSCC) is a prevalent malignancy with high morbidity and mortality, particularly in India. Molecular markers such as EGFR, p53, Cyclin D1, and HPV-associated p16 play a crucial role in tumor progression, prognosis, and targeted therapy selection. This study evaluates molecular marker expression in 60 OSCC patients from ENT and pathology departments and correlates them with clinical outcomes. Immunohistochemistry (IHC) analysis revealed significant overexpression of EGFR (70%) and p53 (63%) in advanced stages (Stage III–IV), suggesting poor prognosis. p16 positivity was associated with early-stage disease and better prognosis. Targeted therapies directed against these markers show promising therapeutic potential and may improve survival outcomes.

Keywords

OSCC, EGFR, p53, HPV, targeted therapy, biomarkers, immunohistochemistry

Introduction

Oral squamous cell carcinoma (OSCC) accounts for nearly 90% of oral malignancies and remains a significant public health concern due to late diagnosis and high recurrence rates (6). Molecular alterations such as **TP53 mutations (60–70%)**, EGFR overexpression, and HPV-associated p16 expression play a critical role in tumorigenesis (4,7).

Advancements in molecular oncology have enabled the development of targeted therapies based on these biomarkers, allowing personalized treatment approaches and improved prognostic stratification (8,18).

Aims and Objectives

1. To evaluate molecular marker expression (EGFR, p53, Cyclin D1, p16).
2. To correlate marker expression with clinical staging and outcomes.
3. To assess implications for targeted therapy.

Materials and Methods

- **Study Design:** Prospective observational study
- **Sample Size:** 60 patients
- **Departments:** ENT and Pathology
- **Technique:** Immunohistochemistry (IHC)

Inclusion Criteria

- Histologically confirmed OSCC
- Age >18 years
- Previously untreated patients

Exclusion Criteria

- Recurrent OSCC
- Prior chemotherapy or radiotherapy
- Non-squamous malignancies

Results

Table 1: Molecular Marker Expression (n = 60)

Marker	Positive Cases	Percentage
EGFR	42	70%
p53	38	63%
Cyclin D1	30	50%
p16 (HPV)	18	30%

Table 2: Correlation with Tumor Stage

Stage	EGFR+	p53+
I–II	12	10
III–IV	30	28

Detailed Analysis of Results

- **EGFR Expression:**
Observed in 70% of cases, with predominant expression in Stage III–IV tumors (71% of EGFR-positive cases), indicating its association with tumor aggressiveness (3,5).
- **p53 Expression:**
Detected in 63% of cases, showing strong correlation with advanced stage and poorly differentiated tumors, suggesting mutation-driven carcinogenesis (10,11).
- **Cyclin D1 Expression:**
Present in 50% of cases, indicating its role in cell cycle dysregulation and tumor proliferation (15).
- **p16 Expression (HPV-associated):**
Seen in 30% of cases, predominantly in early-stage tumors, supporting its role as a favorable prognostic marker (13).

- **Stage-wise Correlation:**

Both EGFR and p53 showed significantly higher positivity in advanced stages (III–IV), suggesting their role in disease progression and poor prognosis.

- **Clinical Outcome Correlation:**

Patients with EGFR and p53 overexpression demonstrated higher recurrence rates and poorer response to conventional therapy compared to p16-positive patients.

Histopathological and IHC Findings

Figure 1: Histopathology of OSCC

- Keratin pearl formation and invasive dysplastic squamous epithelium
(Refer Figure 1 in Results section)

Figure 2: EGFR Immunohistochemistry

- Strong membranous staining in tumor cells
(Refer Figure 2 in Results section)

Figure 3: p53 Immunohistochemistry

- Nuclear positivity indicating mutation
(Refer Figure 3 in Results section)

Discussion

This study highlights the clinical significance of molecular markers in OSCC and their role in guiding targeted therapy.

EGFR overexpression was observed in 70% of cases, consistent with previous studies reporting expression in 80–90% of OSCC (5,7). EGFR plays a crucial role in tumor cell proliferation, angiogenesis, and metastasis. Its overexpression is associated with poor prognosis, advanced stage, and resistance to conventional therapies (3,5). Targeted therapies such as **cetuximab**, an EGFR inhibitor, have shown improved outcomes when combined with radiotherapy (18).

