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Expression of Stathmin and P53 in oral potentially malignant disorders and oral squamous cell carcinoma - An immunohistochemical study

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Abstract

Background: Oral squamous cell carcinoma (OSCC) arises from genetic alterations triggered by carcinogens, often associated with oral potentially malignant disorders (OPMD) like leukoplakia and oral lichen planus (OLP). Tumor markers, including intracellular phosphoprotein called Stathmin (STMN1) that are vital for chromosomal alignment, show abnormal expression leading to mutations, increasing chromosomal instability. The mutant form of the tumor suppressor gene P53 up-regulates STMN1.

Aim: Compare STMN1 and P53 expression via immunohistochemistry in oral lichen planus, oral epithelial dysplasia, and oral squamous cell carcinoma.

Materials and methods: 40 Formalin fixed paraffin embedded sections, diagnosed histopathologically as OSCC, oral epithelial dysplasia (OED), OLP, and normal tissue were categorized into four groups. Immunohistochemical assessment of STMN1 and p53 expression was carried out in these groups, and the results were statistically analyzed.

Results: Significant STMN1 expression variations were observed: 0% in normal mucosa, 50% in OLP, 80% in OED, and 100% in OSCC ($p<0.001$). Positive predictive values were 100% for lichen planus and dysplasia, with negative predictive values of 66.7% and 83.3%, respectively. P53 levels also significantly differed ($p<0.001$): 60% in normal mucosa, 90% in OLP and OED, and 100% in OSCC. Positive predictive values for p53 were 100% across all groups, with variable negative predictive values.

Conclusion: STMN1 and P53 showed significant expression variations among the four groups, highlighting their diagnostic potential and emphasizing their valuable role in oral malignancy prognosis and potential clinical applications.

Keywords: Oral potentially malignant disorders, oral squamous cell carcinoma, oral lichen planus, P53 gene, Stathmin.

Introduction

Oral Squamous cell carcinoma (OSCC) represents the primary type of head and neck squamous cell carcinoma. Notably, oral potentially malignant disorders (OPMDs) play a significant role in the development of oral squamous cell carcinoma, underscoring the importance of early identification and treatment of OPMDs to prevent malignant progression. The concept of malignant transformation of the oral mucosa was first documented by Sir James Paget in 1870 and later confirmed by Schwimmer in 1877. The World Health Organization classifies precancerous lesions and conditions affecting the oral cavity as "oral potentially malignant disorders," which include conditions like leukoplakia and oral lichen planus (OLP).[1]

Early diagnosis can prevent most malignancies and associated complications. Unfortunately, OPMDs are sometimes discovered too late because of a lack of understanding among the public and even among medical experts. In this study, we assessed the expression of an oncoprotein termed "stathmin" and a mutant of the tumour suppressor gene "p53," which may be contributing factors to the malignant transformation of the potentially malignant disorders stated above. Effective integration of these underutilized tumor markers facilitates early identification of high-risk patients with OPMDs, leading to improved prognosis and management in clinical practice, thereby benefiting individuals at risk for oral cancer.

Stathmin (STMN1), from the Greek "stathmos" meaning "relay," plays a pivotal role in modulating microtubule polymerization during signal transduction. This 149-amino-acid protein is divided into four domains (I-IV) through restricted proteolysis.[2] Stathmin plays a vital role in mitosis and potentially other cellular processes.[3]

It is believed to be a prognostic marker because it is overexpressed in some human malignancies, linked to a poor prognosis and chemoresistance.[4] In malignant tumors, aneuploidy is associated with chromosome instability due to abnormalities in the mitotic checkpoint. This includes challenges with chromosome cohesion, spindle attachment, and the effectiveness of the mitotic checkpoint response. Mutations or improperly formed proteins like stathmin can elevate chromosomal instability, contributing to aneuploidy.[5]

Human p53 (TP53), a tumor suppressor on chromosome 17, discovered in 1979 by Arnold Levine, was initially thought to be an oncogene. Now termed "the policeman of the oncogenes" and "the defender of the genome," p53 mutations are early events in HNSCC carcinogenesis. Mutated p53 yields a non-functional protein lacking tumor-suppressive properties, detectable via immunohistochemistry.[6] Stathmin is controlled by mutant p53 during transcription.[7]

Stathmin and P53 may be possible independent prognostic biomarkers and also may contribute significantly to a panel of markers that may efficiently predict prognosis in OPMDs and OSCC.

