

## A STUDY OF SPECTRUM OF NEOPLASTIC AND NON-NEOPLASTIC LESIONS OF SALIVARY GLAND AND THEIR CYTOLOGICAL CORRELATION WITH HISTOPATHOLOGY

P NEERAJA<sup>1</sup>, C LAKSHMI KALAVATHI<sup>1\*</sup>, C BHAKTHAVATSALA REDDY<sup>2</sup>

<sup>1</sup>Department of Pathology A. C. Subba Reddy Government Medical College, Nellore, Andhra Pradesh, India. <sup>2</sup>Department of Cardiology, Narayana Medical College and Hospitals, Nellore, Andhra Pradesh, India. Email: drclk30@gmail.com

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### ABSTRACT

**Objective:** This current study analyzed the diagnostic accuracy of cytology of various salivary gland lesions and correlated with histopathological findings.

**Method:** A study of 45 samples for fine-needle aspiration cytology (FNAC) were obtained from patients who were posted to the department of pathology. Aspirate from all salivary gland lesions and corresponding histopathological (HPE) specimens were included.

**Results:** Cytologic (FNAC) diagnosis reveals non-neoplastic, benign, and malignant lesions in 23% (12), 68% (31), and 4% (2) of 45 samples, respectively. While histopathological (HPE) diagnosis revealed non-neoplastic, benign, and malignant lesions in 20% (9), 62% (28), and 18% (8) of cases, respectively. The most common lesion in cytology and histology was discovered to be pleomorphic adenoma, which has a high sensitivity and specificity and can thus be used to screen all salivary gland tumors for a better therapeutic approach. The higher sensitivity, specificity, and diagnostic accuracy of FNAC confirms its important role in conjunction with radiological and clinical findings to provide the best initial assessment. There is a statistically significant relationship between the consistency, location, and cellularity of the lesion in benign and malignant tumours. Study concluded that on FNAC, 48% were benign in nature and 24% were malignant in nature. The sensitivity of FNAC was 86.5%, specificity was 100%, positive predictive value was 100%, negative predictive value was 86%, and diagnostic accuracy was 92.5%.

**Conclusion:** The study confirms the utility of FNAC as a safe and cost-effective method of distinguishing benign and malignant salivary gland lesions. FNAC had a sensitivity of 86.5%, a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 86%, and a diagnostic accuracy of 92.75%. FNAC and histopathology complemented each other to provide infallible diagnoses that are critical in planning future management.

**Keywords:** Salivary gland tumors, Histopathology, Fine-needle aspiration cytology, pleomorphic adenoma.

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### INTRODUCTION

Salivary gland tumors are extremely rare, accounting for 0.3% of all malignancies and 2–6.5% of head-and-neck tumors [1]. The global annual incidence ranges from 0.4 to 6.5 cases/100,000 people [2]. The vast majority of salivary gland tumors were benign. The majority of salivary gland tumors (75–80%) arise from the parotid glands, and 50% of tumors found in the submandibular glands are benign. Sublingual gland tumors are extremely rare, but if they do occur, they are almost always malignant. The palate is the most common location for minor salivary gland tumors. The most common benign tumour encountered is pleomorphic adenoma of the salivary glands. The most common oral cancers are [3,4] and squamous cell carcinoma [5,6]. Peak incidence occurs in 6–7<sup>th</sup> decades.

Fine-needle aspiration cytology (FNAC) provides immediate information about the nature of the lesion under examination. The technique has few contraindications and risks, and it can be used in the ambulatory setting. FNAC distinguishes between non-neoplastic and neoplastic lesions, removing the need for surgical intervention in lesions that can be treated conservatively. The purpose of FNAC is to determine the nature of the lesion, which can be classified as inflammatory, benign, or malignant, and in some cases, to provide a specific diagnosis [7,8]. For an accurate diagnosis, adequate cellularity of the smears and proper sampling of lesions are required [9]. The high sensitivity, specificity, and diagnostic accuracy of FNAC confirm its vital role, along with clinical and radiological findings, to provide the best possible initial evaluation, which in turn guides the treatment options [10].

