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Original Research Article

# Cytologic Spectrum of Major Salivary Gland Lesions with Histopathological Correlation: A Prospective Study

**T. Anitha[1], M. Kavitha[2], K. Booma[3]**

[1]Assistant Professor, Department of Pathology, Government Sivagangai Medical College, Sivagangai, Tamil Nadu, India

[2]Associate Professor of Pathology, Government medical College, Tiruppur, Tamil Nadu, India

[3]Assistant Professor, Department of Pathology, Government Sivagangai Medical College, Sivagangai, Tamil Nadu, India

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**Corresponding author: Dr. T. Anitha**

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**Abstract**

**Background:** Fine needle aspiration cytology (FNAC) is a widely accepted, minimally invasive, and cost-effective first-line diagnostic tool for salivary gland lesions. The morphological heterogeneity of these tumors presents significant diagnostic challenges. This study evaluates the diagnostic accuracy, sensitivity, and specificity of FNAC in major salivary gland lesions and correlates findings with histopathological diagnosis.

**Methods:** A prospective study of 45 patients presenting with major salivary gland swellings was conducted at the Department of Pathology, Coimbatore Medical College and Hospital, over a 12-month period (August 2018–July 2019). FNAC was performed with a 23–24 gauge needle; smears were stained with Hematoxylin & Eosin (H&E) and May-Grünwald Giemsa (MGG). Histopathological specimens were processed and stained with H&E. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated using histopathology as the gold standard.

**Results:** Parotid gland was the most frequently involved site (60%). Male predominance was observed (60%), with a mean age of 47.7 ± 11.9 years. On FNAC, 27% of cases were non-neoplastic, 69% benign, and 4% malignant; histopathology confirmed 20% non-neoplastic, 62% benign, and 18% malignant. Pleomorphic adenoma was the most common benign neoplasm (42.2% on HPE) and mucoepidermoid carcinoma the most common malignancy (13.3% on HPE). FNAC showed a sensitivity of 85% and specificity of 100% for benign lesions, and sensitivity of 87.5% and specificity of 100% for malignant lesions.

**Conclusions:** FNAC demonstrates high sensitivity, specificity, and diagnostic accuracy in salivary gland lesions and remains an invaluable pre-operative tool when interpreted in conjunction with clinical and radiological findings. Awareness of cytomorphological pitfalls, particularly the pleomorphic adenoma/mucoepidermoid carcinoma interface, is essential to minimize diagnostic errors.

**Keywords:** FNAC, Salivary Gland, Pleomorphic Adenoma, Mucoepidermoid Carcinoma, Histopathological Correlation, Diagnostic Accuracy, Cytomorphology.

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## Introduction

Salivary gland lesions account for 2–5% of all head and neck neoplasms, with an age incidence extending from children to adults over 80 years of age. [1,2,3] The pathology of these lesions is diverse, encompassing developmental, inflammatory, benign, and malignant tumors, which can be primary or metastatic. These glands are generally not subjected to incisional or core needle biopsy because of the possible risk of fistula formation and tumor seeding. [4] Fine needle aspiration cytology (FNAC), first reported by Kun in 1847 and reintroduced for head and neck lesions by Martin & Ellis in 1930, and further promoted by Enroth et al. in the 1950s–60s, has since emerged as the preferred first-line pre-operative diagnostic modality. [5]

FNAC is of particular relevance in the head and neck area because of the easy accessibility of the target site, excellent patient compliance, minimally invasive nature, and its ability to avoid surgery in inflammatory and non-neoplastic conditions. [2] It enables categorization of lesions into inflammatory, reactive, benign, and malignant categories, directly influencing therapeutic management. [2,3,6]

The purpose of FNAC is not merely to provide a definitive specific diagnosis; it is used in conjunction with clinical and radiological findings to provide the best possible initial assessment from which management can be planned. [7,6] Ultrasonography continues to act as a bridge between surgery and pathology, and its adjunct use with FNAC significantly improves diagnostic accuracy. [8] The risk of malignancy prior to FNAC varies by site: 20–25% in the parotid gland and 40–50% in the submandibular gland. The most common source of diagnostic error remains inadequate sampling, as FNAC derives material only from a small area. [9] Though histopathology remains the most accurate definitive method of diagnosis, the role of FNAC in initial salivary gland diagnosis is significant. [10]

This study aims to: (1) analyze the cytological, clinical, and histological features of major salivary gland lesions; (2) correlate FNAC findings with histopathological diagnosis; and (3) identify the reasons for diagnostic pitfalls in cases with cytohistological discrepancy.

**Review of Literature:** Over the past three decades, FNAC has been well recognized as the first diagnostic tool in the workup of salivary gland lesions. It is widely accepted as a simple, safe, and cost-effective technique. [2] Salivary gland tumors constitute about 3–10% of head and neck tumors, and when performed and analyzed by experienced hands, FNAC has the advantage of delivering valuable diagnostic data within a relatively short period of time [1, 3, 5].