Materials and Methods

The study obtained approval from the Institutional Ethical Committee. Forty confirmed cases of formalin-fixed paraffin-embedded tissue blocks, representing four groups: normal mucosa, oral Lichen Planus (OLP), OED, and OSCC were sourced from the department's archives. Tissue sections, 4-5 microns thick, were prepared and assessed for STMN1 and p53 expression using immunohistochemical staining. The primary

antibodies used were Rabbit Anti- Human stathmin 1 (STMN1) monoclonal antibody and mouse anti-human p53 monoclonal antibody.

Two pathologists examined the slides, assessing positive STMN1 expression in normal mucosa, OLP, OED, and OSCC by manually examining 300 cells in at least 5 microscopic fields. The mean percentage of positively stained cells was determined. Each sample was then assigned one of the following staining scores: 0 – Less than 10%, 1 – 11 to 25%, 2 – 26 to 50%, 3 – 51 to 75%, 4 – 76 to 90%, and 5 – 91 to 100%. When no positive cells were found, the intensity was rated as 0; faint staining was rated as 1; moderate staining was rated as 2; and high staining was rated as 3.[8]

p53 immunoexpression was positive. Scores were recorded at 400x magnification on five random fields. Based on staining intensity and percentage, a semi-quantitative method was used to grade the level of immunological reactivity, and the following criteria were used to determine the positive cells. The proportion of positive cells was rated as 0 when it was 0 to 10%, 1 when 11–30%, 2 when 31–50%, and 3 when it was >50%. When no positive cells were found, the intensity was rated as 0, faint staining as 1, moderate staining as 2, and high staining as 3. The final index score was the sum of the labeled percentage positivity score and stain.[9] The results were tabulated and statistically analyzed.

Results

The primary aim was a comparative analysis of prognostic markers, P53 and STMN1, across the groups. Additionally, the study evaluated the significance of immunohistochemical expression of STMN1 and p53 in oral epithelial dysplasia and oral lichen planus.

The negative control group consisted of normal mucosa samples obtained during crown lengthening procedures.[10] The positive control group included OSCC samples, while the study group comprised the remaining two groups. The samples, ranging in age from 40 to 70 years, included 47.5% males and 52.5% females in the total of eighty samples, with Group I samples having no associated harmful habits.

Group II was composed of twenty samples of oral lichen planus, including eight reticular variants and twelve erosive variants. These cases were distributed among anatomical sites as follows: 60% from the buccal mucosa, 30% from the tongue, and 10% from the retromolar trigone. Notably, out of the twenty samples in this group, sixteen exhibited detrimental habits such as tobacco chewing, betel quid chewing, tobacco smoking, and alcoholism

Group III encompassed twenty samples of OED. These cases were distributed among anatomical sites, with 60% from the buccal mucosa, 20% from the tongue, 10% from the floor of the mouth, and 10% from the palate. It is worth noting that among these samples in this group, 80% exhibited harmful habits, including tobacco chewing, betel quid chewing, tobacco smoking, and alcoholism.

Group IV comprised twenty samples of OSCC, consisting of twelve well-differentiated and eight moderately differentiated cases. These cases were distributed as follows: 50% from the buccal mucosa, 20% from the tongue, 20% from the palate, and 10% from the retromolar trigone. Notably, all samples in this group exhibited deleterious habits such as tobacco chewing, betel quid chewing, tobacco smoking, and alcoholism.

Among the samples of normal oral mucosa, none exhibited positive STMN1 expression. In contrast, among the samples of OLP, 50% samples displayed

positive STMN1 expression. Furthermore, 80% samples of OED demonstrated positive STMN1 expression. All cases of OSCC exhibited positive STMN1 expression. The mean STMN1 scores were as follows: 0.0 in normal mucosa, 3.6 in OLP, 6.12 in OED, and 20.7 in OSCC. Statistical analysis using the Kruskal-Wallis test revealed a highly significant p-value of <0.001, indicating the data's statistical significance (Table 1, Graph 1).

The mean STMN1 values were pairwise compared between groups using the Bonferroni test. The differences between normal mucosa and OLP, between normal mucosa and OED were not statistically significant, with p-values of 0.654 and 0.055, respectively. However, the differences between OLP and OSCC and between OED and OSCC were statistically significant, with p-values of 0.005 and 0.116, respectively.

