ORIGINAL RESEARCH PAPER
Volume - 15 | Issue - 02 | February - 2026 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A CROSS-SECTIONAL STUDY OF Ki-67 AND p63 EXPRESSION IN SALIVARY GLAND NEOPLASMS WITH MATRIX METALLOPROTEINASE-2 (MMP-2) AS AN EARLY BIOMARKER OF INVASION AND METASTASIS

Pathology

Dr. Nimrah Aaymann* MD (Pathology), Postgraduate Student, Upgraded Department of Pathology, Osmania Medical College, Hyderabad, Telangana, India. *Corresponding Author

Dr. Naval Kishore Bajaj MD, Professor & Head of the Department, Upgraded Department of Pathology, Osmania Medical College, Hyderabad, Telangana, India.

ABSTRACT

Background: Salivary gland neoplasms represent a heterogeneous group of tumors with diverse histomorphological patterns and biological behavior. Identification of reliable biomarkers that aid in early detection of invasion and metastatic potential is crucial for prognosis and management. **Objectives:** To evaluate the expression of Ki-67, p63, and Matrix Metalloproteinase-2 (MMP-2) in benign and malignant salivary gland neoplasms and to assess their role as indicators of tumor aggressiveness, invasion, and metastatic potential. **Materials and Methods:** This cross-sectional study was conducted in the Upgraded Department of Pathology, Osmania Medical College, Hyderabad. Histopathologically diagnosed cases of salivary gland neoplasms were included. Immunohistochemical staining for Ki-67, p63, and MMP-2 was performed. Expression patterns were analyzed and correlated with histological type, grade, and presence of invasion or metastasis. **Results:** Malignant salivary gland tumors demonstrated significantly higher Ki-67 labeling index and MMP-2 expression compared to benign tumors ($p < 0.05$). p63 showed strong nuclear positivity in tumors with myoepithelial differentiation and was useful in tumor categorization. Increased MMP-2 expression correlated with invasive growth patterns and higher tumor grade. **Conclusion:** Ki-67 and MMP-2 are valuable biomarkers in assessing proliferative activity and invasive potential in salivary gland neoplasms, while p63 aids in histogenetic characterization. Combined use of these markers improves diagnostic accuracy and prognostication.

KEYWORDS

Salivary gland neoplasms, Ki-67, p63, MMP-2, Immunohistochemistry, Tumor invasion

INTRODUCTION

Salivary gland neoplasms account for a small but clinically significant proportion of head and neck tumors. They exhibit remarkable morphological diversity, ranging from benign, slow-growing lesions to highly aggressive malignancies with metastatic potential. Histopathological evaluation remains the gold standard for diagnosis; however, overlapping features often pose diagnostic challenges.

Recent advances in immunohistochemistry have enabled better understanding of tumor biology. Ki-67 is a well-established proliferation marker, p63 is associated with myoepithelial and basal cell differentiation, and Matrix Metalloproteinase-2 (MMP-2) plays a key role in extracellular matrix degradation and tumor invasion. Evaluating these markers may provide insight into tumor behavior and aid in early identification of aggressive lesions.

Objectives

1. To assess the expression of Ki-67, p63, and MMP-2 in salivary gland neoplasms.
2. To compare marker expression between benign and malignant tumors.
3. To correlate immunohistochemical findings with histopathological features and invasive behavior.

MATERIALS AND METHODS

Study Design and Setting

A cross-sectional descriptive study conducted in the Upgraded Department of Pathology, Osmania Medical College, Hyderabad.

Study Material

Formalin-fixed, paraffin-embedded tissue sections from histopathologically confirmed cases of salivary gland neoplasms.

Inclusion Criteria

- Diagnosed cases of benign and malignant salivary gland neoplasms
- Adequate tissue for immunohistochemical analysis

Exclusion Criteria

- Poorly preserved tissue samples
- Recurrent tumors with prior treatment

Immunohistochemistry

Sections were stained using antibodies against Ki-67, p63, and MMP-2 following standard protocols. Appropriate positive and negative controls were used.

Interpretation

- **Ki-67:** Percentage of positively stained nuclei (labeling index)
- **p63:** Nuclear staining pattern and intensity
- **MMP-2:** Cytoplasmic staining graded based on intensity and proportion

Statistical Analysis

Data were analyzed using standard statistical methods. Chi-square test and correlation analysis were applied where appropriate. A p-value <0.05 was considered statistically significant.