FNAC has been used for the diagnosis of salivary gland lesions for more than three decades and is beneficial not only in rendering a diagnosis but also in differentiating neoplastic from non-neoplastic lesions. [11,2,3] It is useful in pre-operative assessment of parotid swellings particularly in resource-limited settings, where tuberculosis and metastatic squamous cell carcinoma invading perisalivary lymph nodes may mimic primary parotid pathology. [8] Additionally, FNAC allows grading of malignant lesions, which determines the extent of surgery, including preservation of the facial nerve and the indication for neck dissection in the case of malignant parotid tumors. [5]

Assessment of FNAC should follow a stepwise approach: the first aim is to decide whether the lesion is of salivary gland origin; [12] the next step is to identify cells and their morphology to classify them as non-neoplastic or neoplastic. [6] A five-group cytomorphological approach has been proposed [13] for systematic categorization:

- **Myxoid-Hyaline group:** Benign mixed tumor, adenoid cystic carcinoma, carcinoma ex pleomorphic adenoma, polymorphous low-grade adenocarcinoma
- **Basaloid group:** Basal cell adenoma, solid variant of adenoid cystic carcinoma, small cell undifferentiated carcinoma
- **Oncocytoid group:** Warthin's tumor, oncocytoma, acinic cell carcinoma, Hürthle cell carcinoma
- **Lymphoid group:** Chronic sialadenitis, lymphoepithelial lesions, Warthin's tumor, lymphoepithelial carcinoma, metastasis to intra/periparotid lymph nodes
- **Squamoid group:** Retention cyst, squamous cell carcinoma, branchial cleft cyst, dermoid cyst

Many factors influence the adequacy of salivary gland FNAC, including aspiration technique (manual vs. ultrasound-guided), nature of the lesion (solid vs. cystic), sample collection and preservation method, preparation technique artifacts, calibre of needle, and the presence of obscuring blood or other material. [11] Ultrasound guidance and rapid on-site evaluation (ROSE) by a cytopathologist improve accuracy.

Foschini et al. 2008 stated that a non-diagnostic aspirate is one that for qualitative and quantitative reasons provides insufficient material for an informative interpretation. Kim et al. 2018 found a diagnostic accuracy of FNAC of 92% in differentiating malignant from benign salivary gland tumors. Fakhry et al. 2012 evaluated the sensitivity and specificity of FNAC to be 80% and 89.5% respectively.

Neha Sikdar et al. 2018 [11 ]observed plasmacytoid cells and poorly cohesive clusters of epithelial cells in a fibromyxoid background in pleomorphic adenoma, and further suggested that high-grade mucoepidermoid carcinoma containing malignant squamous epithelial cells is difficult to distinguish from metastatic squamous cell carcinoma. Sharma M et al. 2015 [9] reported an incidence of 68.7% for pleomorphic adenoma and 12.5% for chronic sialadenitis among all salivary gland lesions.

Kakoty S et al. 2017 [14] reported an incidence of 44% for pleomorphic adenoma among all cases, and suggested that the presence of goblet cells or squamous metaplasia in pleomorphic adenoma should be approached cautiously as it could represent low-grade mucoepidermoid carcinoma. S.V. Ramana et al. 2017 [1] found that Warthin's tumor constituted 4.12% on cytological diagnosis and 3.09% on histological diagnosis, and suggested that rapid enlargement of a previously stable pleomorphic adenoma should raise suspicion of carcinoma ex pleomorphic adenoma.

Joshi AR et al. 2017 [15] reported approximately 21.9% cases of chronic sialadenitis among salivary

gland lesions. Viguer et al. 1997 [16] stated that metaplastic cells such as oncocytic, sebaceous, and squamous cells may occasionally be seen in pleomorphic adenoma, adding diagnostic complexity.

Klijanienko and Vielh et al. 1997 [17] suggested that mast cells are commonly associated with oncocytes in Warthin's tumor aspirates, and in acinic cell carcinoma mild to moderate anisokaryosis with bland chromatin can be seen. E.D. Rossi et al. 2017 suggested that a salivary gland lesion should be classified as suspicious for malignancy when some, but not all, criteria for a specific malignant diagnosis are present yet the overall cytologic features are suggestive of malignancy. Foschini et al. 2008 stated that a non-diagnostic aspirate is one that provides insufficient material for an informative interpretation, emphasizing that sample adequacy is of paramount importance.

Swati Sahni et al. 2017 [7] reported interpretation difficulty in cases of pleomorphic adenoma harboring mucin, constituting a potential trap for erroneous mucoepidermoid carcinoma diagnosis. They also reported that the predominance of lymphoid cells in Warthin's tumor may lead to misdiagnosis as lymphoepithelial cyst. Das et al. 2004 [18] suggested that pleomorphic adenoma is commonly misdiagnosed as adenoid cystic carcinoma due to the presence of hyaline stromal globules, but chondromyxoid stroma and foci of squamous metaplasia are absent in adenoid cystic carcinoma.

