

# Comparative study of Fine-Needle Aspiration Cytology and Histopathological diagnosis of salivary gland swelling

Balaprasanth J<sup>1</sup>, Vinod PB<sup>2</sup>

## Abstract

**Introduction:** Fine-needle aspiration cytology (FNAC) of salivary gland swelling helps differentiate benign and malignant lesions, thereby allowing clinicians to plan proper management. Ultrasound-guided FNAC is more accurate than other methods of FNAC. It is simple and safe and lacks significant complications. It is also inexpensive and can be repeated if needed.

**Methods:** This study is a prospective study of 80 patients subjected to FNAC followed by surgery and histopathological examination, from September 2017 to July 2019. Histopathology reports were compared with the preoperative FNAC reports. In all 80 cases, informed consent was obtained prior to surgery.

**Results:** True-positive, true-negative, false-positive, and false-negative rates for carcinomatous lesions of salivary gland swelling were assessed. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 81.82%, 97.10%, 81.82%, 97.10%, and 95%, respectively for FNAC when compared against histopathology.

**Conclusion:** FNAC is a sensitive, specific, and accurate diagnostic test used for the preoperative evaluation of patients with salivary gland swelling. FNAC is very commonly used as an initial routine investigation.

**Keywords:** FNAC; Histopathology; Salivary gland swelling; Sensitivity; Specificity.

## Author affiliations:

<sup>1</sup> Department of Plastic surgery, Christian Medical College, Vellore, Tamilnadu, India.

<sup>2</sup> Department of General Surgery, Government TD Medical College, Alappuzha, Kerala, India

## Correspondence:

Dr Vinod P B,  
Associate Professor,  
Department of General Surgery,  
Government TD Medical College,  
Alappuzha, Kerala, India

Email: pbdrvinod@gmail.com

## Disclosures:

**Ethical Clearance:** Taken

**Conflict of interest:** None

**Financial aid:** None

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## How to cite this article:

Balaprasanth J, Vinod PB. Comparative study of Fine needle aspiration cytology and histopathological diagnosis of salivary gland swelling. J Soc Surg Nep. 2022; 25(2):46-52.

## DOI:

<https://doi.org/10.3126/jssn.v25i2.50810>

## Introduction

The salivary glands consist of the parotid, submandibular, sublingual, and minor glands. The minor salivary glands are widely distributed throughout the mouth and oropharynx. Approximately 3% of all head and neck neoplasms are salivary gland tumors.<sup>1</sup> About 80% are located in the parotids, 10% are located in the submandibular glands, and the remainder is distributed between the sublingual and countless minor salivary glands.<sup>2</sup> Major salivary gland tumors tend to be benign, whereas minor tumors tend to be malignant.<sup>3</sup>

Fine needle aspiration cytology (FNAC) was introduced in the 1920s and quickly gained wide acceptance among clinicians due to the ease of its performance and its rapid diagnosis.<sup>4</sup> FNAC is the main diagnostic tool used for the evaluation of salivary gland swelling due to its superficial location and easy accessibility.<sup>5,6</sup> Due to the large variety of salivary gland neoplasms and the lack of tumor markers, diagnosing submandibular tumors is challenging for clinicians and pathologists.

The inherent morphological heterogeneity of the lesions, technical expertise of the performer, quality of the cytological smear preparations and finally, the experience of the cytopathologist in reviewing and diagnosing the lesions alter the ultimate diagnosis, treatment protocol, and outcome.<sup>7-10</sup>

Clinical examination and imaging without FNAC are not able to distinguish benign from malignant lesions.<sup>11</sup> FNAC can better identify malignancy than any other investigations such as ultrasonography (USG), computed tomography (CT), or magnetic resonance imaging (MRI) in the majority of cases. FNAC for salivary gland lesions has been shown to be adequately sensitive and specific for diagnosing and treating salivary gland pathologies<sup>12,13</sup> and is simple, safe, cost-effective, and can be repeated if necessary. Although many study-reports on the use of FNAC are available in the literature, those addressing populations from coastal areas attending rural medical colleges with no access to frozen sections or MRIs are lacking. This study was conducted to fill this research gap. This study aims to see the correlation between FNAC and histopathology in salivary gland swelling.

