

# Diagnostic Cytological Yield with and without Ultrasound Guided Fine Needle Aspiration Cytology in Salivary Gland Lesions

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## Abstract:

**Background:** Fine Needle Aspiration Cytology is most commonly used primary diagnostic procedure in the salivary gland lesions. It is minimally invasive, well tolerated, rapid, and inexpensive with a high diagnostic accuracy. Fine needle aspiration cytology is sometimes done with the assistance of ultrasonography. Ultrasound guided fine needle aspiration cytology is comparatively more time consuming and costly procedure.

**Objective:** Compare and correlate the diagnostic cytological yield of conventional method of fine needle aspiration cytology with ultrasound guided fine needle aspiration cytology in salivary gland swellings in order to determine if ultrasonography has substantial advantage to justify additional cost and time.

**Materials & Method:** Random selection was used. Half of the randomized patients underwent Fine Needle Aspiration Cytology without help of ultrasonography and the other half underwent ultrasound guided Fine Needle Aspiration Cytology. A cell block was also processed for histology. Histopathological correlation with the surgical specimen was done in cases where surgical excision was carried out. All the stained cytological and histological slides were analyzed and compared. Data was computerized with window Statistical Package of Social Sciences version 22.

**Results:** The mean age of the study population was  $40.44 \pm 16.08$  years. The male to female ratio was 1.16:1. The sample size was 65. The parotid gland was involved in 38 (58.6%) patients, submandibular gland in 21 (32.3%) patients, submental gland in 2 (3.1%) patients and minor salivary gland was involved in 4 (6.2%) patients. The sensitivity of ultrasound guided fine needle aspiration cytology was 100% with specificity of 82.8%, Positive Predictive Value of 75%, Negative Predictive Value of 100% and diagnostic accuracy was 84.8% taking histopathology as gold standard. The sensitivity of conventional fine needle aspiration cytology was 80% with specificity of 96.3%, Positive Predictive Value of 100%, Negative Predictive Value of 96.3% and diagnostic accuracy was 93.75% taking histopathology as gold standard.

**Conclusion:** Fine needle aspiration cytology without additional ultrasound guidance should be used routinely for the diagnosis of salivary gland lesions as it will save the time and decrease the cost of the test with a high diagnostic accuracy.

**Keywords:** Salivary gland tumors, Fine Needle Aspiration Cytology, FNAC, Ultrasound guided FNAC, Cytology, Diagnostic yield

## Introduction

The salivary gland swellings can be broadly classified as non-neoplastic and neoplastic. The non-neoplastic lesions include inflammatory and cystic lesions whereas neoplastic category includes benign and malignant lesions.

Benign tumors are more common in this region and these generally appear after the fourth decade whereas the malignant counterparts can be seen in young age groups but are seen maximally after 60 years. Benign tumors specially of parotid region are more commonly seen in females than males but the incidence of malignant tumors is equal in both the genders.<sup>1</sup>The most common site for primary epithelial tumors of salivary gland origin is parotid glands, next in frequency is submandibular gland and less commonly is sublingual and minor salivary glands.<sup>2</sup> The commonest benign neoplasm of salivary glands is

