



Original Article

A Retrospective Institutional Study with Emphasis on Fine Needle Aspiration Cytology of Pleomorphic Adenoma

Shubhani Singh¹, Bhagyashree², Ojasvi Ramesh³, Rituraj⁴

¹MBBS, MD (Pathology), Senior resident, Department of Pathology, VCSGGIMS&R, Srinagar, Uttarakhand, 246178 India.

^{2,3,4}MBBS, MD (Pathology) Assistant Professor, Department of Pathology, Government Medical College, Haldwani, Uttarakhand, 263139, India.

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Corresponding Author:

Dr. Ojasvi Ramesh

MBBS, MD (Pathology) Assistant Professor, Department of Pathology Government Medical College, Haldwani, Uttarakhand, 263139, India.

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ABSTRACT

Background: Salivary gland lesions include many neoplastic and non-neoplastic lesions. Fine needle aspiration cytology (FNAC) is often the first-line, pre-operative diagnostic procedure. Here, we investigate the cyto-histopathological concordance in salivary gland lesions focusing on pleomorphic adenomas (P.A.).

Methods: A retrospective analysis of 50 salivary gland lesions that were surgically excised over 2 years (2023-2025) was performed. Pre-operative FNAC was performed in 32 of the cases. Calculated values included sensitivity, specificity, positive and negative predictive values, and Cohen's kappa coefficient. For other analyses, FNAC results were compared using Fisher's exact test.

Results: The average age of the patients was 38.1 ± 14.0 years, with ages ranging from 13-77 years, and there was a nearly equal distribution of males and females (M: F=1.08:1). The most frequent diagnosis of the cohort was pleomorphic adenomas (n = 20, 40%). The FNAC had a sensitivity of 89.3% and a specificity of 75% in assessing neoplastic lesions, while a sensitivity of 87.5% and a specificity of 100% were achieved in assessing malignant lesions. The overall concordance of the paired cyto and histopathological assessments was 78.1% (n = 32). For neoplastic lesions, Cohen's kappa was 0.529, while assessment of malignant lesions yielded a kappa of 0.909, and for pleomorphic adenomas kappa was 0.936, indicating almost perfect concordance. The rate of inadequate FNAC was determined to be 9.4%.

Conclusion: FNAC is particularly accurate for salivary gland lesions, pleomorphic adenomas, and malignant lesions. FNAC is a good diagnostic, economical, and reliable pre-operative procedure. There are challenges with inadequate FNAC and diagnosis of lesions with similar morphologies, and therefore FNAC results should be correlated with clinical and imaging findings.

Keywords: Salivary gland; pleomorphic adenoma; FNAC; cytology; histopathology; cyto-histopathological correlation; Cohen's kappa.

INTRODUCTION

Salivary gland neoplasms are approximately 6% of head and neck tumours and have a wide histopathological spectrum with more than 40 variants in WHO classifications. The clinical similarity of these lesions is high, and the biological heterogeneity is given the need for an accurate diagnosis well before surgery.¹

Fine needle aspiration cytology (FNAC) is a rapid, cost effective and minimally invasive technique for preliminary diagnosis of salivary gland masses.² However, because of the morphological complexity and inter-tumor heterogeneity of salivary gland neoplasms, diagnostic difficulties may arise resulting in negative, positive and equivocal FNAC reports despite the lower morbidity associated with FNAC.^{3,4}

Pleomorphic adenoma (P.A.) is the most common benign salivary gland neoplasm and characterized by a unique dual epithelial-myoepithelial differentiation and marked histological variety. P.A. requires FNAC to be correctly diagnosed and to avoid misdiagnosis as low- grade malignancy. The sensitivity of FNAC is reported to be 85-96% for P.A. but there are reports of misdiagnosis in the presence of keratinous cysts, squamous metaplasia and myxoid stroma.⁵

The present study is aimed to analyse the cyto-histopathological data of patients with salivary gland lesions in a tertiary care teaching hospital. To evaluate the diagnostic efficacy of FNAC in benign, malignant and non-neoplastic salivary gland lesions and describe the cytological tracings necessary for the diagnosis of P.A.