## Methods

After approval was received from the Institutional Research Committee and the Institutional Ethics Committee, this prospective study was launched. Patients attending surgery outpatient department with swelling in the neck and oral cavity were identified. Patient histories were collected and detailed clinical examinations of the neck and oral cavity were conducted to identify salivary gland swelling. Data were obtained using a pre-structured proforma after the study participants gave their written informed consent. The research was carried out from September 2017 to July

2019. The study enlisted the participation of 80 patients. Male and female patients with salivary gland swelling between the ages of 13 and 70 were included. All patients subjected to FNAC followed by surgery and histopathological examination due to salivary gland swelling were included. Patients below age 13 are referred to pediatric surgery, so they were not included. Patients with inoperable tumors and patients not fit for surgery were excluded.

Patient histories were collected and detailed clinical examinations were conducted to locate the lesion for aspiration. USG of the neck was done. In selected cases where there was fixity to the structures like muscles, nerves, skin, or bone, a CT scan was also done. In cases where the origin or fixity to the adjacent structures on clinical examination was unclear, ultrasound and CT scans were done prior to FNAC. In straightforward cases, FNAC was done in the first visit before the imaging studies. Ultrasound-guided FNAC was not practiced routinely in our institution, so it was not utilized in our study.

After consent was obtained, aspiration was done directly on the percutaneous or transoral root as an operative procedure. All the aspiration was done by the same team of cytotechnicians, and examinations of slides were done by the same team of cytopathologists. The aspirate was obtained under aseptic conditions with a 23-gauge needle and a 10cc disposable syringe. Under negative-pressure, needle was passed in multiple directions without taking it out of the tumor, and for large tumors, aspiration was done at various sites. Smear-prepared on multiple slides fixed with ether-95% alcohol solution and stained using Papanicolaou's stain. After the FNAC report was obtained, patients were re-evaluated, and additional investigations like a CT scan were conducted for selected cases, after which patients were subjected to surgery with a proper anesthesia check-up. For all cases, informed written consent was obtained. Since there is no facility for the frozen sections in our center, surgery for the swelling was planned based on the clinical examination, FNAC, and scan report. Specimens were assessed by post-operative histopathological evaluation. Cytologically benign tumors of the parotid from the superficial lobe underwent superficial parotidectomy and total parotidectomy for swelling arising from the deep lobe. For cytologically malignant cases, total parotidectomy with removal of the lymph nodes was done. For submandibular swelling, total excision of the gland was done for cytologically benign cases, and for malignant cases, total excision of the gland with removal of the lymph nodes and adjacent structures was done in indicated cases. For minor salivary gland tumors, excision with an adequate margin was done. Cytological diagnosis and histopathological diagnosis were correlated. The sensitivity, specificity, positive predictive value, and negative predictive value of FNAC were calculated, and the diagnostic accuracy of FNAC was assessed.

## Results

Eighty patients with salivary gland swelling subjected to FNAC followed by surgery and histopathological examination were included in this study. Patients between the ages of 13 and 70 were included in the study, of which 45 (56.25%) were females and 35 (43.75%) were males. The age group most commonly affected was 41–50 years (24 cases). The mean age of the patients was 39. The duration of swelling ranged from 3 months to 15 years; the mean duration was seven years and seven months (**Table 1**).

FNAC results revealed that there were 47 (58.75%) cases of pleomorphic adenoma, 10 (12.5%) cases of chronic sialadenitis, eight (10%) cases of Warthin's tumor, four (5%) cases of cystic lesions, five (6.25%) cases of mucoepidermoid carcinoma, two (2.5%) cases of acinic cell carcinoma, and four (5%) cases of adenoid cystic carcinoma. After FNAC, no patients had major complications. Only nine patients complained of pain at the site, and three showed bruising at the site.

