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FROM NORMAL TO NEOPLASTIC: A CROSS SECTIONAL LOOK AT P53 AND CYCLIN D1 IN ORAL LESIONS

Pathology

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ABSTRACT

Background: Oral squamous cell carcinoma remains one of the most prevalent malignancies in India, largely attributed to widespread tobacco and areca nut consumption. Delayed diagnosis and biological heterogeneity contribute to poor outcomes. Molecular alterations, particularly involving the tumor suppressor p53 and the cell-cycle regulator Cyclin D1, play a crucial role in the transition from normal mucosa to potentially malignant disorders and invasive carcinoma.**Objectives:** To evaluate and compare the immunohistochemical expression of p53 and Cyclin D1 across a spectrum of oral proliferative lesions and normal oral mucosa, and their association with histopathological diagnosis. **Materials and Methods:** A cross-sectional analytical study comprising 50 histopathologically confirmed cases was conducted over two years at a tertiary ENT hospital. The sample included normal mucosa (n=5), dysplasia (n=5), verrucous hyperplasia (n=10), and OSCC (n=30). Tissue sections underwent hematoxylin–eosin staining followed by immunohistochemistry for p53 and Cyclin D1. Expression was recorded qualitatively and semi-quantitatively using the Immunoreactive Score (IRS). Statistical analysis was performed using chi-square tests. **Results:** p53 expression was positive in 90% of cases, increasing progressively from normal mucosa to dysplasia, verrucous hyperplasia, and OSCC. Cyclin D1 positivity was observed in 70%, with strongest expression in malignant lesions. Combined p53 and Cyclin D1 positivity occurred in 68% of cases. Both markers showed statistically significant associations with histopathological severity (p53: $p < 0.001$; Cyclin D1: $p = 0.006$). **Conclusion:** The study demonstrates a clear escalation of p53 and Cyclin D1 expression across the continuum of oral carcinogenesis. Combined assessment enhances diagnostic utility and may serve as an effective adjunct in identifying high-risk lesions requiring closer surveillance and timely intervention.

KEYWORDS

Oral squamous cell carcinoma, Oral potentially malignant disorders, p53, Cyclin D1

INTRODUCTION:

OSCC constitutes nearly 90% of oral cancers and imposes a major health burden in India due to widespread exposure to tobacco and areca nut. Outcomes remain suboptimal, driven by late presentation and tumour heterogeneity. Molecularly, loss of p53 function and overactivity of Cyclin D1–CDK4/6 signalling are frequent and biologically plausible hallmarks of progression from potentially malignant lesions to invasive cancer. We evaluated and compared IHC expression of p53 and Cyclin D1 across a spectrum of oral proliferative lesions versus normal mucosa within one institutional cohort

MATERIALS AND METHODS:

Cross-sectional analytical study over two years at a tertiary ENT hospital. Ethical approval and written informed consent were obtained.

Fifty biopsies were included: non-dysplasia (n=5), dysplasia (n=5), verrucous hyperplasia (n=10), OSCC (well-differentiated WDSCC, n=18; moderately differentiated MDSCC, n=10; poorly differentiated PDSCC, n=2). Inclusion required histopathological confirmation; inflammatory/infective lesions and inadequate tissue were excluded.

Formalin-fixed, paraffin-embedded sections underwent H&E and IHC for p53 and Cyclin D1. Positivity (nuclear for both markers) and IRS (combining proportion and intensity) were recorded. Statistics were performed using Excel/SPSS; chi-square tested associations between marker status and histopathology

Table 1. Sample characteristics (n=50)

Characteristic	Category	n (%)
Age (Years)	41 - 50	16 (32%)
Sex	Male	40 (80%)
Histopathology	No Dysplasia	05 (10%)
	Dysplasia	05 (10%)
	Verrucous hyperplasia	10 (20%)
	OSCC	30 (60%)

RESULTS

Biomarker Expression

p53:

- Positive in 90% (45/50)
- Negative only in non-dysplastic mucosa
- High IRS (4–9) in 50%

Chart 1:

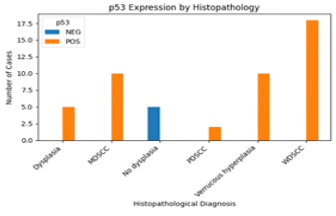


Figure 1: Negative staining of p53 in normal Oral mucosa

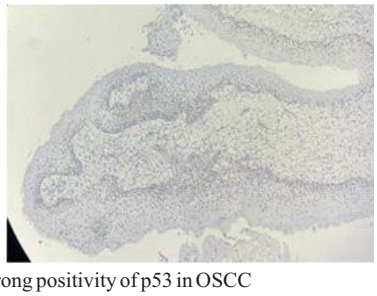
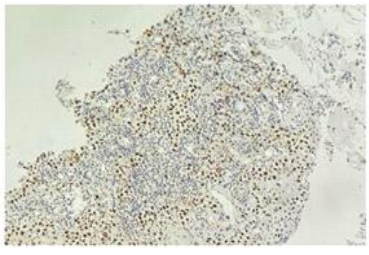