While the Bonferroni test did not show statistical significance, the predictive values indicated a high level of significance, with STMN1 demonstrating a 100% positive predictive value in OED and OLP. The negative predictive value of STMN1 in OED and OLP was 83.3% and 66.7%, respectively.

The pairwise comparison of mean STMN1 values between normal mucosa and OSCC was carried out using the Bonferroni test, and the predictive values indicated a significant diagnostic potential. The mean difference between Normal Mucosa and OSCC was -20.740, with a p-value of <0.001 (Table 1). Remarkably, the positive predictive value and the negative predictive value of STMN1 in OSCC were both 100% (Table 3).

In the present study, positive P53 expression was observed in 60% normal oral mucosa samples, 90% OLP cases, 90% OED cases, and all OSCC cases. The mean P53 scores escalated from 0.52 in normal mucosa to 12.79 in OSCC, with a highly significant p-value of <0.001 according to the Kruskal-Wallis test, emphasizing the statistical significance of the data (Table 2, Graph 2).

Statistical analysis, employing the Bonferroni test for pairwise comparisons of mean P53 values, revealed significant differences between various groups. The mean differences and associated p-values were as follows: Normal Mucosa vs. OLP (-3.16, p=0.324), Normal Mucosa vs. OED (-6.94, p=0.013), normal mucosa vs. OSCC (12.271, p<0.001), OLP vs. OSCC (-9.111, p=0.008), and OED vs. OSCC (-5.331, p=0.236). Despite a relatively smaller difference between dysplasia and carcinoma, the findings indicate a high level of statistical significance (Table 2). p53 exhibited consistent positive predictive values of 60% in OLP and OED, with a slightly higher value of 62.5% in OSCC. The negative predictive values for p53 in OLP, OED, and OSCC were 66.7%, 83.3%, and 100%, respectively, as demonstrated in Table 4.

Both P53 and STMN1 demonstrated highly significant sensitivity and specificity values in all three groups: Group II, Group III, and Group IV. In the case of OLP, STMN1 displayed 50% sensitivity and 100% specificity, while P53 exhibited 90% sensitivity and 40% specificity. In OED, STMN1 showed 80% sensitivity and 100% specificity, and P53 displayed 90% sensitivity and 40% specificity. Notably, in OSCC, both STMN1 and P53 exhibited 100% sensitivity. Specifically, in OSCC, P53 demonstrated 90% sensitivity and 40% specificity.

Table 1: Comparison of mean stathmin score between groups using Kruskal wallis test followed by Bonferroni post hoc test

Groups	Mean	Group 1 vs Group 2	Mean difference	P value
Normal mucosa (Negative control)	0 ± 0	Normal mucosa vs Lichen planus	-3.6	0.654
Dysplasia	6.12 ± 7.12	Normal mucosa vs Dysplasia	-6.12	0.055
Squamous cell carcinoma (Positive control)	20.704 ± 10.14	Normal mucosa vs Squamous cell carcinoma	-20.704	<0.001#
Lichen planus	3.6 ± 5.23	Lichen planus vs Dysplasia	-2.52	1.000
P value <0.001*		Lichen planus – Squamous cell carcinoma	-17.104	0.005#
		Dysplasia – Squamous cell carcinoma	-14.584	0.116

*Kruskal wallis test #Post hoc analysis

Graph 1:

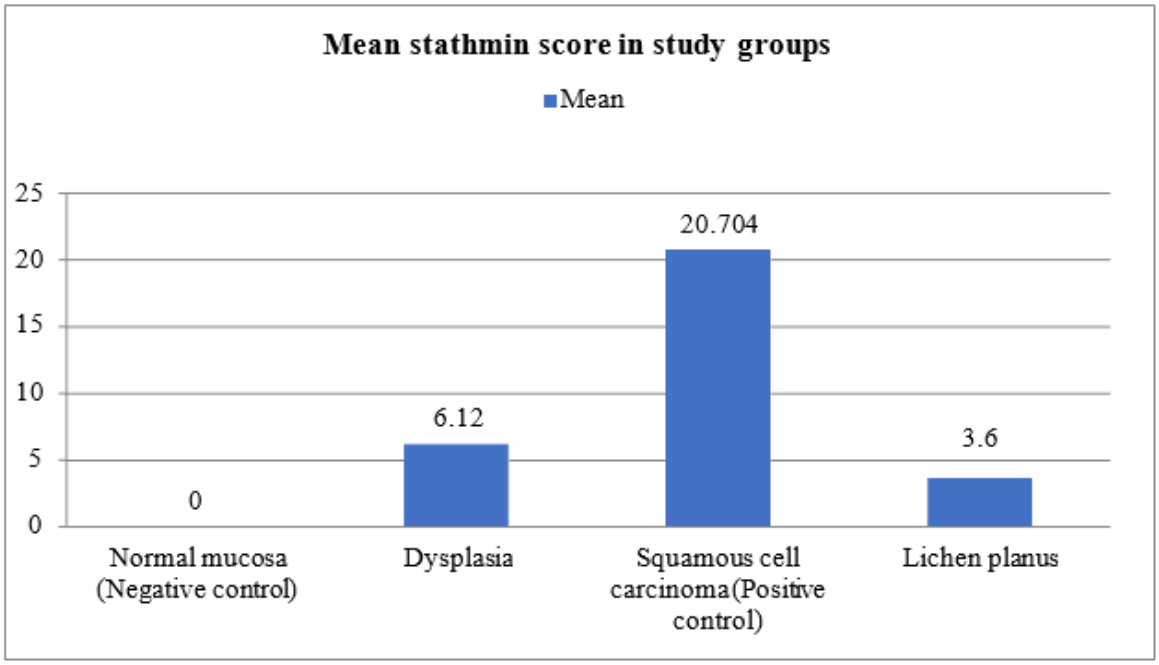


Table 2: Comparison of mean p53 score between groups using Kruskal Wallis test followed by Bonferroni post hoc test

Groups	Mean ± SD	Group 1 vs Group 2	Mean difference	P value
Normal mucosa (Negative control)	0.52 ± 0.492	Normal mucosa vs Lichen planus	-3.16	0.324
Dysplasia	7.46 ± 4.753	Normal mucosa vs Dysplasia	-6.94	0.013#
Squamous cell carcinoma (Positive control)	12.791 ± 1.375	Normal mucosa vs Squamous cell carcinoma	-12.271	<0.001#
Lichen planus	3.68 ± 3.20	Lichen planus vs Dysplasia	-3.78	1.000
		Lichen planus vs Squamous cell	-9.111	0.008#

P value <0.001*	carcinoma		
	Dysplasia vs Squamous cell carcinoma	-5.331	0.236

*Kruskal wallis test #Post hoc analysis

Graph 2:

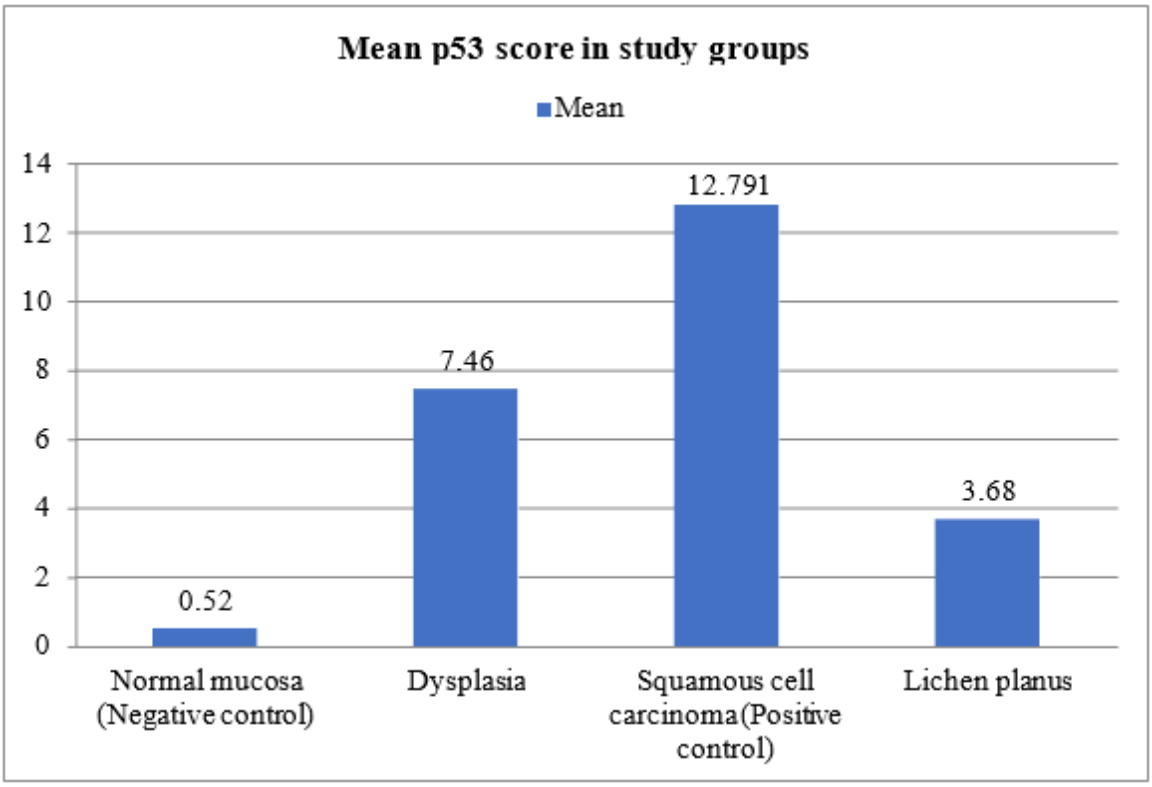


Table 3: Predictive value of diagnostic markers p53 and stathmin

	Dysplasia		OSCC		Lichen planus	
	p53	Stathmin	p53	Stathmin	p53	Stathmin
Sensitivity	90%	80%	100%	100%	90%	50%
Specificity	40%	100%	40%	100%	40%	100%
Positive predictive value	60%	100%	62.5%	100%	60%	100%
Negative predictive value	80%	83.3%	100%	100%	80%	66.7%
Likelihood ratio of positive result(LR+)	1.5	α	1.7	α	1.5	α
Likelihood ratio of negative result(LR-)	0.25	0.2	0	0	0.25	0.5
Accuracy	65%	90%	70%	100%	65%	75%
Misclassification rate	0.35	0.1	0.3	0	0.35	0.25
Diagnostic odds ratio	6	α	α	α	6	α

Discussion

The oral cavity acts as a direct interface with the external environment providing a unique perspective on the development of OPMDs and OSCC. Oral leukoplakia, a common OPMD, poses a 20% risk of progressing to OSCC, heightened with moderate to severe dysplasia. Investigating OSCC initiation within leukoplakia reveals genetic alterations like 3p14 and 9p21 loss of heterozygosity and dysregulated EGFR and PI3K-AKT-mTOR signaling. While previous research identified contributing factors, a comprehensive exploration of cellular landscapes during the precancerous stage remains underexplored, offering valuable insights into OSCC initiation near leukoplakia.[11,12]

In a study by de Lanna, C.A., da Silva, B.N.M et al, the transformation potential of OLP into OSCC has been studied. The research scrutinizes gene expression profiles in OLP and various OSCC stages, identifying common patterns related to keratinization, keratinocyte differentiation, cell proliferation, and immune response. Specific dysregulated genes, including PI3, SPRR1B, KRT17, and IL1B, are highlighted, providing insights into their potential role in OLP progression to OSCC. [13]

Although not all cases of leukoplakia and OLP have the potential to progress into OSCC the risk of transformation varies depending on several factors. Regular monitoring and early intervention are crucial to promptly detect and address any signs of malignant transformation. Continuous research is crucial for predicting and detecting the progression of OPMDs to cancer due to their varied characteristics. A multifaceted approach involving a panel of markers, such as STMN1 and p53, is necessary for accurate evaluation, enhancing early detection precision. This study compares the prognostic significance of TP53 and STMN1 in the transformation of OLP and OED, aiming to identify complementary markers for improved patient outcomes, emphasizing the need for rigorous validation and standardization in the complex context of oral cancer.

Genetic alterations in the p53 pathway play a pivotal role in the development of HNSCC. Mainly located in the DNA-binding domain, TP53 mutations hinder normal p53 function, preventing the activation of target genes. Mutant p53 not only suppresses the activity of remaining normal p53 but also gains new functions. High-risk TP53 mutations promote cellular transformation, accelerate tumor development, and confer resistance to chemotherapy. As a transcription factor, p53 is crucial for regulating cell cycle arrest and apoptosis in response to DNA damage, essential for preserving genomic integrity in HNSCC progression.[14-16]