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considered to be pleomorphic adenoma and most common malignant tumor is adenoid cystic carcinoma. Most of the tumors in the parotid gland are benign (66%) whereas majority of (82%) minor salivary gland tumors are malignant.<sup>1</sup> Over the years there has been a tremendous development in salivary gland cytology and now there is a unique system for reporting salivary gland lesions, the Milan classification.<sup>3</sup> Fine needle aspiration cytology gives a good preservation of cellular architecture with minimal damage and a very low risk of seeding of malignant cells and does not interfere with subsequent surgical management as compared to pre-operative surgical biopsy which was done previously.<sup>4</sup> FNAC gives rapid results and it can be repeated several times to obtain more material for diagnosis or special studies.<sup>5</sup> The interpretation of FNAC is a multistep process, the first step is to recognize whether the lesion is of salivary gland origin or not, next step is the recognition of cells and their morphology to correctly classify them into cystic, inflammatory or neoplastic lesion.<sup>6</sup> On the other hand, due to heterogenous nature of salivary gland lesions the cytological interpretation could be confusing in the diagnosis of rare entities or in cases where there is a considerable overlap in the cytological features specially when the aspirate is scanty or the lesion is deep seated. The restricted range of the angle of approach, localization of the lesion and other procedural limitations can increase false-negative rates to as high as 19%.<sup>7</sup> In such cases image guided aspiration can yield better results while minimizing risks. Imaging criteria can be used confidently to diagnose a few benign conditions such as cysts and lymph nodes. However, it is insufficient to differentiate benign from malignant lesions on hypoechoic imaging criteria as both lesions are mostly hypoechoic. The characteristics which are suggestive of malignant lesions like posterior shadowing, or heterogenous internal echogenicity, irregular margins and enlarged lymph nodes are suggestive of malignancy but there are no conclusive imaging features available which distinguishes neoplastic from non-neoplastic lesions including Doppler evaluation.<sup>8</sup> Few other limitations of USgFNAC are that the procedure can be time consuming due to longer duration for appointment with radiologists which also increases the cost of the test. Another limitation is higher rate of unsatisfactory aspiration from small lesions especially in the absence of on-site cytopathologist. USgFNAC does not yield a conclusive cytological diagnosis in the presence of poor cellular

quality, one study reports insufficient cellularity in about 6% to 25.5% of cases.<sup>9</sup>

Only a few large comparative studies have been done for evaluating this procedure for the assessment of salivary gland lesions. The main rationale of doing this study was to evaluate whether USgFNAC provides a better diagnostic cytological yield in salivary gland lesions as compared to the conventional method of FNAC without Ultrasound guidance or not.

## **Patients & Methods**

The present cross-sectional comparative study was conducted at Shaikh Zayed hospital Lahore during two years from Dec.2012 to Dec.2014. 65 patients were selected randomly. A signed informed consent and complete history was taken before doing any study related procedure and the patients were thoroughly counselled regarding the procedure. The sample size for this study was 65. It was estimated using already published literature using 95% confidence level, 10% precision with expected sensitivity of 93.3% and specificity of 95.7% for the diagnosis of benign and malignant lesions by FNAC with prevalence of 75%.<sup>5</sup> Half of the selected patients underwent Fine Needle Aspiration cytology without ultrasound guidance and the other half underwent USgFNAC in the radiology department.

### **Sampling Technique**

The sampling technique used was convenient sampling and we randomized the patients alternatively into either study group. This selection was done by alternate method. The lesions were aspirated using 22-gauge needle and 10 cc syringe attached to it. Alcohol fixed slides were stained with Hematoxylin and Eosin stain and Papanicolaou stain. May-Grunwald-Giemsa (MGG) method was used for staining the remaining half slides which were air dried. A cell block was also processed for histology examination. All the slides were examined under microscope and the lesion classified accordingly.

The formalin fixed specimens were stained with Hematoxylin and Eosin stain for histopathological correlation in cases where surgical excision was carried out. All the stained cytological and histological slides were analyzed and compared.

### **Data Analysis Plan:**

Data was entered and analyzed by using Statistical Package for Social Sciences (SPSS) version 22.0

Data for the type of lesion was reported by using frequency and percentages.

The diagnostic efficacy parameters included Sensitivity, Specificity, Positive Predictive Value

(PPV), Negative Predictive Value (NPV) and Accuracy of FNAC against histological findings for each type of lesion. It was presented separately for guided aspirates and for those done blindly.

Overall Accuracy of FNAC was reported which were carried out with and without ultrasound guidance.

### Results & Discussion

In this present study total 65 cases were enrolled. The mean age of the patients was 40.44±16.08 years with minimum and maximum ages of 4 & 75 years respectively. 53.85% patients were male and 46.15% patients were females. The male to female ratio of the patients was 1.16:1. The study results showed that the parotid gland was involved in 38 (58.6%) patients, submandibular gland in 21 (32.3%) patients and submental gland in 2 (3.1%) patients whereas the minor salivary glands were involved in 4 (6.2%) patients only.