W.C. Faquin et al. 2015 suggested that the common pitfall in chronic sialadenitis is the misinterpretation of metaplastic or atrophic ductal cells as a basaloid neoplasm, while chronic sialadenitis lacks the three-dimensional epithelial groups and degree of cellularity found in aspirates of a basaloid neoplasm. Tessy PJ et al. [19] emphasized that distinction between salivary duct carcinoma and high-grade metastasis to the salivary gland from a primary elsewhere is of critical diagnostic importance. The WHO Classification of Tumors of the Head and Neck20 and TNM staging for major salivary gland carcinomas provides the current gold-standard framework for lesion classification and pathological staging.

## Materials and Methods

**Study Design and Setting:** A prospective observational study was conducted at the Department of Pathology, Coimbatore Medical College and Hospital, Coimbatore, Tamil Nadu, India, over 12 months (August 2018–July 2019). Informed written consent was obtained from all patients, and appropriate institutional ethical clearance was in place.

**Study Population:** A total of 45 patients presenting with major salivary gland swellings were enrolled, irrespective of age and sex. All patients who had an adequate FNAC smear and a corresponding histopathological specimen were included.

### Inclusion and Exclusion Criteria

**Inclusion Criteria:** All aspirates from major salivary gland lesions with corresponding histopathological specimens.

**Exclusion Criteria:** Smears with low cellularity; hypocellular smears; smears obscured by blood, mucus, or inflammatory cells; inadequate specimens.

**FNAC Technique:** FNAC was performed using a 23–24 gauge needle with a 10 mL syringe under negative pressure. Aspirated material was smeared on clean glass slides. Wet-fixed smears were stained with Hematoxylin and Eosin (H&E) and air-dried smears were stained using May-Grünwald Giemsa (MGG). MGG was preferred for its superior demonstration of chondromyxoid stroma, its crisp chromatin rendering, and metachromatic staining of mucoid material. [6] Clinical data including duration, associated pain, facial nerve findings, and cervical lymphadenopathy were recorded for each patient.

**Histopathological Processing:** Surgical resection specimens were fixed overnight in 10% neutral buffered formalin, grossly examined, processed through standard paraffin embedding, sectioned at 4–5 µm, and stained with H&E. Immunohistochemistry was applied in selected cases as clinically indicated to resolve diagnostic ambiguity.

### Cytological Categorization

FNAC diagnoses were classified into five operational categories:

- Category I: Non-diagnostic (insufficient/acellular material or peripheral blood)
- Category II: Non-neoplastic lesions
- Category III: Benign neoplastic lesions
- Category IV: Suspicious for malignancy
- Category V: Positive for malignancy

**Statistical Analysis:** Sensitivity, specificity, PPV, and NPV were calculated with histopathological diagnosis as the gold standard, using standard 2×2 contingency tables. Pearson chi-square test was applied for comparative analysis; a p-value $< 0.05$ was considered statistically significant.

## Results

**Demographic Profile:** Of the 45 cases enrolled, the age range was 15–70 years (mean 47.7 ± 11.9

years; S.D. 11.9 years). The largest proportion (31.1%, n=14) fell in the 41–50-year age group, followed by 51–60 years (24.4%, n=11). Male patients constituted 60% (n=27) and female patients 40% (n=18) of the cohort.

**Clinical and Anatomical Distribution:** The parotid gland was involved in 60% (n=27) and the submandibular gland in 40% (n=18) of cases. The majority of patients (33.3%, n=15) presented with a lesion duration of 2 months; malignant cases showed consistently longer symptom duration. Lesion size ranged from 3–6 cm, with 4 cm being the most common (48.9%, n=22). By consistency: firm 77.8% (n=35), doughy 17.8% (n=8), hard 4.4% (n=2). By cellularity on FNAC: highly cellular 77.8% (n=35) and moderately cellular 22.2% (n=10).

**Cytological Diagnosis:** On FNAC, lesions were distributed as: non-neoplastic 12 cases (26.7%), benign neoplastic 31 cases (68.9%), and malignant 2 cases (4.4%). Pleomorphic adenoma was the single most frequent diagnosis (35.6%), followed by Warthin's tumor and chronic sialadenitis (17.8% each). Six cases received a dual differential diagnosis — 4 as PA/low-grade MEC and 2 as Warthin's tumor/MEC — reflecting the morphological overlap at these interfaces. [Table 1]

**Histopathological Findings:** Histopathology confirmed: non-neoplastic 9 cases (20%), benign 28 cases (62.2%), and malignant 8 cases (17.8%). Pleomorphic adenoma was the most common benign entity (n=17, 42.2%) followed by Warthin's tumor (n=8, 17.8%). Among malignancies, mucoepidermoid carcinoma was most frequent (n=7, 13.3%), followed by salivary duct carcinoma (n=1). [Table 2]