Stathmin plays a vital role in cell-cycle regulation and microtubule dynamics, impacting cell proliferation and the p34cdc pathway during mitosis. Its interaction with tubulin can hinder or facilitate polymer formation. Overexpression in cancers, including OSCC, makes it a potential oncobiological marker. Elevated levels correlate with increased cancer cell proliferation, indicating its role in tumor initiation and progression. In head and neck cancers, high stathmin expression is associated with advanced stages, higher grades, and poor prognosis, emphasizing its significance in predicting the prognosis of oral potentially malignant disorders progressing to OSCC.[17-19]

In the present study, comparative analysis of prognostic markers, P53 and STMN1, in four groups: normal oral mucosa, OLP, OED, and OSCC was assessed. Among the 10 samples of normal oral mucosa, none exhibited positive STMN1 expression, while in OSCC, all cases showed positive STMN1 expression. In OLP, 50% cases

displayed positive STMN1 expression, and in OED, 80% cases demonstrated positive STMN1 expression. The mean STMN1 scores increased from normal mucosa to OSCC, with highly significant statistical differences.

The present study reveals a clear increase in mean STMN1 scores from normal mucosa to OSCC, indicating a correlation between STMN1 expression and the severity of oral conditions. This aligns with Vadla et al.'s study on oral leukoplakia, where STMN1 staining scores increased with the progression of dysplasia. Additionally, Satyadev Rana et al.'s examination of OSCC showed a positive correlation between Stathmin expression and tumor proliferation, particularly in poorly differentiated OSCC, suggesting a potential role of Stathmin in tumor progression and differentiation status.[20]

To the best of our knowledge, our study is the first to investigate stathmin expression in OLP. 50% of samples displayed positive stathmin expression. Notably, all these stathmin- positive cases were associated with the erosive variant of lichen planus.

Regarding P53, in normal mucosa, 60% samples exhibited mild positive P53 expression, and in OSCC, all cases displayed positive P53 expression. In OLP and OED, 90% samples\ showed positive P53 expression. The mean P53 scores also increased from normal mucosa to OSCC, with highly significant statistical differences.

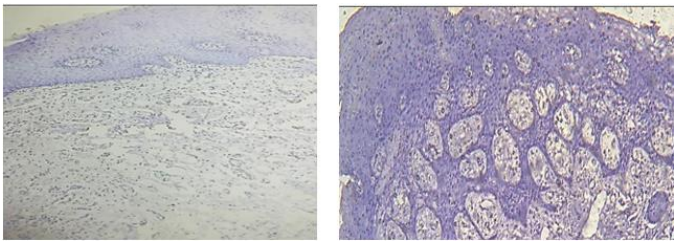
Cuevas Gonzalez, Gaitan Cepeda et al found p53-positive nuclei in 80% of OLP cases, with lower percentages in older and higher in younger patients. Intense p53 staining in keratinocytes, even with a low count, may indicate a stable mutant form. The study emphasized p53's potential role in monitoring disease progression and assessing malignant transformation risk, noting an inverse relationship between highly expressed civatte bodies and p53-positive cells, with no correlation to apoptosis. Among OSCCs, 44.6% were p16-positive, and 40.1% were p53-positive. Notably, no statistical link was found between histological grading and these markers, but strong p16 expression correlated with moderately differentiated OSCCs, while strong p53 expression was prevalent in poorly differentiated OSCCs.[21]

Comparing our findings with the study done by Cuevas Gonzalez, Gaitan Cepeda et al, indicated positive p53 expression in all cases, suggesting its consistent presence in potentially malignant disorders. However, the correlation between p53 expression and histological grading was not statistically significant. This implies that p53 expression in OSCC may not strongly correlate with the degree of differentiation, contributing valuable insights into its role in disease progression and differentiation status.

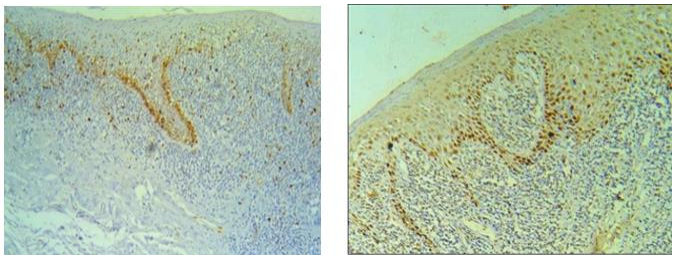
The present study compared prognostic markers P53 and STMN1, revealing distinct sensitivity and specificity. P53 showed 60-90% sensitivity and 40-100% specificity, while STMN1 exhibited 50-100% sensitivity with consistent 100% specificity. Expression patterns varied, notably increasing in OSCC, emphasizing their potential as valuable prognostic indicators in diverse oral conditions.