The need for an accurate, timely, and well-structured pathology report has become increasingly important in this age, considering a society

that is both erudite and critical. FNAC is shown to be a safe and reliable method that overcomes these problems by providing a minimally invasive means to rapid diagnosis of intraoral lesions, and if necessary, a re-aspiration can be done immediately [11]. This technique has rarely been used to diagnose oral and pharyngeal lesions but has become a diagnostic test of choice for salivary gland lesions [12].

Keeping histopathological diagnosis as the gold standard, sensitivity, specificity, and diagnostic accuracy of FNAC were calculated.

Relevant clinical data, radiological findings, and collaboration between the clinician and cytopathologist are essential for making the best use of FNAC.

Thus, the current study aims to investigate the sensitivity, specificity, and diagnostic accuracy of FNAC of salivary gland lesions with histopathological correlation, as well as to identify discrepancies that contribute to diagnostic pitfalls.

### METHODS

This study included 45 FNAC samples obtained from patients posted to the pathology department with various major salivary gland disorders. Our study included major salivary gland lesions. Patients' demographics, clinical history, and ultrasonogram findings were all documented. Patients with all relevant clinical history and investigations who presented with superficial palpable and nodular salivary gland lesions were included. Patients with contraindications to FNAC, such as vascular lesions or patients on anticoagulant therapy, were excluded. All salivary gland lesions were aspirated, and the corresponding histopathological specimens were evaluated.

**FNAC-procedure**

FNAC was performed with a 23–24 gauge needle and a 10 mL syringe under negative pressure. Smears were either wet fixed or air fixed and stained with hematoxylin and eosin and Giemsa, respectively. The histopathological specimens were fixed overnight in 10% formalin and subjected to gross examination, processing, paraffin embedding, section cutting staining with hematoxylin and eosin, and mounting with DPX.

Maygrunwald Giemsa stain is a combination of two neutral stains. MayGrunwald stain is made up of an acidic stain (eosin) and a basic stain (methylene blue). Giemsa stain is made up of eosin and metachromatic stain.

**Procedure**

Smears are air dried, May Grunwald stain for 2 min, Blueing for 5 min, Giemsa stain for 3 min, blueing for 5 min, Dry, xylene, and DPX mount.

The data were entered into a Microsoft Excel spreadsheet, and the statistical analysis was carried out using SPSS version 21.0. Continuous measurement results were presented as mean±SD (min-max), while categorical measurement results were presented as frequency (%). To evaluate the relationship between the two categorical variables, the Chi-square test was used. For continuous variables, the Student *t*-test is used to compare intergroup variation. Histopathological findings were used as the gold standard to calculate sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy.

True positive: Positive for malignancy on FNAC and histopathology.

False positive: Positive for malignancy on FNAC but was declared negative after histopathology.

False negative: Negative for malignancy on FNAC but was declared positive for malignancy after histopathology.

True negative: Negative for malignancy both on histopathology and FNAC.

**RESULTS**

The present study includes the 18–70 years age group and the highest number of cases are in the age group 41–50 years, accounting 31.1%, followed by 24.4% of cases in 51–60 years, 17.8% in 31–40 years, 17.8% in >60 years, and 2.2% in <20 years age group, respectively. Predominance of males constituting 60% of total cases. Based on clinical diagnosis in 45 cases, result shows that incidence of non-neoplastic and benign lesions were higher (98.2%, n=42) than malignant (1.8%, n=3) (Table 1).

The study is consistent with the finding that patients with malignant neoplasm having a long duration. The study included cases with the size of the swelling ranging from 3 to 6 cm. The most common being 4 cm constituting about 48.9% (Table 2).

The lesions were firm in the majority of the cases contributing to 77.8% (n=35). Doughy consistency was noted in 8 (17.8%) cases proven to be Warthin's tumor on histopathology (Table 3).

The frequency of salivary gland lesions in parotid and submandibular in the present study was 60% (n=27) and 40% (n=18), respectively. The parotid gland is the most commonly involved gland which is consistent with other studies too (Table 4).