These results are almost in accordance with a study done by Anwar et al in which the mean age of patients was 41.28±13.06 years, the ages varied from 20 to 78 years and parotid gland was involved in 59.6% of cases.<sup>10</sup>

Conventional FNAC was done in 32 cases, out of which 1 sample was inadequate or non-diagnostic so the diagnostic cytological yield was 97%. Whereas ultrasound guided FNAC was done in 33 cases and 5 out of these aspirates came out to have an inadequate or non-diagnostic cytological yield with a diagnostic cytological yield of 85%.

**Table 1: Frequency distribution of the lesions diagnosed on FNAC**

|                  | Conventional FNAC                   | USgFNAC   | Total     |    |
|------------------|-------------------------------------|-----------|-----------|----|
| <b>Benign</b>    | Benign cystic lesion                | 1         | 2         | 3  |
|                  | Sialadenitis                        | 2         | 1         | 3  |
|                  | Chronic-granulomatous inflammation  | 4         | 3         | 7  |
|                  | Reactive lymph node                 | 0         | 1         | 1  |
|                  | Pleomorphic adenoma                 | 17        | 15        | 32 |
|                  | Warthin tumor                       | 3         | 2         | 5  |
|                  | <b>Inadequate</b>                   | 1         | 5         | 6  |
| <b>Malignant</b> | Adenocarcinoma                      | 1         | 0         | 1  |
|                  | Metastatic carcinoma                | 0         | 2         | 2  |
|                  | Undifferentiated/malignant neoplasm | 3         | 2         | 5  |
| <b>Total</b>     | <b>32</b>                           | <b>33</b> | <b>65</b> |    |

FNAC results (Table 1) showed that out of total 65 cases, 51 (78.4%) were classified as benign lesions, 8(12.3%) as malignant and 6 could not be classified or diagnosed due to scanty aspirate. Further in the

benign category 3 were diagnosed as benign cystic lesions, 7as sialadenitis, 7 were diagnosed as chronic granulomatous inflammation, 1 came out to be reactive lymph node, 32 were diagnosed as pleomorphic adenomas and 5 Warthin’s tumors. Out of the 8 malignant lesions diagnosed on FNAC 1 was an adenocarcinoma, 2 were diagnosed as metastatic carcinomas and 5 as malignant or undifferentiated malignant neoplasms

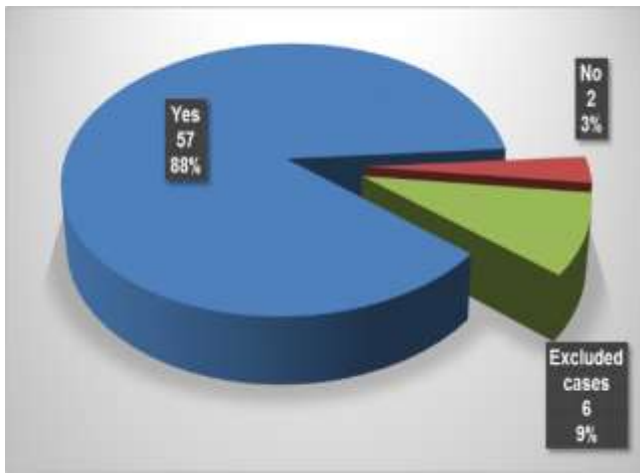
The histopathological analysis (Table 2) of the surgical specimen of the 6 inadequate cases including 1 conventional and 5 USgFNAC was also done later on. The one inadequate aspirate on conventional FNAC was diagnosed as chronic sialadenitis, whereas out of 5 cases diagnosed as inadequate with USgFNAC, 2 were diagnosed later as benign cystic lesions, 1 as pleomorphic adenoma and 2 histological specimens (which were the cell blocks) did not have enough material to correctly diagnose them so they were labeled as inadequate or non-diagnostic.