While P53 serves as a prevalent diagnostic and prognostic marker, the integration of STMN1 enriches its significance, providing supplementary insights for assessing diverse oral conditions. When strategically combined, these biomarkers create a potent tandem, leveraging their strengths to enhance collective diagnostic and prognostic efficacy. Optimal deployment requires a comprehensive understanding of each

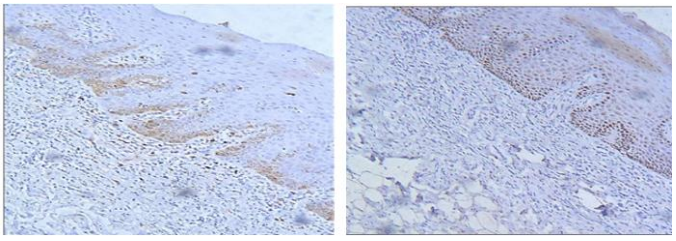
marker's distinct attributes: P53 establishes a robust foundation, while Stathmin, as a refined complement, adds nuance to the assessment. This collaborative approach ensures enhanced diagnostic precision, prognostic accuracy, and an overarching standard of clinical excellence.



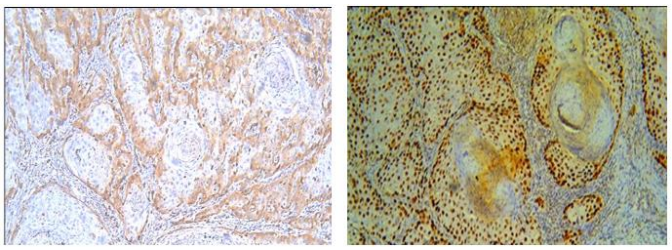
Pictomicrograph showing negative STMN 1 expression in normal mucosa (H&E staining; 100x) and negative P53 expression in normal mucosa (IHC staining; 100x) (left to right)



Pictomicrograph showing positive STMN 1 expression in oral lichen planus (H&E staining; 100x) and positive P53 expression in oral lichen planus (IHC staining; 100x) (left to right)



Pictomicrograph showing positive STMN 1 expression in oral epithelial dysplasia (H&E staining; 100x) and positive P53 expression in oral epithelial dysplasia (IHC staining; 100x) (left to right)



Pictomicrograph showing positive STMN 1 expression in oral epithelial dysplasia (H&E staining; 100x) and positive P53 expression in oral epithelial dysplasia (IHC staining; 100x) (left to right)

Conclusion

The study delves into the intricate dynamics of the progression from conditions like oral leukoplakia and oral lichen planus to oral squamous cell carcinoma. Highlighting the importance of genetic markers P53 and STMN1, the research underscores the need for a combined approach for enhanced diagnostic precision and prognostic accuracy, elevating the standard of clinical excellence in managing these disorders. The limitation of this study is its sample size, anticipated to be addressed in future studies, given its pilot nature. Furthermore, exploring common markers such as Ki-67, p16, and cyclin D1 along with stathmin and p53 could enhance the prognostic panel for oral potentially malignant disorders.

References

1. Hamed Mortazavi, Maryam Baharvand, Masoumeh Mehdipour. Oral Potentially Malignant Disorders: An Overview of More than 20 Entities. J Dent Res Dent Clin Dent Prospect 2014;8(1):6-14 | doi: 10.5681/joddd.2014.002
2. John Nemunaitis. Stathmin 1: a protein with many tasks. New biomarker and potential target in cancer. Expert Opin. Ther. Targets (2012) 16(7):631-634
3. Camelia Iancu Rubin and George F. Atweh. The Role of Stathmin in the Regulation of the Cell

Cycle. Journal of Cellular Biochemistry 93:242–250 (2004) | DOI 10.1002/jcb.20187