On cytology diagnosis, study showed high cellularity in most of the cases, constituting of 78%. Among the benign neoplastic lesions, pleomorphic adenoma was the most common constituting 35.6%. Mucoepidermoid carcinoma is the most common malignant neoplasm, constituting 2.2%. While on histopathology, pleomorphic adenoma is the most common benign neoplasm constituting 42.2%, and mucoepidermoid carcinoma is the most common malignant neoplasm constituting 13.3% (Table 5).

**Table 1: Distribution of neoplastic lesions according to histopathological diagnosis and site of location**

Histopathology diagnosis	Parotid	Sub-mandibular	Total cases
Pleomorphic adenoma	11	6	17
Mucoepidermoid Carcinoma	5	2	7
Warthin's tumor	8	0	8
Oncocytoma and myoepithelioma	2	1	3
Salivary duct Carcinoma	1	0	1
Total	27	9	36

**Table 2: Distribution of cases based on cellularity, cytology, and histopathology diagnosis**

Diagnosis	Frequency	%
Cellularity		
Highly cellular	35	77.8
Moderately cellular	10	22.2
FNAC diagnosis		
Pleomorphic adenoma	16	35.6
Warthin's tumor	8	17.8
Inflammatory lesion	1	2.2
Chronic sialadenitis	8	17.8
Lymphoepithelial cyst	4	8.9
Mucoepidermoid carcinoma	1	2.2
Salivary duct carcinoma	1	2.2
Pleomorphic adenoma/ mucoepidermoid carcinoma	4	8.9
Warthin's tumor/mucoepidermoid carcinoma	2	4.4
HPE diagnosis		
Pleomorphic adenoma	17	42.2
Warthin's tumor	8	17.8
Myoepithelioma	2	2.2
Chronic sialadenitis	8	15.6
Lymphoepithelial cyst	1	2.2
Mucoepidermoid carcinoma	7	13.3
Oncocytoma	1	2.2
Salivary duct carcinoma	1	4.4

FNAC: Fine-needle aspiration cytology, HPE: Histopathological

**Table 3: Cytology and histopathological categorization of lesions**

Diagnosis	No.	%
FNAC diagnosis		
Benign	31	68.9
Malignant	2	4.4
Non-neoplastic lesions	12	26.7
HPE diagnosis		
Benign	28	62.2
Malignant	8	17.8
Non-neoplastic lesions	9	20.0

On cytology diagnosis, non-neoplastic lesions constitutes 27%. Benign neoplasm constitutes 69% of total cases. Malignant neoplasm is the least common neoplasm of 4%.

On histopathology diagnosis, the non-neoplastic lesions constitute about 20%, the most common benign neoplasm constitutes 62%, and malignant neoplasm is the least, which accounts for 18%.

The diagnostic accuracy of benign lesions was predicted as 85%, and the diagnostic accuracy of malignant lesions was predicted as 86.5%.

**DISCUSSION**

Major salivary gland lesions are common, and the associated histopathology is extremely varied and complex due to the presence

Table 4: Correlation of cytology and histopathological assays

HPE	Number of cases	Pleomorphic adenoma	Warthin's tumor	Myoepithelioma	Chronic Sialadenitis	Lymphoepithelial Cyst	Mucoepidermoid Carcinoma	Salivary Duct Carcinoma	Oncocytoma
Pleomorphic adenoma	16	14	2						
Warthin's tumor	8	5		2					1
Inflammatory Lesion	1			1					
Chronic Sialadenitis	8		3		5				
Cystic lesion	4	3				1			
Mucoepidermoid Carcinoma	1						1		
Salivary Duct Carcinoma	1							1	
Oncocytoma									
Pleomorphic adenoma/Mucoepidermoid Carcinoma	4						4		
Warthin' tumor/Mucoepidermoid Carcinoma	2						2		
TOTAL	45	17	8	2	8	1	7	1	1

Table 5: Diagnostic accuracy in benign and malignant neoplastic lesions of salivary gland

FNAC	HPE		%
	+ve	-ve	
Benign lesions			
-ve	4	8	
+ve	24	0	
True negatives	4		Positive predictive value 100%
False negatives	8		Negative predictive value 65%
True positives	24		Sensitivity 84%
False positives	0		Specificity 100%
Malignant lesions			
+ve	1	28	
-ve	7	0	
True positive	7		Sensitivity 86.5%
False positive	0		Specificity 100%
True negative	1		PPV 100%
False negative	28		NPV 95.5%