**Cytohistopathological Correlation:** Pleomorphic adenoma was the most common lesion, with 16 histopathologically confirmed cases, of which 14 were correctly identified on cytology, reflecting a high cytological accuracy for this benign tumor. Warthin's tumor accounted for 8 histopathological cases, but only 5 were correctly diagnosed on cytology, with 2 cases misdiagnosed as chronic sialadenitis and 1 as oncocytoma, suggesting cytological overlap with other lesions. Chronic sialadenitis showed 8 histopathological cases, yet cytology correctly identified only 5, with 3 being called Warthin's tumor, highlighting the challenge of distinguishing reactive inflammatory changes from neoplastic oncocytic proliferations. Among the 4 cystic lesions on histopathology, 3 were cytologically diagnosed as pleomorphic adenoma, indicating that cystic degeneration in pleomorphic adenoma can mimic simple cystic lesions and vice versa.

Malignant lesions such as mucoepidermoid carcinoma and salivary duct carcinoma showed perfect cytology-histopathology concordance in the single straightforward cases, demonstrating that overtly malignant tumors are reliably identified on FNAC. However, 4 cases histologically diagnosed as pleomorphic adenoma and 2 as Warthin's tumor were cytologically called mucoepidermoid carcinoma, representing false-positive malignant diagnoses — a clinically significant finding that could lead to overtreatment.

No case of oncocytoma was confirmed histopathologically, yet one was diagnosed cytologically in a Warthin's tumor case, reinforcing that oncocytic cells are a common source of diagnostic confusion. Overall, the table underscores that while FNAC is reliable for common benign tumors like pleomorphic adenoma; diagnostic pitfalls exist particularly around cystic, oncocytic, and low-grade malignant lesions in salivary glands. [Table 3]

**Diagnostic Accuracy:** The diagnostic accuracy of FNAC for benign salivary gland lesions was 85%, with a sensitivity of 85% and a specificity of 100%, indicating no false positive benign diagnoses on cytology. Out of 28 confirmed benign cases, FNAC correctly identified 24 (true positives), with 4 false negatives, yielding an NPV of 66%, reflecting occasional under-diagnosis on cytology.

For malignant lesions, FNAC achieved a sensitivity of 87.5% and specificity of 100%, correctly detecting 7 of 8 malignant cases with zero false positives. The PPV was 100% in both categories, confirming that every positive FNAC diagnosis — benign or malignant — was validated by histopathological examination.

Overall, FNAC proved to be a highly specific and reliable pre-operative tool with diagnostic accuracy of 85% (benign) and 87.5% (malignant), supporting its routine use in salivary gland lesion workup. [Table 4].Pearson chi-square analysis with 2×2 contingency tables demonstrated statistically significant associations ($p < 0.05$) between malignancy and: (i) hard lesion consistency; (ii) parotid location; and (iii) high cellularity on FNAC smear.[Table 5]

**Table 1: Cytological diagnosis of salivary gland lesions**

| Cytology Diagnosis | Cases | |
|---|---|---|
| | No | % |
| 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 |
| Total | 45 | 100 |

**Table 2: Histopathological Diagnosis of salivary gland lesions**

| Histopathology Diagnosis | Cases | |
|---|---|---|
| | No | % |
| 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 |
| Total | 45 | 100.0 |

**Table 3: Cytohistolopathological correlation of the diagnoses**

| Histopathological Diagnosis | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Cytology Diagnosis** | **N0 Of Cases** | **Pleomorphic adenoma** | **Warthin' tumor** | **Myoepithelioma** | **Chronic Sialadenitis** | **Lymphoepithelial Cyst** | **Mucoepidermoid Carcinoma** | **Salivary Duct Carcinoma** | **Oncocytoma** |
| Pleomorphic adenoma | 16 | 14 | | 2 | | | | | |
| Warthin' tumor | 8 | | 5 | | 2 | | | | 1 |
| Inflammatory Lesion | 1 | | | | 1 | | | | |
| Chronic Sialadenitis | 8 | | 3 | | 5 | | | | |
| Cystic lesion | 4 | 3 | | | | 1 | | | |
| Mucoepidermoid Carcinomo | 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 4: Diagnostic Performance of FNAC vs. Histopathology**