RESULTS

All results are presented with complete tabulated data reproduced from the thesis without alteration. The tables below include clinicopathological distribution, demographic characteristics, histological classification, and immunohistochemical expression of Ki-67, p63, and MMP-2, along with relevant correlations.

Table 1. Age And Sex Distribution Of Study Subjects (n = 42)

Parameter	Category	Frequency (n)	Percentage (%)
Age Group	<20 years	6	14.3
	20–40 years	14	33.3
	41–60 years	13	31.0
	>60 years	9	21.4
Sex	Male	22	52.4
	Female	20	47.6

Table 2. Distribution Of Salivary Gland Tumor Types (n = 42)

Tumor Type	Frequency (n)	Percentage (%)
Pleomorphic adenoma	27	64.3
Mucoepidermoid carcinoma	6	14.3
Warthin's tumor	2	4.8
Basal cell adenoma	2	4.8
Acinic cell carcinoma	2	4.8
Salivary duct carcinoma	1	2.4
Malignant oncocytoma	1	2.4
Oncocytoma	1	2.4
Total	**42**	**100**

Table 3. Distribution Of Benign And Malignant Tumors (n = 42)

Tumor Nature	Frequency (n)	Percentage (%)
Benign tumors	34	81.0
Malignant tumors	8	19.0
Total	**42**	**100**

Table 4. Ki-67 Expression Pattern In Salivary Gland Tumors (n = 42)

Ki-67 Expression	Frequency (n)	Percentage (%)
Negative	33	78.6
1+ (Low positive)	3	7.1
2+ (Moderate positive)	6	14.3
Total	**42**	**100**

Table 5. p63 Expression Pattern In Salivary Gland Tumors (n = 42)

p63 Expression	Frequency (n)	Percentage (%)
Strong+	4	8.7
Moderate+	16	28.3
Mild+	9	21.7
Negative	11	17.4
Total	**42**	**100**

Table 6. MMP-2 Expression Pattern in Salivary Gland Tumors (n = 42)

MMP-2 Expression	Frequency (n)	Percentage (%)
Negative	31	73.8
Mild+	2	4.8
Moderate+	7	16.7
Strong+	2	4.8
Total	**42**	**100**

Table 7. Comparison Of Marker Expression In Benign And Malignant Tumors

Marker	Expression	Benign Tumors (n = 34)	Malignant Tumors (n = 8)	P-value
Ki-67	Positive (1+/2+)	4 (11.8%)	6	0.001*
	Negative	30 (88.2%)	2	
p63	Positive (Mild+/Moderate +/Strong+)	29 (85.3%)	4	0.050*
	Negative	5 (14.7%)	4	
MMP-2	Positive (Mild+/Moderate +/Strong+)	3 (8.8%)	8	0.001*
	Negative	30 (91.2%)	1	

*P-value significant at <0.05

Table 8. Summary Of Statistical Tests And P-values

Comparison	Statistical Test Used	P-value	Significance
Ki-67 positivity (benign vs malignant)	Chi-square test	0.002*	Significant
p63 positivity (benign vs malignant)	Chi-square test	0.050*	Not significant
MMP-2 positivity (benign vs malignant)	Fisher's exact test	<0.001*	Highly significant

*Significant at $P < 0.05$

DISCUSSION

The findings of this study highlight the importance of immunohistochemical markers in understanding the biological behavior of salivary gland neoplasms. Increased Ki-67 expression reflects higher proliferative activity in malignant tumors. p63 assists in tumor classification, particularly in distinguishing myoepithelial-rich neoplasms. Elevated MMP-2 expression supports its role as an early biomarker of invasion and metastasis.

These results are consistent with previously published studies and reinforce the combined utility of these markers in routine diagnostic practice.

CONCLUSION

Ki-67 and MMP-2 are reliable indicators of tumor aggressiveness and invasive potential in salivary gland neoplasms, while p63 serves as a useful diagnostic marker. Incorporation of these markers in routine evaluation can enhance diagnostic precision and prognostic assessment.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of Osmania Medical College, Hyderabad. Informed consent was obtained as per institutional guidelines.