MATERIALS AND METHODS

Study Design and Case Selection

This was a retrospective study conducted in the Department of Pathology of a tertiary care hospital. The organized histopathology archives of the department from 2023 to 2025 were reviewed. All the histopathology records of salivary gland lesions were included, regardless of patient age.

Data collection

Patient age and sex, affected gland site, clinical diagnosis, and histopathological and cytopathological diagnosis (if any) were all documented. Findings were confirmed by reviewing the respective slides.

Classification

Diagnoses were classified into (1) Benign Neoplastic (2) Malignant Neoplastic, and (3) Non-neoplastic/Inflammatory. Additionally, FNAC was classified into adequate neoplastic, adequate non-neoplastic, suspicion of malignancy, and inadequate/unsatisfactory. Cyto-histo-pathological concordance was also assessed at the level of neoplastic vs. non-neoplastic, and at the level of specific entity, when applicable.

Statistical Analysis

For discrete data, counts and percentages were used, while means and standard deviations (SD) were used for continuous data. In the context of this study, histopathological diagnosis was considered the gold standard. Hence, the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and test accuracy, and the overall accuracy of the test, were also determined. Due to small sample sizes, significance was determined by Fisher's exact test. Cohen's Kappa was calculated to determine the degree of concordance between FNAC and histopathology. Cohen's Kappa was also calculated for the classification of neoplasia as malignant and benign, and for the classifications of non-neoplastic and inflammatory. Kappa values of <0.2 were considered to indicate slight, fair, and moderate agreement; values between 0.61-0.8 were taken as substantial agreement, and 0.81-1.0 as near-perfect agreement. A Kappa value of <0.05 was deemed statistically significant. The analyses were done in Python.

RESULTS

Demographic Profile

Of the 50 included specimens, the age of patients ranged between 13 and 77 years with a mean of 38.1 years with a standard deviation (SD) of 14.0 years. The gender distribution was 26 males and 24 females with a male to female ratio of 1.08.

Table 1: Demographic and Gland-wise Distribution of Salivary Gland Lesions (n=50)

Parameter	Number (n=50)	Percentage (%)
Male	26	52.0%
Female	24	48.0%
Age (mean $\pm$ SD)	38.1 $\pm$ 14.0 yrs	(range: 13–77)
Parotid gland	29	58.0%
Submandibular gland	10	20%
Minor salivary glands	11	22%

Gland-wise Distribution

The parotid gland was the most involved (n=29) in this study. Other sites were the minor salivary glands(n=11,22%), and the submandibular glands (n=10,20%).

Histopathological Diagnoses

The most frequent diagnosis was pleomorphic adenoma (n=20, 40%). This included one recurrent case and one case of the cellular variant of pleomorphic adenoma. Of the 50 cases, (n=7,14%) were malignant salivary gland tumors. Non-neoplastic lesions (n=17, 34%) included chronic sialadenitis (n=6, 12%) and retention cysts/mucoceles (n=5, 10%) as the most frequent lesions.

Table 2: Distribution of Histopathological Diagnoses (n=50)

Histopathological Diagnosis	N	%
BENIGN NEOPLASMS		
Pleomorphic Adenoma (P.A.)	20	40.0
(including Recurrent P.A.)	(1)	
Warthin Tumour	1	2.0
Basal Cell Adenoma	1	2.0
MALIGNANT NEOPLASMS		
Adenoid Cystic Carcinoma	4	8.0
Mucoepidermoid Carcinoma	2	4.0
Acinic Cell Carcinoma	1	2.0
Squamous Cell Carcinoma	1	2.0
Polymorphous Adenocarcinoma	1	2.0
Low Grade Intraductal Carcinoma	1	2.0
Poorly Differentiated Metastatic Carcinoma	1	2.0
NON-NEOPLASTIC LESIONS		
Chronic Sialadenitis	5	10.0
Retention Cyst / Mucocoele	5	10.0
Mild Chronic Parotitis / Fibrosis	3	6.0
Sjogren's Syndrome / Sicca	2	4.0
Chronic Sclerosing Sialadenitis (Kuttner)	1	2.0
Normal	1	2.0
TOTAL	50	100