| Test / Gold standard ⇨ | HPE Positive | HPE Negative | Total | Metric/Value |
|---|---|---|---|---|
| **BENIGN LESIONS (n = 36)** | | | | **Performance Metrics** |
| **FNAC Positive (+)** | 24 (TP) | 0 (FP) | 24 | Sensitivity = 85% |
| **FNAC Negative (−)** | 4 ( FN) | 8 (TN) | 12 | Specificity = 100% |
| **Total** | **28** | **8** | **36** | **PPV = 100%** |
| | | | | NPV = 66% |
| | | | | **Diagnostic Accuracy = 85%** |
| **MALIGNANT LESIONS (n = 36)** | | | | **Performance Metrics** |
| **FNAC Positive (+)** | 7 (TP) | 0 (FP) | 7 | Sensitivity = 87.5% |
| **FNAC Negative (−)** | 1 (FN) | 28 (TN) | 29 | Specificity = 100% |
| **Total** | **8** | **28** | **36** | **PPV = 100%** |
| | | | | NPV = 96.5% |
| | | | | **Diagnostic Accuracy = 87.5%** |
| TP = True Positive \| FP = False Positive \| FN = False Negative \| TN = True Negative | | | | |
| PPV = Positive Predictive Value \| NPV = Negative Predictive Value \| FNAC = Fine Needle Aspiration Cytology \| HPE = Histopathological Examination | | | | |

**Table 5: Clinical Parameters — Benign vs. Malignant (Chi-square, p<0.05)**

| Parameter | Category | Benign (no) | Benign (%) | Malignant (no) | Malignant (%) | Total | P value |
|---|---|---|---|---|---|---|---|
| **Consistency** | Doughy | 8 | 28.6% | 0 | 0.0% | 8 | |
| | Firm | 20 | 71.4% | 6 | 75.0% | 26 | |
| | Hard | 0 | 0.0% | 2 | 25.0% | 2 | |
| | Total | 28 | 100% | 8 | 100% | 36 | <0.05* (S) |
| **Site of Lesion** | Parotid | 17 | 60.7% | 7 | 87.5% | 24 | |
| | Submandibular | 11 | 39.3% | 1 | 12.5% | 12 | |
| | Total | 28 | 100% | 8 | 100% | 36 | <0.05* (S) |
| **Cellularity** | Moderate | 26 | 92.9% | 0 | 0.0% | 26 | |
| | High | 2 | 7.1% | 8 | 100% | 10 | |
| | Total | 28 | 100% | 8 | 100% | 36 | <0.05* (S) |

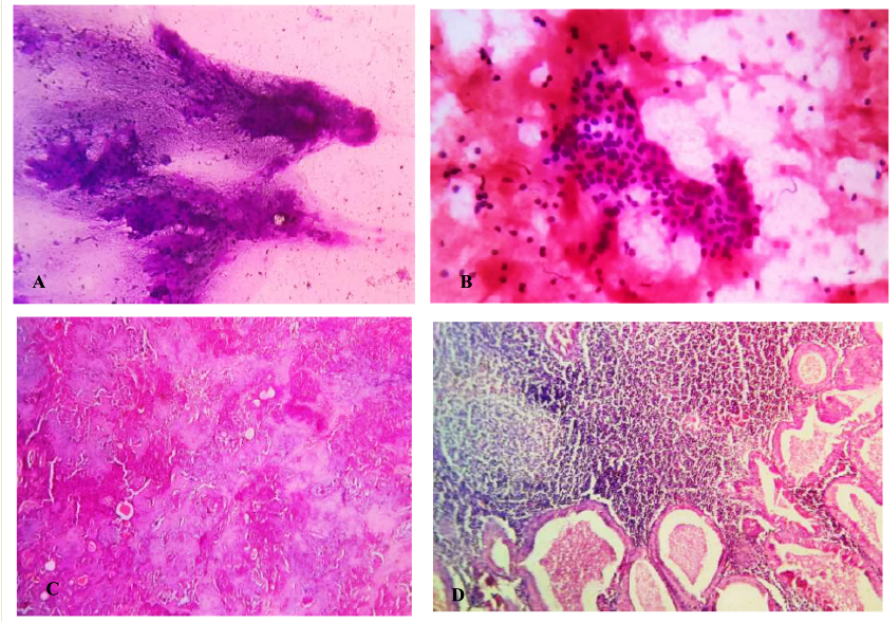


**Figure 1: Cyto-histopathological correlation of benign salivary gland tumors (A) H&E, 40 X magnification, cytology of pleomorphic adenoma (B) H&E, 40 X magnification, cytology of warthin's tumor (C) H&E, 20 X magnification, histopathology of pleomorphic adenoma (D) H&E, 20 X magnification, histopathology of warthin's tumor**