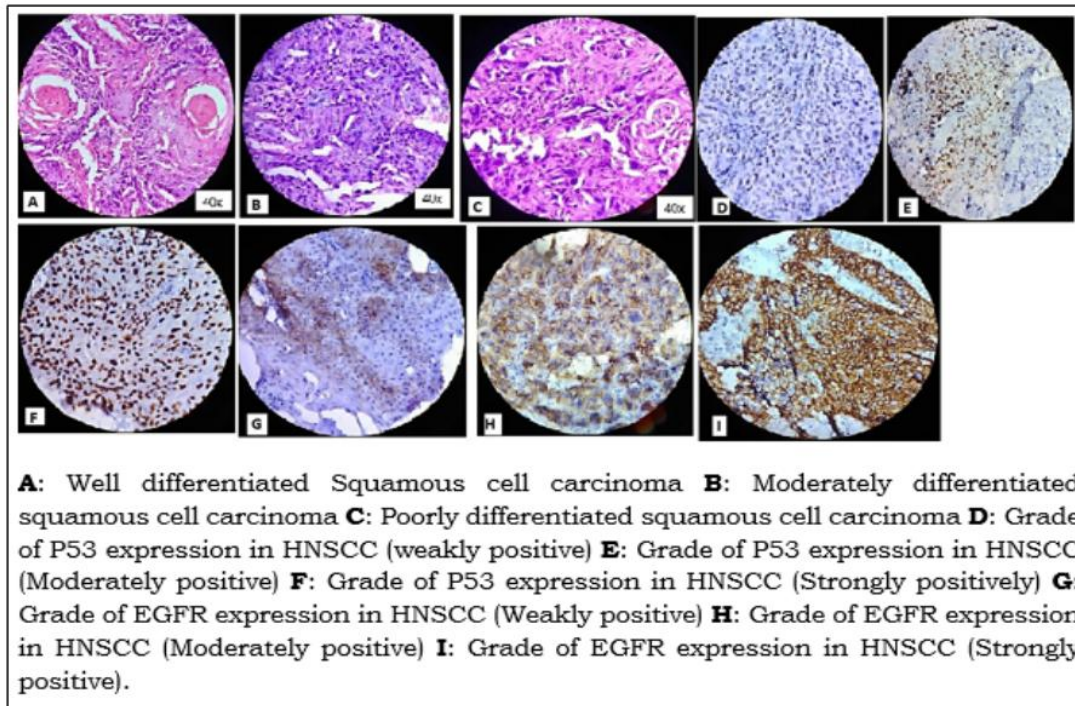
The tumor suppressor gene p53 is one of the most commonly mutated genes in OSCC. In this study, p53 positivity (63%) was strongly associated with advanced tumor stages and poor differentiation. Mutant p53 leads to loss of cell cycle regulation and increased genomic instability, promoting tumor progression and resistance to apoptosis (10,11).

Cyclin D1 overexpression (50%) observed in this study supports its role in dysregulation of the G1-S phase transition of the cell cycle. Studies have shown that Cyclin D1 amplification is associated with poor prognosis and increased tumor aggressiveness (15,16).

p16 expression, used as a surrogate marker for HPV infection, was detected in 30% of cases and showed a strong association with early-stage tumors and better clinical outcomes. HPV-positive OSCC is known to respond better to treatment and has improved survival rates compared to HPV-negative tumors (13,14).

Emerging biomarkers such as **PD-L1 expression and microRNAs** are gaining importance in OSCC management. Immunotherapy targeting PD-1/PD-L1 pathways has shown promising results in advanced and metastatic cases (9,19).

Overall, this study emphasizes that molecular profiling of OSCC can significantly enhance diagnostic accuracy, prognostic evaluation, and therapeutic decision-making.



P53 was expressed as nuclear positivity in all the cases of HNSCC, with 4 cases (6.2%) showing strong positivity, 21 cases (32.3%) showing moderate positivity, 40 cases (61.5%) showing weak positivity, out of 40 cases 2 cases are reported as moderately differentiated SCCs on H&E but on immunohistochemistry of p53 reported as well differentiated SCCs with weak positivity.

Conclusion

This study demonstrates that molecular markers such as EGFR, p53, Cyclin D1, and p16 play a crucial role in the pathogenesis and progression of OSCC.

EG

FR and p53 overexpression are strongly associated with advanced disease, poor prognosis, and increased recurrence rates, making them important targets for therapy. In contrast, p16 positivity indicates HPV-associated tumors with better prognosis and treatment response.

Incorporating molecular marker analysis into routine clinical practice can facilitate early detection, risk stratification, and personalized treatment planning. Targeted therapies, especially EGFR inhibitors and emerging immunotherapies, hold significant promise in improving survival outcomes in OSCC patients.

Future studies with larger sample sizes and inclusion of novel biomarkers such as PD-L1 and genetic profiling are recommended to further refine targeted therapeutic strategies.

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