Cyto- Histo-Pathological Correlation

Of the 32 cases, 25 (78.1%) FNAC and histopathology were concordant. In the 7 discordant cases (21.9%), 3 cases were of inadequate FNAC sample. In the remaining 4 cases, active discordance between FNAC and histopathology was noted. The discordant cases included: (1) inadequate FNAC sample for Polymorphous Adenocarcinoma (P.A.); (2) misdiagnosed case of sialadenitis as NHL (poorly differentiated malignant tumor) on FNAC (Figure 1a,1b); (3) polymorphous adenocarcinoma with unsatisfactory (SUMP) FNAC; (4) adenoid cystic carcinoma reported as 'suspicious for malignancy' on FNAC; and (5) squamous cell carcinoma reported as poorly differentiated adenocarcinoma NOS (Figure 2a,2b) (6) Inadequate FNAC sample and necrosis reported as chronic sialadenitis (Figure 3a,3b) (7) The cellular case of P.A. was reported as inadequate (INAD) on FNAC.

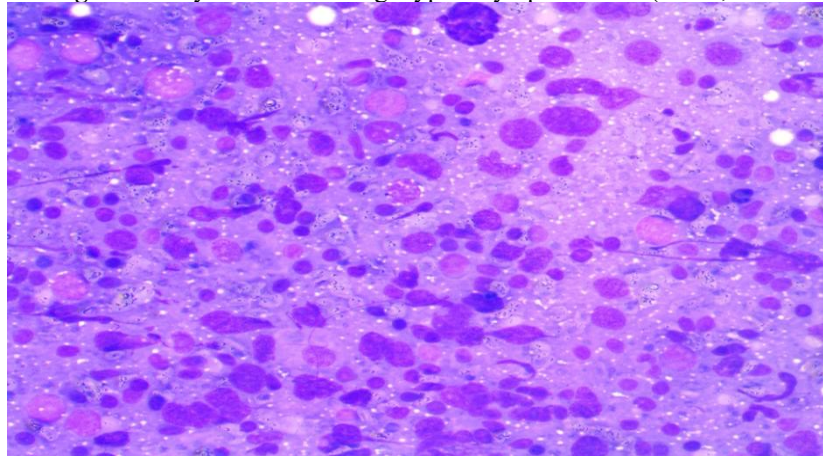
Figure 1a: Cytosmear showing atypical lymphoid cells (MGG, x400)

Figure 1b: Histopathological section showing dense lymphocytic infiltration with prominent lymphoid aggregates replacing salivary gland parenchyma, consistent with chronic sialadenitis (H&E, ×400)