**Table 2: Frequency distribution of the lesions diagnosed on Histopathology**

|                  | Histopathology                            | Frequency |
|------------------|---|-----------|
| <b>Benign</b>    | Benign cystic lesion                      | 5         |
|                  | Sialadenitis                              | 4         |
|                  | Chronic-granulomatous inflammation        | 7         |
|                  | Reactive lymph node                       | 1         |
|                  | Pleomorphic adenoma                       | 33        |
|                  | Warthin tumor                             | 5         |
|                  | Inadequate cases                          | 2         |
| <b>Malignant</b> | Adenoid cystic CA                         | 1         |
|                  | Mucoepidermoid CA                         | 1         |
|                  | Ca ex pleomorphic adenoma                 | 1         |
|                  | Squamous cell CA                          | 1         |
|                  | Metastatic CA                             | 1         |
|                  | Poorly differentiated malignant neoplasms | 3         |
| <b>Total</b>     | <b>65</b>                                 |           |

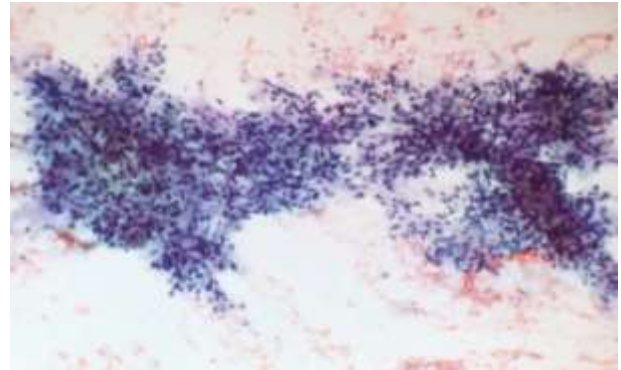
Histopathological correlation confirmed 8 (12.3%) cases as malignant and 55 (84.6%) were confirmed benign. 2 samples (cell blocks) were inadequate for diagnosis. In the benign category 5 were classified as benign cystic lesions, 4 as sialadenitis, 7 chronic granulomatous inflammation, 1 as a reactive lymph node, 33 pleomorphic adenomas and 5 Warthin’s tumors. Out of the 8 cases diagnosed as malignant on histopathology there was 1 mucoepidermoid carcinoma, 1 adenoid cystic carcinoma, 1 carcinoma ex

pleomorphic adenoma, 1 squamous cell carcinoma, 1 metastatic carcinoma and 3 as poorly differentiated malignant neoplasm.

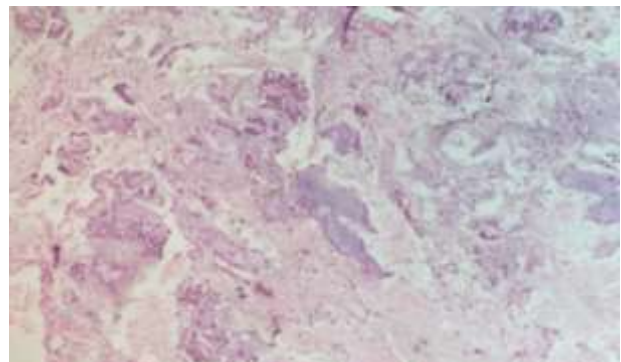


**Figure 1: Concordance between FNAC & histopathology diagnosis**

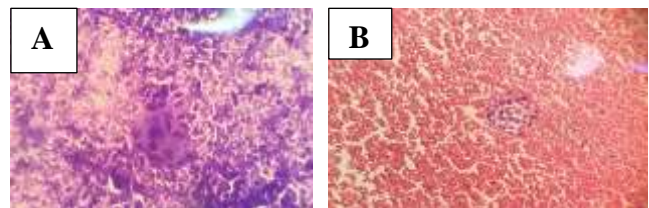
There was only one discordant case in this category in which the FNAC diagnosis was given as a malignant salivary gland lesion (most likely a mucoepidermoid carcinoma) but on histopathology and review of the FNAC slides the diagnosis of pleomorphic adenoma with squamous metaplasia and cystic change was given. All other cases were concordant with histology. Similarly, there was one discordant case in conventional FNAC which was given as a pleomorphic adenoma but on histopathological diagnosis it was diagnosed as adenoid cystic carcinoma. There are few factors which can cause such misinterpretations. One of the commonest is that pleomorphic adenoma is a frequently diagnosed salivary gland lesion observed in routine practice. (Figures 1-5) Pleomorphic adenoma can be misdiagnosed due to certain cytological features including dominance of one cell type, cytological atypia, cystic change, mucin production, squamous, mucinous and sebaceous metaplasia. As in one of the cases the solid and cystic areas, squamous metaplasia, cytological atypia raised the suspicion of malignancy and was falsely labeled as malignant. It can also have certain cytological features that resemble adenoid cystic carcinoma such as basaloid cells and hyaline globules of basement membrane material and some degree of cytologic atypia that can lead to a false diagnosis or observer bias.<sup>11</sup>