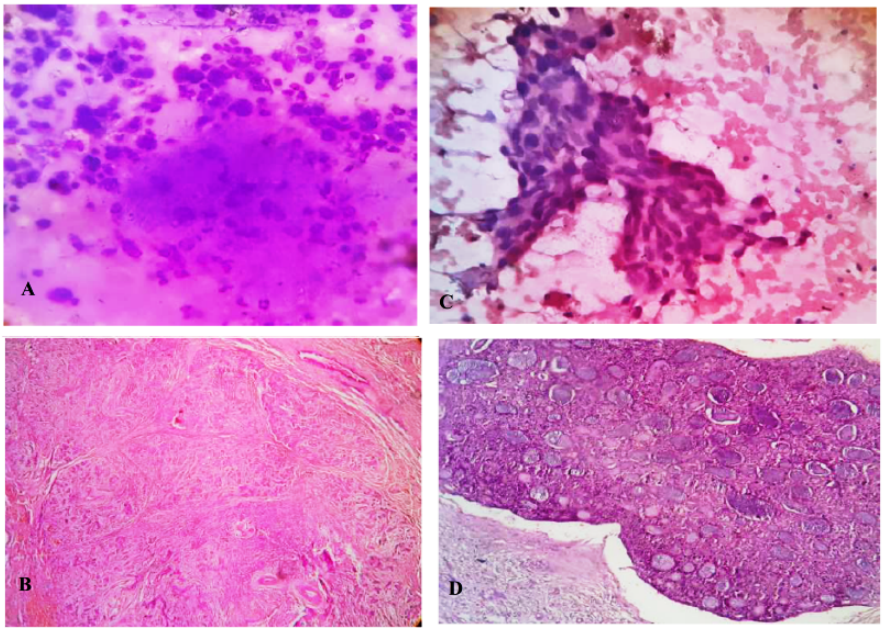


**Figure 2: Cyto-histopathological correlation of malignant salivary gland tumors (A) H&E, 40 X magnification, cytology of mucoepidermoid carcinoma (B) H&E, 20 X magnification, histopathology of mucoepidermoid carcinoma (C) H&E, 40 X magnification, cytology of adenoid cystic carcinoma (D) H&E, 20 X magnification, histopathology of adenoid cystic carcinoma**

## Discussion

Major salivary gland lesions are common and the associated histopathology is extremely varied and complex, due to the co-occurrence of non-neoplastic lesions, epithelial and non-epithelial neoplasms, metastatic tumors, and lymphomas. Though the typical morphology of most salivary gland lesions is predictable, many confounding factors make FNAC smears difficult to interpret — cytomorphology alone is often insufficient to conclude a definitive malignant diagnosis, and some salivary gland malignancies can only be differentiated from their benign counterparts by the presence of capsular invasion, which is not assessable by FNAC.

**Demographics and Clinical Profile:** The present study demonstrates a male predominance (60%) with a mean age of 47.7 ± 11.9 years, consistent with data from Sharma et al. [9] (2015), Kakoty et al. [14] (2017), and Ramana et al. [1] (2017). Parotid gland involvement (60%) was consistent across the cited literature. [11,3,5,21] Malignant lesions showed statistically longer symptom duration ($p < 0.05$) — an important clinical predictor. Hard consistency was exclusively associated with malignancy, while doughy consistency uniformly predicted Warthin's tumor on histopathology. High cellularity on smears showed a 100% correlation with malignant diagnosis ($p < 0.05$), emphasizing its value as a rapid screening parameter. The significant associations between consistency, site, and cellularity with the nature of the lesion ($p < 0.05$) reinforce the indispensable role of clinical parameters in cytopathological interpretation. [6,13]

**Non-Neoplastic Lesions:** In the present study, sialadenitis constituted 20% of all cases, representing the most common non-neoplastic lesion. [3,9] Histopathological correlation was accurate in 50% of non-neoplastic cases. Joshi AR et al. [15] (2017) reported about 21.9% cases of chronic sialadenitis, and Sharma M et al. [9] (2015) reported about 12.5% — values broadly similar to the present findings. The submandibular gland was more frequently involved in sialadenitis (n=4) than the parotid (n=2), consistent with the higher prevalence of sialolithiasis-associated ductal obstruction in Wharton's duct. [21]

Among the 2 cases of sialadenosis reported cytologically showing clusters of large vacuolated acinar cells, Christensen et al. 2016 cautioned that in sialadenosis, numerous acinar cells with maintained architectural arrangement should not be confused with well-differentiated acinic cell carcinoma — the clinical and radiological context, particularly bilateral painless parotid enlargement associated with systemic conditions (diabetes, hypothyroidism, alcoholic cirrhosis), is decisive. [22] W.C. Faquin et al. 2015 highlighted that the common pitfall in chronic sialadenitis is the misinterpretation of metaplastic or atrophic ductal cells as a basaloid neoplasm. In contrast, chronic sialadenitis lacks the three-dimensional epithelial groups and degree of cellularity characteristic of aspirates from a basaloid neoplasm.

Three of 8 cytologically diagnosed chronic sialadenitis cases were histopathologically confirmed as Warthin's tumor — a discrepancy attributable to the lymphocyte-rich background shared by both entities. Swati Sahni et al. [7] (2017) similarly reported that predominance of lymphoid cells in Warthin's tumor may lead to misdiagnosis as lymphoepithelial cyst. Collela et al. 2015 reported that acinic cell carcinoma (which often has a lymphocyte-rich stroma), malignant lymphoma, benign lymphoepithelial lesions, and lymphoepithelial cysts all share lymphocyte-rich aspirate backgrounds, compounding this diagnostic challenge.