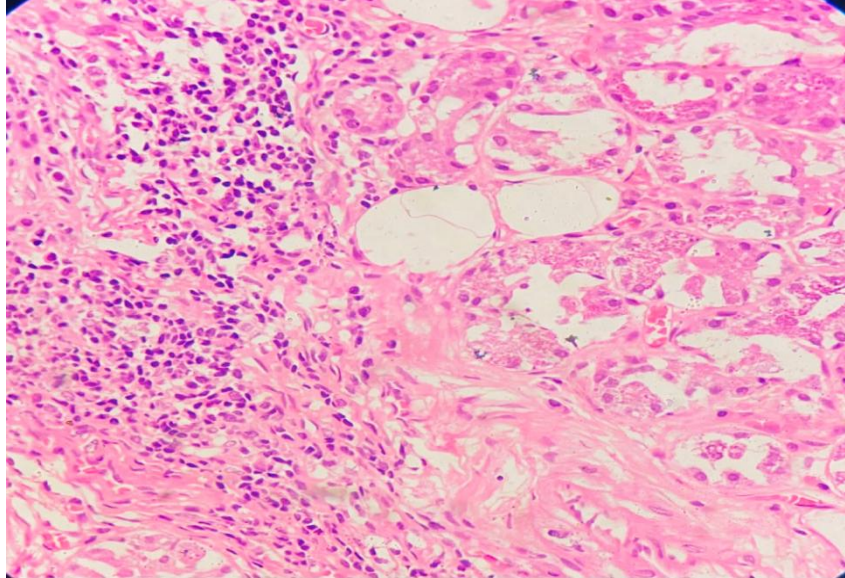


Figure 2a: FNAC smear showing discohesive pleomorphic malignant epithelial cells (MGG, X400)

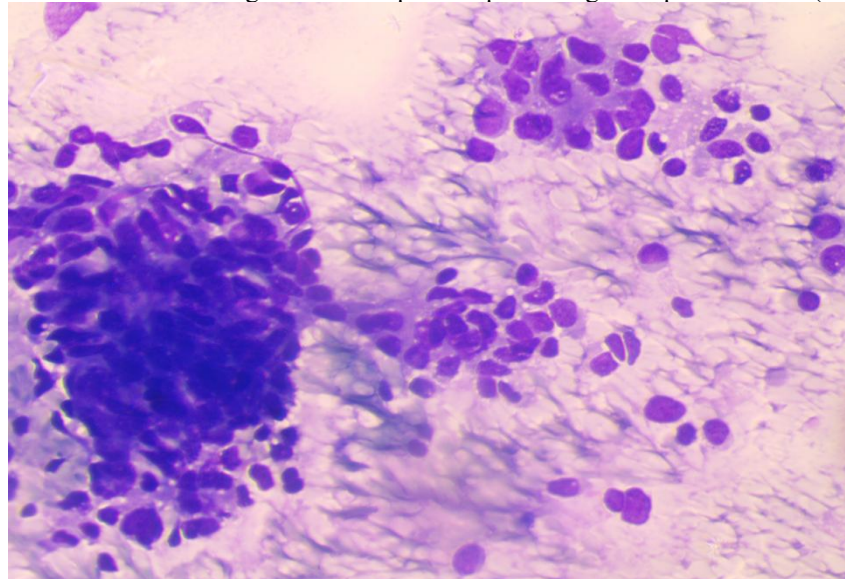


Figure 2b: Histopathological section showing infiltrating nests and sheets of malignant squamous cells exhibiting nuclear pleomorphism, hyperchromasia, and keratinization, consistent with squamous cell carcinoma (H&E, X400).

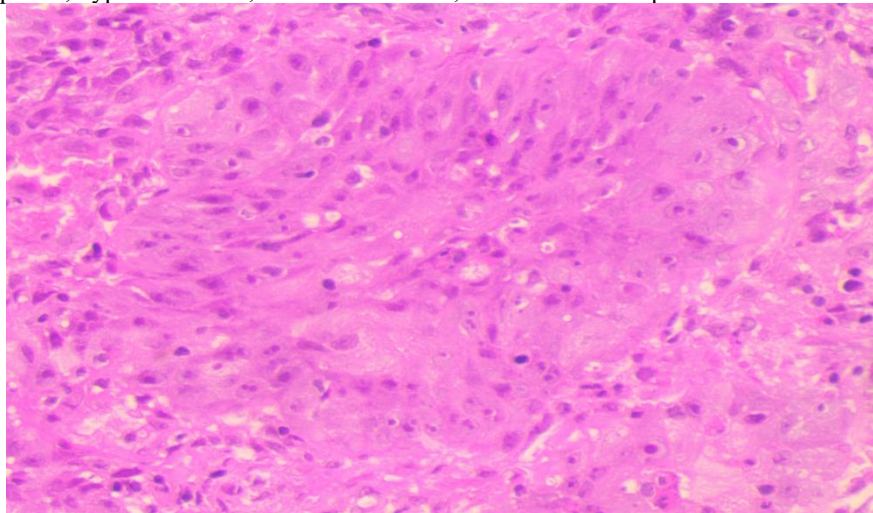


Figure 3a: Cytosmear showing necrosis (MGG, X400)