Table 6: Comparison of site of Lesion-Benign versus Malignant and Cellulary - Benign versus Malignant and Consistency - Benign versus Malignant

Characteristics	Benign	Malignant	p value
Site of lesion			
Parotid	17	7	0.023
Submandibular	11	1	
Cellulary			
Moderate	26	0	0.042
High	02	8	
Consistency			
Doughy	8	0	0.0025
Firm	20	6	
Hard	0	2	

of non-neoplastic lesions, epithelial and non-epithelial neoplasms, metastatic tumours, and lymphomas.

Among the study population, the age group 41-50 years accounts for 31.1% of cases, followed by 24.4% of cases in 51-60 years, 17.8% in 31-40 years, 17.8% in >60 years, and 2.2% in <20 years.

In our study, the parotid gland was involved in 60% of the study population and the submandibular gland in 40%. Similar findings were revealed by Alghamdi *et al.* [13] and Verma [14].

In our study, among the study population, 51.1% of the swelling were of <6 months duration, and 6.6% of the swellings were of >5 years.

In our study, 26.7% of the lesions were non-neoplastic, 69% were benign, and 4.4% were malignant in nature.

According to Shalley *et al.* [15], non-neoplastic, benign, and neoplastic lesions were found in 18.47%, 74.28%, and 21.53% of patients, respectively.

On histopathology, 13.3% of the cases were mucoepidermoid carcinomas, with pleomorphic adenoma accounting for 42.2% of the benign neoplasms. Based on FNAC and histopathology, seven cases were reported to be positive for malignancy. False positive for malignancy indicates that there is no malignancy.

There is one false-negative case.

True negative shows eight cases that were declared negative for malignancy on the basis of both histopathology and FNAC. The sensitivity of FNAC was 86.5%, specificity was 100%, positive predictive

value was 100%, negative predictive value was 86% and diagnostic accuracy was 92.5%.

Similarly, Stow [16] study shows sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of were 86.9%, 92.3%, 96.8%, 86.6%, and 92.3%, respectively.

Kakoty *et al.* [17] reported an incidence of 44% of cases, and Sharma *et al.* [18] reported an incidence of 68.7% of the total cases of pleomorphic adenoma.

Vaidya *et al.*'s [19] study shows sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were 96.55%, 81.82%, 100%, 100%, and 95.9%, respectively.

Alghamdi *et al.* study shows sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were of 90.3%, 100%, 100%, 57.1%, and 91.4% respectively.

Dhanani *et al.*'s [20] study show sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were of 88.9%, 97.9%, 93%, 96.7%, and 95.8%, respectively.

Verma study shows sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were of 88%, 96.6%, 91.7%, 95%, and 94.05%, respectively.

The higher sensitivity, specificity, and diagnostic accuracy of FNAC confirms its important role in conjunction with radiological and clinical findings to provide the best initial assessment, which in turn guides management options.

The most common lesion in cytology and histology was found to be pleomorphic adenoma, which has a high sensitivity and specificity for screening salivary gland tumours.

In our study, there is a statistically significant relationship between lesion consistency, location, and cellularity in benign and malignant tumors.

Histopathology revealed that two cases of pleomorphic adenoma were myoepithelioma in the current study.

When myoepithelial cells have clear cytoplasm, the diagnostic considerations include epithelial-myoepithelial carcinoma, sebaceous adenoma, myoepithelial carcinoma, and even metastasis.

In the current study, two cases with a differential diagnosis of Warthin's tumor/mucoepidermoid carcinoma were found to be mucoepidermoid in histopathology.

Sahni *et al.* [21] reported that the predominance of lymphoid cells in cases of Warthin's tumor may lead to a misdiagnosis of lymphoepithelial cyst.

Many salivary gland neoplasms, including myoepithelioma, mucoepidermoid carcinoma, and pleomorphic adenoma, can have oncocytic features.

All cases of Warthin's tumor should be distinguished from intraparotid lymph nodes, lymphoepithelial sialadenitis, lymphoepithelial cyst, and oncocytoma.