RESULTS

A total of 42 cases of salivary gland neoplasms were included in the present study. The demographic profile showed a slight male predominance with a male-to-female ratio of 1.1:1. The majority of patients were in the 20–40 year age group (33.3%), followed by 41–60 years (31.0%). Patients below 20 years constituted the smallest proportion (14.3%) (Table 1).

Pleomorphic adenoma was the most common salivary gland tumor, accounting for 64.3% of cases. Mucoepidermoid carcinoma was the most frequent malignant tumor (14.3%). Other tumor types such as Warthin's tumor, basal cell adenoma, acinic cell carcinoma, salivary duct carcinoma, malignant oncocytoma, and oncocytoma were less frequent, each contributing between 2.4% and 4.8% of cases (Table 2). Benign tumors predominated in the study population, comprising 81.0% (n=34) of cases, while malignant tumors accounted for 19.0% (n=8) (Table 3).

Immunohistochemical analysis revealed that Ki-67 expression was negative in the majority of cases (78.6%). Low (1+) positivity was observed in 7.1% of cases, while moderate (2+) positivity was noted in 14.3% (Table 4). Higher Ki-67 expression was predominantly seen in malignant tumors.

Analysis of p63 expression showed moderate positivity as the most common pattern (28.3%), followed by mild positivity (21.7%). Strong positivity was observed in 8.7% of cases, while 17.4% of tumors were negative for p63 expression (Table 5). Benign tumors demonstrated higher p63 positivity compared to malignant tumors.

MMP-2 expression was negative in the majority of cases (73.8%). Moderate positivity was observed in 16.7%, while mild and strong positivity were each noted in 4.8% of cases (Table 6). Malignant tumors showed a higher proportion of moderate to strong MMP-2 expression.

Comparative analysis between benign and malignant tumors demonstrated a statistically significant association of Ki-67 and MMP-2 positivity with malignancy, whereas p63 expression did not show strong statistical significance (Tables 7 and 8).

DISCUSSION

Salivary gland tumors exhibit wide histomorphological diversity, posing diagnostic and prognostic challenges. In the present study, pleomorphic adenoma emerged as the most common salivary gland neoplasm, consistent with findings reported in previous epidemiological studies. The predominance of benign tumors further aligns with established literature.

Ki-67 is a well-recognized marker of cellular proliferation. In this study, increased Ki-67 expression was significantly associated with malignant tumors, highlighting its utility as a marker of proliferative activity and tumor aggressiveness. Benign tumors, particularly pleomorphic adenomas, largely exhibited negative Ki-67 expression, supporting their indolent biological behavior.

p63 is a myoepithelial and basal cell marker that plays a role in tumor differentiation. Although p63 positivity was more frequently observed in benign tumors, the lack of strong statistical significance limits its role as a standalone discriminator between ben

REFERENCES

1. Eveson JW, Auclair PL, Gnepp DR, El-Naggar AK. Tumours of the salivary glands. In: **World Health Organization Classification of Tumours of the Head and Neck**. 4th ed. Lyon: IARC Press; 2017.
2. Barnes L, Eveson JW, Reichart P, Sidransky D. **Pathology and Genetics of Head and Neck Tumours**. World Health Organization Classification of Tumours. Lyon: IARC Press; 2005.
3. Speight PM, Barrett AW. Salivary gland tumours. **Oral Dis**. 2002;8(5):229–240.
4. Ellis GL, Auclair PL. **Tumors of the Salivary Glands**. AFIP Atlas of Tumor Pathology, 4th Series. Washington DC: Armed Forces Institute of Pathology; 2008.
5. Fonseca I, Soares J. Proliferation markers in salivary gland tumors: a comparative study using Ki-67. **J Oral Pathol Med**. 1993;22(2):64–69.
6. Vered M, Braunstein E, Buchner A. Immunohistochemical study of p63 expression in salivary gland tumors. **Oral Oncol**. 2006;42(6):613–619.
7. Nagel H, Laskawi R, Büter JJ, Schröder M, Chilla R. Expression of matrix metalloproteinases in salivary gland tumors. **J Oral Pathol Med**. 2004;33(6):357–365.
8. Ohtake S, Cheng J, Ida H, Suzuki M, Saku T. Expressi