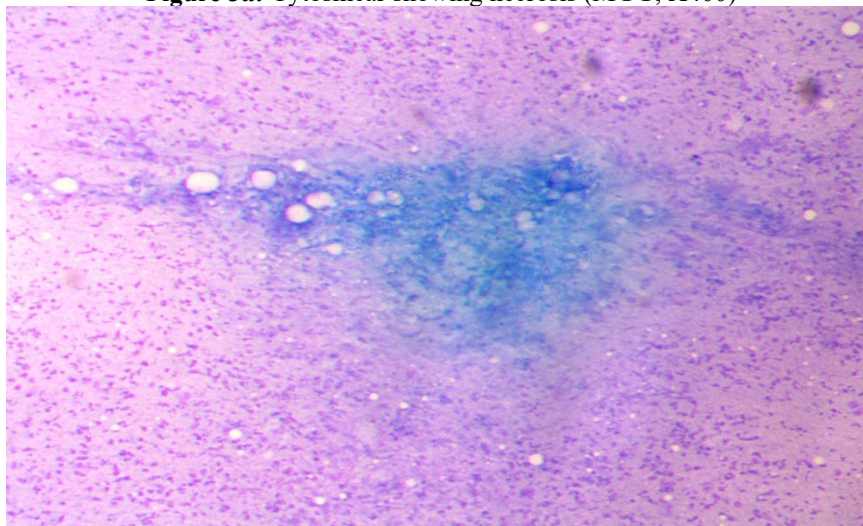


Figure 3b: Histopathology revealing chronic sialadenitis characterized by dense lymphoid aggregates with associated acinar destruction and ductal preservation (H&E, ×100).

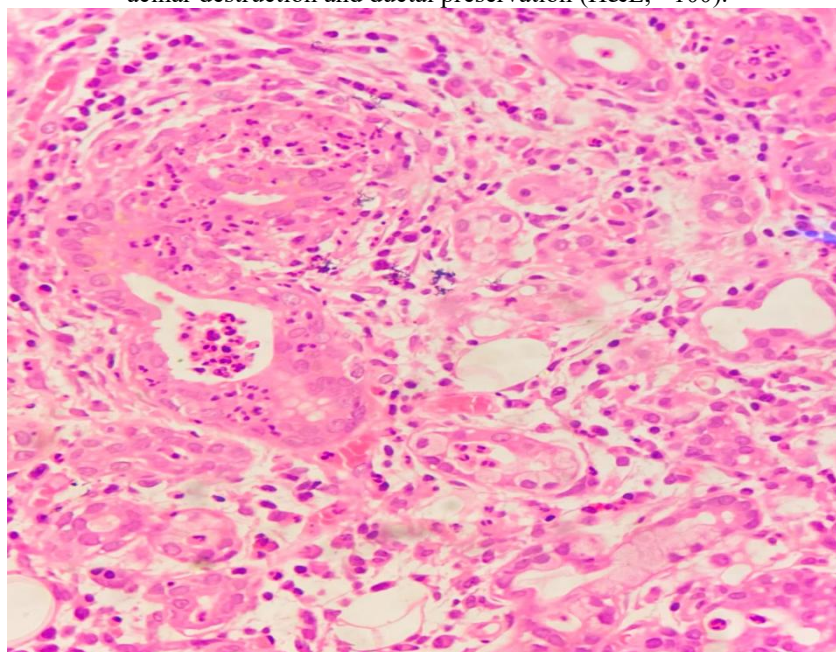


Table 3: Cyto-Histopathological Correlation Matrix (n=32 paired cases)