Lymphoepithelial sialadenitis lacks oncocytic epithelium and dirty cystic debris.

A case of granulomatous lesion involving the parotid gland was reported, revealing groups of epithelioid histiocytes, multinucleated giant cells, and inflammatory cells, but no histopathological correlation could be established.

Mihashi *et al.* [22] suggested that in cases of prominent granulomas, caution should be exercised to avoid misinterpreting epithelioid histiocytes with moderate eosinophilic cytoplasm and curved nuclei as epithelial neoplasm.

In 2 cases, the FNAC diagnosis was broadly given as a cystic lesion, and a possibility of cystic degeneration was suggested. On follow-up, the 2 cases were diagnosed with low-grade mucoepidermoid carcinoma on histopathology.

Among the malignant lesions, mucoepidermoid was the most common, constituting about 14% of cases. Similar observations were reported by Sharma *et al.*, Yogambal *et al.* [23], Kakoty *et al.*, Ramana *et al.* [24] It has a diagnostic accuracy of 66% which is significantly more than other studies.

Overall, malignancy was more common in parotid (7 cases) 20%, as compared with the submandibular gland (1 case) 3%.

In our study, 12 (23%) cases had non-neoplastic lesions, 31 (68%) cases had benign lesions, and 2 (4%) cases had malignant lesions.

While histopathological diagnosis revealed that 9 (20%) cases were non-neoplastic, 28 (62%) cases were benign lesions, and 8 (18%) cases were malignant.

We discovered a strong correlation between FNAC and final histology.

The high sensitivity, specificity, and diagnostic accuracy of FNAC confirms its important role in conjunction with radiological and clinical findings to provide the best initial assessment, which in turn guides management options.

Multiple sampling from different sites helps to avoid misinterpretation by concluding with a type-specific diagnosis. The most common lesion in cytology and histology was discovered to be pleomorphic adenoma, which has high sensitivity and specificity and can thus be used to screen all salivary gland tumors for a better therapeutic approach.

The study included 45 cases of aspirates from major salivary gland lesions.

Cytologic distribution of 45 cases was as follows: 12 cases (23%) were non-neoplastic, 31 (68%) cases were benign lesions, and 2 (4%) cases were malignant lesions.

Histopathological confirmation of 45 cases revealed that 9 (20%) cases were non-neoplastic, 28 (62%) cases were benign lesions, and 8 (18%) cases were malignant.

In our study, there is a statistically significant relationship between lesion consistency, location, and cellularity in benign and malignant tumors.

We discovered a strong correlation between FNAC and final histology. The high sensitivity, specificity, and diagnostic accuracy of FNAC confirm its significance. Histopathology confirmed one case of salivary duct carcinoma found on cytology.

Tessy *et al.* suggested that distinguishing high-grade metastasis to the salivary gland from primary elsewhere is critical in these cases. The current study confirms the higher incidence of benign neoplastic lesions compared to their malignant counterpart.

There was nearly perfect agreement and fairly good accuracy between the cytological and histological diagnoses in the study.

Some of the common salivary gland lesions like various cysts, basal cell adenoma, Acinic cell carcinoma, Adenoid cystic carcinoma, and Epithelial-myoeplithelial carcinoma were not encountered in the

present study as it had a limitation period of 1 year in spite of an effective study population.

## CONCLUSION

The study concluded that 48% of FNAC were benign and 24% were malignant. The FNAC had a sensitivity of 86.5%, a specificity of 100%, a positive predictive value of 100%, a negative predictive value of 86%, and a diagnostic accuracy of 92.5%. The study confirms the utility of FNAC as a safe and cost-effective method of distinguishing benign and malignant salivary gland lesions. FNAC and histopathology complemented each other to provide infallible diagnoses that are critical in planning future management.

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## AUTHORS' CONTRIBUTIONS

Neeraja, Bhakthavatsala Reddy- conceptualization, methodology, formal analysis, writing - original draft, writing - reviewing and editing; Neeraja, Lakshmi kalavathi- data curation, writing - reviewing and editing; Neeraja, Bhakthavatsala Reddy, Lakshmi kalavathi- investigation, formal analysis.

## COMPETING INTERESTS

There are no conflicts of interest.

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