4. Qingyan Mao Zhen Chen Kun Wang Renfang Xu Hao Lu Xiaozhou He. Prognostic Role of High Stathmin 1 Expression in Patients with Solid Tumors: Evidence from a Meta- Analysis. Cell Physiol Biochem 2018; 50:66-78| DOI: 10.1159/00049395
5. Gaijing Han, Zongyong Wu et al. Overexpression of stathmin plays a pivotal role in the metastasis of esophageal squamous cell carcinoma Oncotarget, 2017, Vol. 8, (No. 37)
6. Ruchi Dhuria et al.: p53 Immunoexpression as a Prognostic Indicator of Survival in Head and Neck Squamous Cell Carcinoma American Journal of Medicine and Medical Sciences 2020, 10(2): 86-95.
7. Ma HL, Jin SF, Ju WT, Fu Y, Tu YY, Wang LZ, Jiang-Li, Zhang ZY, Zhong LP. Stathmin is overexpressed and regulated by mutant p53 in oral squamous cell carcinoma. J Exp Clin Cancer Res. 2017 Aug 14;36(1):109.
8. Vadla P, Yeluri S, Deepthi G, Guttikonda VR, Taneeru S, Naramala S. Stathmin! An immunohistochemical analysis of the novel marker in Oral Squamous Cell Carcinoma and Oral Leukoplakia. Asian Pacific Journal of Cancer Prevention: APJCP. 2020 Nov;21(11):3317.
9. Fedchenko N, Reifenrath J. Different approaches for interpretation and reporting of immunohistochemistry analysis results in the bone tissue–a review. Diagnostic pathology. 2014 Dec;9(1):1-2.
10. Gandhi V, Mahajan A, Kansal YP. Establishment of the role of myofibroblasts in invasive process of oral squamous cell carcinoma: A pilot study. J Family Med Prim Care. 2022 Sep;11(9):5485-5489. doi: 10.4103/jfmpc.jfmpc_1123_21. Epub 2022 Oct 14. PMID: 36505558; PMCID: PMC973097
11. Chandra P, Agnihotri PG, Nagarathna S. Expression of p53 protein in premalignancies and squamous cell carcinoma of the oral cavity. Journal of Indian Academy of Oral Medicine and Radiology. 2012 Oct 1;24(4):300.
12. Sun L, Kang X, Wang C, et al. Single-cell and spatial dissection of precancerous lesions underlying the initiation process of oral squamous cell carcinoma. Cell Discov. 2023;9:28.
13. De Lanna CA, da Silva BNM, de Melo AC, et al. Oral Lichen Planus and Oral Squamous Cell Carcinoma share key oncogenic signatures. Sci Rep. 2022;12:20645.
14. Xie TX, Zhou G, Zhao M, Sano D, Jasser SA, Brennan RG, Myers JN. 2013. Serine substitution of proline at codon 151 of TP53 confers gain of function activity leading to anoikis resistance and tumor progression of head and neck cancer cells. Laryngoscope. 123(6):1416–1423.
15. Neskey DM, Osman AA, Ow TJ, Katsonis P, McDonald T, Hicks SC, Hsu TK, Pickering CR, Ward A, Patel A, et al. Evolutionary action score of TP53 identifies high-risk mutations associated with decreased survival and increased distant metastases in head and neck cancer. Cancer Res. 2015;75(7):1527–1536.
16. Sionov RV, Haupt Y. The cellular response to p53: The decision between life and death. Oncogene. 1999;18:6145–6157.
17. Brattsand G, Marklund U, Nylander K, Roos G, Gullberg M. 1994. Cell-cycle-regulated

phosphorylation of oncoprotein 18 on Ser16, Ser25, and Ser38. Eur J Biochem 320:359– 368.

18. Cheng AL, Huang WG, Chen ZC, et al (2008). Identification of novel nasopharyngeal carcinoma biomarkers by laser capture microdissection and proteomic analysis. Clin Cancer Res, 14, 435-45.
19. Nakashima D, Uzawa K, Kasamatsu A, et al (2006). Protein expression profiling identifies maspin and stathmin as potential biomarkers of adenoid cystic carcinoma of the salivary glands. Int J Cancer, 118, 704-13.
20. Rana S, Mondal P, Mandal M, Datta P, Maji I, Chakraborty J. Expression of stathmin in oral squamous cell carcinoma and its correlation with tumour proliferation. J Oral Maxillofac Pathol. 2023 Jan-Mar;27(1):103-108. DOI: 10.4103/jomfp.jomfp_202_22. Epub 2023 Mar 21. PMID: 37234316; PMCID: PMC10207213.
21. Cuevas Gonzalez JC, Gaitan Cepeda LA, Borges Yanez SA, Cornejo AD, Mori Estevez AD, Huerta ER. p53 and p16 in oral epithelial dysplasia and oral squamous cell carcinoma: A study of 208 cases. Indian J Pathol Microbiol. 2016;59: 153.