FNAC Diagnosis	Histology confirmed	Histology discordant	Inadequate/Unsatisfactory	Total
Pleomorphic Adenoma	18	1 (Inadequate)	—	19
Adenoid Cystic Carcinoma	1	—	—	1
Acinic Cell Carcinoma	1	—	—	1
Mucoepidermoid Carcinoma	1	—	—	1
Basal Cell Adenoma	1 (BCA)	—	—	1
Malignant (unclassified/CA)	2	—	—	2
Suspicious for Malignancy	1 (ACC)	—	—	1
Non-neoplastic / Inflammatory	1	1 (NHL/PDMT)	—	2
Normal	1	—	—	1
Inadequate / Unsatisfactory	—	2	1	3
TOTAL	27	4 (discordant)	1	32

Accuracy of FNAC Diagnosis

The sensitivity, specificity, PPV, NPV and overall accuracy of FNAC for detection of neoplastic vs. non-neoplastic lesions were 89.3%, 75.0%, 96.2%, 50.0% and 90.6%, respectively. The Fisher's exact test was significant ($p=0.015$) indicating a significant association between FNAC and histopathological neoplastic categorization.

In neoplastic cases FNAC for detection of malignancy showed sensitivity 87.5%, specificity 100%, PPV 100%, NPV 95.2% and accuracy 96.4%. Fisher's exact test gave $p<0.001$, indicating a highly significant association.

Specifically for P.A. 18 of 19 P.A. cases on histopathology were correctly identified on FNAC (sensitivity 94.7%). No non-P.A. case was misclassified as P.A. (specificity 100% in paired cases). FNAC rate was inadequate in 9.4% (3/32 cases).

Table 4: Diagnostic Performance of FNAC for Salivary Gland Lesions

Category	Sensitivity	Specificity	PPV	NPV	Accuracy
Neoplastic detection	89.3%	75.0%	96.2%	50.0%	90.6%
Malignancy detection	87.5%	100.0%	100.0%	95.2%	96.4%
P.A. specific	94.7%	100%*	100%	92.3%	96.9%

*Specificity for P.A. calculated among neoplastic paired cases only.

Cohen's Kappa Coefficient

Cohen's kappa for neoplastic vs. non-neoplastic classification was 0.529, indicating moderate agreement. For malignant vs. benign differentiation among neoplastic cases, kappa was 0.909, signifying near-perfect agreement. For the P.A.-specific diagnosis, kappa was 0.936, also reflecting near-perfect agreement between FNAC and histopathology.

DISCUSSION

The present study found that the modal age group for most of our patients (31-40 years) was 32%, whereas, for the next group (21-30 years), it was 26%. These findings were in agreement with the studies of Kakoty et al⁶ and S. Srikanth et al,⁷ where the maximum number of patients, (22% and 45%, respectively) were in the same age group. Contrary to these studies was that of A.A. Kumar et al,⁸ wherein the maximum cases were in the age group of 41-50 years (27.3%), followed by 31-40 years (22.7%). This is also in disagreement with the study of M.S. Misakyan et al,⁹ wherein the patients' age group of 51-60 years was (38%). The authors believe this discordance is due to the age demographics of the population of the different regions.

Considering the sex distribution of all salivary gland lesions, the present study noted a slight male predominance (52% vs 48%). This was in agreement with the studies of M.S. Misakyan et al⁹ and Hafiz et al.¹⁰ In these studies, the male population was 62.3% and 59%, respectively. In contrast to our findings were the studies of S. Srikanth et al,⁷ A.A. Kumar et al⁸ and A.U.C. de Melo et al,¹¹ wherein the females predominated and the males constituted 49%, 48%, and 45.17% of the total patients, respectively.