A case of granulomatous lesion involving the parotid gland was reported cytologically, showing groups of epithelioid histiocytes and multinucleated giant cells with inflammatory cells; histopathological correlation could not be obtained in this case. Mihashi et al. 2015 suggested that in cases with marked granulomas, care should be taken to avoid misinterpreting epithelioid histiocytes with moderate eosinophilic cytoplasm as an epithelial neoplasm.

**Benign Neoplastic Lesions:** Pleomorphic Adenoma: Among benign lesions, pleomorphic adenoma was the most common, constituting 42.2% of histopathological cases. The present study showed a diagnostic accuracy of 84% for pleomorphic adenoma and 62% for Warthin's tumor, which were significantly better than the 76% accuracy reported by the Malaysian J Pathol study 2017. [5] Sharma et al. [9] (2015) reported 68.7%, Kakoty et al. [14] (2017) reported 44%, and Nanda et al. 2014 and Cohen et al. 2014 all documented a higher incidence of pleomorphic adenoma in the parotid gland. On cytology, the presence of chondromyxoid stroma, particularly red-staining intercellular aggregates on MGG, is the most characteristic finding.6 Viguer et al. 1997 [16] stated that metaplastic cells — oncocytic, sebaceous, and squamous — may occasionally be seen in pleomorphic adenoma.

Warthin's Tumor: All 8 cytologically diagnosed Warthin's tumors were confirmed on histopathology. They presented as doughy, painless masses exclusively in the parotid gland and periparotid lymph nodes. [21] Klijanienko and Vielh et al. 1997 [17] noted that mast cells are commonly associated with oncocytes in Warthin's aspirates.

The characteristic finding is the combination of bland oncocytic cells in cohesive monolayered sheets, a lymphoid background, and granular amorphous debris on MGG. [17] Oncocytoma must be distinguished from Warthin's tumor: oncocytomas consist of epithelial cells only and lack the dirty cystic background; Cohen et al. 2014 noted that mucin-containing cystic spaces, if present in an oncocytic lesion, should raise suspicion of the oncocytic variant of mucoepidermoid carcinoma.

Cytohistological Discordance — PA vs. Myoepithelioma: Two cases cytologically diagnosed as pleomorphic adenoma were confirmed as myoepithelioma on histopathology. This discordance arises because both share a predominance of myoepithelial cells; however, myoepithelioma lacks the biphasic ductal-myoepithelial pattern and chondromyxoid stroma characteristic of PA. When myoepithelial cells display clear cytoplasm, the differential diagnosis expands to include epithelial-myoepithelial carcinoma, sebaceous adenoma, myoepithelial carcinoma, and even metastasis. Immunostaining with HMW keratin, P63, smooth muscle keratin, and calponin is necessary to confirm myoepithelial differentiation.

**Diagnostic Pitfalls: PA/MEC Interface:** The most clinically significant pitfall in this study was the cytomorphological overlap between pleomorphic adenoma and low-grade mucoepidermoid carcinoma. Four cases given a differential cytological diagnosis of PA/low-grade MEC were all confirmed as MEC on histopathology. Kotwal et al. 2007 observed that smears containing myxoid stroma were diagnosed as pleomorphic adenoma, while excision showed low-grade mucoepidermoid carcinoma; bland intermediate cells were misidentified as myoepithelial cells of PA. Swati Sahni et al. [7] (2017) described an interpretation difficulty in cases of PA harboring mucin, creating a potential trap for erroneous MEC diagnosis. Kakoty S et al. [14 (2017) suggested that goblet cells or squamous metaplasia in PA should be approached cautiously as a possible indicator of low-grade MEC. Baloch et al. 2014 further stated that it is critical to exclude adenoid cystic carcinoma from the differential when facing a matrix-producing tumor.

Practical discriminating criteria for the PA/MEC interface include:

- Myxochondroid and fibrillary stroma is absent in MEC but characteristic of PA [6]
- Plasmacytoid cells are a reliable marker for PA; they have not been described in MEC [11]
- Keratinization in squamous cells is more pronounced in PA than in MEC
- A pure population of intermediate cells in mucoid pools strongly supports MEC

Das et al. 2004 [18] noted that pleomorphic adenoma is commonly misdiagnosed as adenoid cystic carcinoma due to hyaline stromal globules; however, the absence of chondromyxoid stroma

and of foci of squamous metaplasia in adenoid cystic carcinoma is a key discriminating feature.

Postema et al. 2004 added that the nuclei of adenoid cystic carcinoma tend to be hyperchromatic and angulated rather than bland and uniform as in polymorphous low-grade adenocarcinoma.