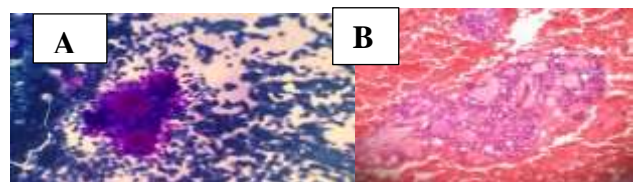
**Fig 2: FNAC Pleomorphic adenoma (May-Grunwald-Giemsa (MGG) X 100)**



**Figure 3: Cell block of Pleomorphic Adenoma (MGG X 200)**



**Figure 4 (A & B): FNAC of a granuloma (MGG X 200) Cell block showing a granuloma (H&E X 40)**



**Figure 5 (A & B): FNAC of adenoid cystic carcinoma basaloid cells surround spheres of matrix with sharp borders and a "cookie-cutter" like appearance A. May Grunwald-Giemsa (MGG) X 100). B. The Cell block showing features of adenoid cystic carcinoma (H&E X 100)**

This study results showed the sensitivity of Conventional FNAC was 80%, specificity of 96.3%, PPV 100%, NPV value was 96.3% and diagnostic

accuracy was 93.75% taking histopathology as gold standard. Razmpa et al<sup>(12)</sup> in his study obtained sensitivity of 82.5%, specificity 93.3%, accuracy 87.5%, PPV 93.3% and NPV of 82.35% for conventional FNAC which is corresponding with this study. In a study conducted by Omhare et al<sup>(13)</sup> sensitivity of conventional FNAC came out to be 88.2%, specificity 97.1%, diagnostic accuracy 95.3%, PPV 88.2% and NPV 97.1%.

Our study results showed sensitivity of USgFNAC to be 100% with specificity of 82.8%, PPV value was 75% NPV value was 100% and diagnostic accuracy was 84.8% taking histopathology as gold standard. Similar study done by Piccioni et al<sup>(14)</sup> showed the sensitivity of USgFNAC to be 81%, specificity 99%, diagnostic accuracy 97%, PPV 93% and NPV 98%. Similarly Wan et al<sup>(15)</sup> concluded a sensitivity of 83%, specificity of 100%, accuracy 97%, PPV 100% and NPV of 96% of USgFNAC in salivary gland lesions.

In this study concordance between FNAC & histopathology was found in 57 (88%) cases excluding 6 (9%) inadequate aspirates and the discordance was observed in 2 (3%) cases as shown in figure 1.

### **Conclusion**

1. Ultrasound guided FNAC as well as conventional FNAC both have high sensitivity, specificity and diagnostic accuracy with subtle differences.
2. Ultrasound guided FNAC has comparatively low diagnostic cytological yield.
3. FNAC without additional ultrasound guidance could be used routinely for the diagnosis of salivary gland lesions as it will save the time and decrease the cost of the test with a high diagnostic accuracy.

### **Limitations**

1. Limited sample size. This study was conducted on 65 patients.
2. Due to ethical considerations including financial burden, more time consumption and hassle of the patient we performed conventional FNAC on half patients and USgFNAC on the other half.

### **Recommendations**

1. Further studies should be done on a large sample size.
2. Both procedures should be done on all the patients so that more reliable results could be achieved.

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- D. Manuscript Writing
- E. Critical Review
- F. Facilitated for Reagents/Material/Analysis