According to the current study, the parotid gland (38%) was the most common location for salivary gland lesions, followed by submandibular (18%) and minor salivary glands (22%). These findings were similar to S. Srikanth et al⁷ (63.75%), A.A. Kumar et al⁸ (72.7%), A.U.C. de Melo et al¹¹ (57.2%). All previous studies identified the parotid gland as the most commonly involved site, while minor salivary glands were reported to account for 16.58%, 24.2%, and 24% of cases, respectively. An inverse statistic was presented by JLS Cunha et al¹², who reported an overall greater frequency of involvement of minor salivary glands versus major salivary glands (68.9% versus 25.6%).

Major salivary glands exhibit higher rates of pathology and neoplasia than minor glands due to: 1. Greater parenchymal volume: A larger mass of functional tissue provides significantly more cellular targets for neoplastic mutations and systemic disease. 2. Complex ductal architecture: Extensive, branching ductal networks increase the risk of mechanical obstruction via sialolithiasis or mucus plugging.

Out of 50 cases, 44% were benign tumours, 34% nonneoplastic lesions followed by 22% malignant tumours of salivary gland. Our inferences were similar to the study by M.S Misakyan et al⁹, where also benign tumours (44.5%) were more prevalent than non-neoplastic lesions (42.3%) and only 13.2% cases comprised of neoplastic tumour. Most of the other studies including A.U.C de melo et al¹¹, GAQ Oliveira et al¹³ and A Hafiz et al¹⁰ didn't take into account non neoplastic lesions but benign tumours still comprised majority of the salivary gland lesions in these studies comprising of 57%, 72% and 79.9% respectively.

Benign salivary tumours occur more frequently than malignant ones primarily because about 80% of these tumours arise in the large parotid glands, where the biological environment strongly favours slower-growing, less aggressive cellular growths like Pleomorphic Adenomas.

Among neoplastic lesions, Pleomorphic Adenoma was the most common benign salivary gland tumour (40%) in our study. The observed findings were similar to almost all the other studies conducted, including studies by Kakoty et al⁶, A Kumar et al⁸ and S. Srikanth et al⁷ in which pleomorphic adenoma was the most common benign tumour comprising of 68%, 44% and 50% cases respectively.

Also, benign tumours predominantly develop from a mix of epithelial and myoepithelial cells. The complex, diverse nature of these cells allows them to proliferate abundantly in major glands without instantly triggering the rapid, invasive characteristics of malignancies. Unlike cancers of the oral cavity, salivary gland tumours are rarely linked to typical carcinogens like tobacco, heavy alcohol use, or HPV. Because the driver mutations aren't constantly spurred by toxic exposures, the baseline cellular growth in the major gland's favors localized, contained, and benign neoplasms over malignant ones.

While Adenoid cystic carcinoma is one of the most common salivary gland malignant tumour overall, it is actually the second most common malignancy in parotid gland. However, results of our study negated this theory, as adenoid cystic carcinoma was the most common MSGT observed, 8% of total cases and all these tumours were found in parotid gland, followed by mucoepidermoid carcinoma comprising of 4% of total cases found equally in parotid gland and submandibular gland respectively. Our result also coincided with the study done by S. Srikanth et al⁷ where, cases of adenoid cystic carcinoma were more than mucoepidermoid Carcinoma (14% vs. 6%). In our literature review, MEC was the most common malignant salivary gland tumour in most of the other studies done followed by adenoid cystic carcinoma. It presented at frequencies of 4% in study done by Kakoty et al⁶.

Among nonneoplastic diseases, parotid gland chronic sialadenitis was the most common diagnosis (79.6%) followed by mucous retention cyst (10%) in our study. This finding is in discordance with the study by A. Hafiz et al¹⁰ in which mucous retention cyst was the most common entity (21.10%). However, sialolithiasis was most common (33.6%) benign diagnosis in the study by Misakyan et al⁹ followed by chronic sialadenitis and abscesses of the parotid gland, which comprised of 8.6% cases.

The present study provides a comprehensive retrospective analysis of 50 salivary gland lesions with emphasis on cyto-histopathological correlation. The findings are broadly consistent with previously published data from tertiary care centres in the Indian subcontinent and globally.