**Diagnostic Pitfalls: Warthin's Tumor/MEC Interface:** Two cases given a differential cytological diagnosis of Warthin's tumor/MEC were both confirmed as MEC on histopathology. The mucoid cystic content of low-grade MEC closely mimics the turbid aspirate of Warthin's tumor. Swati Sahni et al. [7] (2017) reported the same pitfall. Collela et al. 2015 further warned that acinic cell carcinoma, malignant lymphoma, chronic sialadenitis, lymphoepithelial cyst, and benign lymphoepithelial lesions all produce lymphocyte-rich aspirates that can be confused with Warthin's tumor. Lymphoepithelial sialadenitis lacks the oncocytic epithelium and dirty cystic debris that typify Warthin's tumor and should also be excluded; patients with Sjögren's syndrome and lymphoepithelial sialadenitis carry an increased risk of developing extranodal marginal zone lymphoma. [13,21]

**Malignant Lesions:** Among malignant neoplasms, mucoepidermoid carcinoma (MEC) was the most common, constituting 13.3% (n=7) on histopathology. The overall diagnostic accuracy for malignant lesions in this study was 87.5% with a specificity of 100%. Similar findings were reported by Sharma M et al. [9], Yogambal M et al. [2] (2015), Kakoty S et al. [14] (2017), and S.V. Ramana et al. [1] (2017). Neha Sikdar et al. [11] (2018) suggested that high-grade MEC containing malignant squamous epithelial cells is difficult to distinguish from metastatic squamous cell carcinoma; a preceding history of head and neck cutaneous SCC and the absence of mucin-positive epithelial cells assists in the differential. Overall malignancy was more common in the parotid gland (7 cases, 20%) compared to the submandibular gland (1 case, 3%).

Two cases reported cytologically as 'cystic lesion with possibility of cystic degeneration' were diagnosed as low-grade mucoepidermoid carcinoma on histopathology, demonstrating that cystic salivary gland lesions should never be dismissed without follow-up histopathological evaluation.

One case of salivary duct carcinoma on FNAC was confirmed by histopathology. Tessy PJ et al. [19] emphasized that distinguishing salivary duct carcinoma from high-grade metastasis to the salivary gland from a primary elsewhere (breast, prostate, and lung) is of critical clinical importance, requiring immunohistochemistry and clinical correlation.

Klijanienko, El-Naggar, and Vielh 1999 found that carcinoma ex pleomorphic adenoma carries the highest false negative rate on FNAC, and Verma and Kapila 2002 reported that all cases of carcinoma ex pleomorphic adenoma in their series were misinterpreted as benign on cytology — a warning particularly relevant for cases of a rapidly growing longstanding parotid mass. [21]

**Clinical Implications and Reporting Framework:** FNAC should be discouraged in patients without a palpable or radiologically detectable mass, as the risk of false negative diagnosis is high. Rapid on-site evaluation (ROSE) is recommended wherever feasible, as it allows immediate assessment of adequacy, reduces repeat FNAC rates, and facilitates triage of material for cell blocks, flow cytometry, and immunophenotypic analysis for suspected lymphomatous lesions. [22] E.D. Rossi et al. 2017 emphasized that the reporting system should emphasize risk stratification rather than specific diagnosis alone, providing management ranges for each risk category rather than a binary benign/malignant outcome for every case. FNAC has some acknowledged complications including localized bleeding, post-aspiration squamous metaplasia, fibrosis, and necrosis on final histopathological examination; however, these generally do not interfere with the final diagnosis and do not alter the favorable risk-benefit profile of the procedure.

**Limitations:** This study is limited by its single-center prospective design, a 12-month study period, and a sample of 45 cases. Common salivary gland lesions such as lymphoepithelial sialadenitis, various cysts (branchial, thyroglossal, dermoid), basal cell adenoma, acinic cell carcinoma, polymorphous low-grade adenocarcinoma, and epithelial-myoepithelial carcinoma were not encountered due to this limited timeframe, restricting the scope of pitfall analysis for these entities. Ultrasound guidance was not uniformly applied, which may have contributed to the cystic lesion misclassification noted above.

## Conclusions

The present study confirms that FNAC is a safe, economical, and high-accuracy pre-operative technique for major salivary gland lesions, with sensitivity of 85% and 87.5%, and specificity of 100% for benign and malignant lesions respectively. There was almost perfect agreement between cytological and histological diagnosis; FNAC complemented histopathology to make the final diagnosis reliable and accurate for therapeutic planning. The most common lesion in both

cytology and histology was pleomorphic adenoma, while mucoepidermoid carcinoma was the most common malignancy. Clinical parameters — consistency, site, and cellularity — showed statistically significant associations ($p < 0.05$) with the nature of the lesion and should routinely guide cytological interpretation. The PA/MEC interface and Warthin's tumor/MEC overlap represent the most important diagnostic pitfalls; awareness of their distinguishing cytomorphological criteria is essential for practice.

Multiple sampling from various sites reduces misinterpretation. FNAC remains the cornerstone of pre-operative workup for all major salivary gland swellings and, when interpreted in conjunction with clinical findings and imaging, delivers consistently high diagnostic accuracy.

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