Figure2: Strong positivity of p53 in OSCC



Cyclin D1:

- Positive in 70% (35/50)
- Strongest expression in OSCC
- Verrucous hyperplasia showed mixed expression (50% positive)

Chart 2:

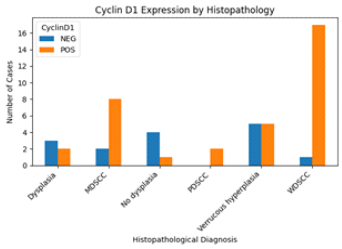


Figure 3: Negative staining of Cyclin D1 in Normal Oral mucosa

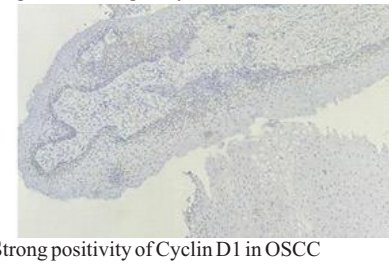
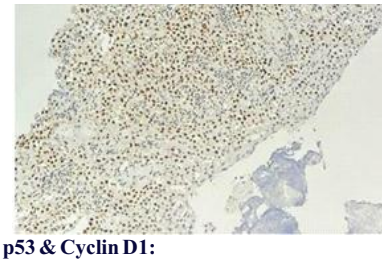


Figure 4: Strong positivity of Cyclin D1 in OSCC



Combined p53 & Cyclin D1:

- Double-positive in 68%
- Only 8% double-negative

Statistical significance:

- p53 vs histopathology: $p < 0.001$
- Cyclin D1 vs histopathology: $p = 0.006$

Table 2. Marker positivity by diagnosis (n=50)

HPE Diagnosis	p53 + / Total	Cyclin D1 + / Total
No Dysplasia	0/5	1/5
Dysplasia	5/5	2/5
Verrucous hyperplasia	10/10	5/10
OSCC	30/30	27/30
Overall	45/50	35/50

DISCUSSION:

This single-centre study demonstrates a clear gradient of both p53 and Cyclin D1 expression from non-dysplastic mucosa through dysplasia and verrucous hyperplasia to OSCC, mirroring the biological continuum of oral carcinogenesis. The demographic skew towards middle-aged men.

p53: Universal p53 positivity in dysplasia, verrucous hyperplasia, and OSCC—contrasted with negativity in non-dysplasia—supports early and pervasive disruption of TP53 signalling in oral tumorigenesis. The high proportion with elevated p53 IRS further underlines clonal expansion of genomically unstable keratinocytes during progression.

Cyclin D1: Concentration of Cyclin D1 positivity in SCC and its step-up from OPMDs is concordant with its role as a proliferative driver and with reported CCND1 copy-number gains in oral cancer. The mixed Cyclin D1 profile in verrucous hyperplasia (50% positive) is consistent with its classification as a potentially malignant, proliferative lesion.

Combined assessment. The 68% double-positive rate supports the complementary prognostic value of evaluating genomic surveillance (p53) and proliferative drive (Cyclin D1) together. Significant chi-square associations highlight the potential utility of these markers to augment routine histopathology for risk stratification and surveillance planning, particularly in resource-limited, high-incidence settings.

Clinical implications. In practice, (1) OPMDs with strong p53 and/or Cyclin D1 expression may warrant intensified follow-up or early intervention; (2) routine IHC panels incorporating these markers can standardise and objectify assessments where histological grading is equivocal; and (3) screening efforts should prioritise high-risk demographics (middle-aged males with tobacco/areca exposure) and predilection sites (lateral tongue/buccal mucosa).

LIMITATIONS:

As a cross-sectional, single-centre study (n=50), causal inference and survival correlations are not addressed; longitudinal validation and integration with broader molecular panels would refine prognostic accuracy.

CONCLUSION:

p53 and Cyclin D1 expression escalate along the histopathological continuum from non-dysplastic mucosa to OSCC. Combined IHC assessment improves lesion risk appraisal beyond single-marker analysis and should be considered as an adjunct to routine histopathology in oral proliferative lesions, particularly in high-burden settings.

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Institutional Ethics Committee approval and written informed consent were obtained; patient confidentiality was maintained. No external funding is declared. We thank the pathology department of the tertiary ENT centre, Osmania Medical College, Hyderabad.

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