The overall cyto-histopathological concordance of 78.1% in our study is comparable to, though slightly lower than, some published series reporting concordance rates of 85–95%. This may be attributable to the small sample size, the inclusion of morphologically challenging entities, and the 9.4% inadequate aspirate rate, which itself falls within the published range of 5–12% for FNAC of salivary gland lesions.

The kappa coefficient of 0.936 for P.A. reflects the high reliability of FNAC for this entity. The characteristic cytological triad cohesive epithelial cell clusters, plasmacytoid myoepithelial cells, and fibrillary metachromatic stroma renders P.A. cytologically distinctive. The single discordant P.A. case in our series yielded an inadequate aspirate, likely attributable to tumour consistency or suboptimal sampling technique. Importantly, one P.A. case demonstrated squamous metaplasia and numerous keratinous cysts on histopathology; FNAC in such cases must be interpreted with awareness of these potential pitfalls to avoid over-diagnosis as mucoepidermoid carcinoma or squamous cell carcinoma.

The near-perfect kappa (0.909) for malignant vs. benign classification underscores FNAC's high specificity for malignant salivary gland tumours (100% in our series). The false-negative case an adenoid cystic carcinoma reported as 'suspicious' reflects a well-recognized cytological challenge due to the morphological overlap between ACC and cellular P.A. with basaloid features. The case of squamous cell carcinoma reported as poorly differentiated adenocarcinoma NOS on FNAC illustrates a diagnostic pitfall in determining precise tumour type on cytology alone, though the clinically important neoplastic/malignant categorization was correctly identified.

The moderate kappa at the neoplastic vs. non-neoplastic level (0.529) was driven largely by three factors: the three inadequate aspirates, one non-neoplastic case (chronic sialadenitis) reported as NHL/poorly differentiated malignant tumour on FNAC, and one polymorphous adenocarcinoma yielding an unsatisfactory SUMP smear. These cases highlight the inherent limitations of FNAC in non-neoplastic lesions where aspirates may be paucicellular, and in rare malignancies where cytological recognition is difficult.

Retention cysts and mucocoeles (n=5) were all managed surgically without preoperative FNAC at our institution, consistent with practice in many centres where cystic swellings of minor glands are directly excised. Chronic sclerosing sialadenitis (Kuttner's tumour) is a rare entity that can clinically mimic a neoplasm and is best diagnosed on histopathology.

The study is limited by its retrospective design, the relatively small sample size over the study period, the absence of FNAC in 18 cases (predominantly non-neoplastic lesions of minor glands), and the lack of immunohistochemical correlation for rare entities. Prospective multicentre studies with larger cohorts are warranted.

CONCLUSION

FNAC is a reliable preoperative diagnostic tool for salivary gland lesions with high sensitivity and specificity, particularly for pleomorphic adenoma ($\kappa=0.936$) and malignant tumours (sensitivity 87.5%, specificity 100%). Overall, cyto-histopathological concordance was 78.1% in our series. The principal limitations are inadequate aspirate rates and diagnostic challenges in morphologically overlapping and rare entities. A multi-disciplinary approach integrating FNAC findings with clinical presentation and imaging is essential for optimal patient management. Histopathological examination remains the definitive gold standard.

Author Contributions (CRediT Taxonomy)

Shubhani Singh: Conceptualization, Methodology, Data Curation, Formal Analysis, Writing – Original Draft, Writing – Review & Editing.

Bhagyashree: Data Curation, Investigation, Writing – Review & Editing.

Ojasvi Ramesh: Data Curation, Investigation, Writing – Review & Editing, Supervision.

Rituraj: Conceptualization, Supervision, Project Administration, Writing – Review & Editing.

DECLARATIONS

Ethics Approval: The study was conducted in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee.

Consent to Participate: Patient consent was waived by the IEC given the retrospective, anonymised nature of the study.

Competing Interests: The authors declare no competing interests.

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Data Availability: Data are available from the corresponding author on reasonable request.

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