In the postoperative histopathological diagnosis, out of 47 cases of pleomorphic adenoma, 44 cases showed the same diagnosis as FNAC and three cases showed different diagnoses (Warthin's tumor: 1, mucoepidermoid carcinoma: 1, carcinoma ex pleomorphic adenoma: 1). Out of 10 cases of chronic sialadenitis, eight showed the same diagnosis as FNAC, and two cases showed different diagnoses (pleomorphic adenoma: 2). In the cases of Warthin's tumor, cystic lesions, and acinic cell carcinoma, all cases showed the same diagnosis as FNAC. Out of five cases of mucoepidermoid carcinoma, four showed the same diagnosis as FNAC, and one case showed a different diagnosis (pleomorphic adenoma). Out of four cases of adenoid cystic carcinoma, three showed the same diagnosis as FNAC, and one case showed a different diagnosis (pleomorphic adenoma).

The histopathological diagnosis showed 48 (60%) cases of pleomorphic adenoma, eight (10%) cases of chronic sialadenitis, nine (11.25%) cases of Warthin's tumor, four (5%) cases of cystic lesions, five (6.25%) cases of mucoepidermoid carcinoma, two (2.5%) cases of acinic cell carcinoma, one (1.25%) case of carcinoma ex pleomorphic adenoma, and three (3.75%) cases of adenoid cystic carcinoma. There were 11 (13.75%) malignant cases, 57 (71.25%) benign cases, and 12 (15%) non-neoplastic cases. There were 68 (85%) and 12 (15%) neoplastic and nonneoplastic cases, respectively. Among the 57 cases of benign neoplasm, 48 (84.21%) cases were pleomorphic adenoma and nine (15.78%) cases were Warthin's tumors. Out of the 11 malignant cases, the most common was mucoepidermoid carcinoma at five (45.45%) cases, followed by adenoid cystic carcinoma at three (27.27%) cases, acinic cell carcinoma at two (18.18%) cases, and carcinoma in pleomorphic adenoma at one (9.09%) case (**Table 3**).

False-positive cases included one mucoepidermoid carcinoma of the parotid gland in a 45-year-old male who underwent total parotidectomy that proved to be a pleomorphic adenoma on histopathological examination. One adenoid cystic carcinoma of the parotid gland in a 55-year-old female proved to be a pleomorphic adenoma. False-negative cases were two cases of pleomorphic adenoma, one from the parotid gland and one from the palate, that proved to be carcinoma in ex-pleomorphic adenoma and mucoepidermoid carcinoma, respectively. For the former, since it arose from the deep lobe, the patient underwent total parotidectomy. For the latter, arose from the palate, the patient underwent re-excision in view of malignancy.

**Table 1. Age and sex distribution of the study group (n=80)**

Age	Total	Female	Male
13–20	3	2	1
21–30	6	3	3
31–40	21	12	9
41–50	24	14	10
51–60	19	10	9
60–70	7	4	3
Total	80	45	35

The male: female ratio was 1:1.28.

**Table 2. Distribution of salivary gland lesions (n=80)**

Site	Number	Percentage
Parotid	63	78.75
Submandibular	16	20
Minor salivary gland	1	1.25

## Discussion

Salivary gland swelling in male and female patients between the ages of 13 and 70 years old was examined in the study. The highest number of patients was seen in the age group of 41–50 years old. The male: female ratio was 1:1.28, consistent with a study that claimed that salivary gland lesions are more common in females.<sup>11</sup>

In our study, the frequency of swelling in the parotid, submandibular, and minor salivary glands was 78.75%, 20%, and 1.25%, respectively. This is consistent with the results of the majority of previous studies. Most patients had a history of a gradually increasing mass of variable duration. Facial nerve involvement was seen in one case, fixity to the underline structure was seen in two cases, and lymphadenopathy was seen in two cases. Most of the instances of malignant swelling were clinically similar to those of benign swelling, so the primary challenge of aspiration cytology was to differentiate benign tumors from malignant ones and then to differentiate the various types of malignancy.<sup>14</sup>

**Table 3. Comparison of FNAC and histopathological results (HPR) (n=80)**

Cases	N(%) (FNAC)	Same HPR	Different HPR	Discordant Cases	Total Cases HPR
Pleomorphic adenoma	47 (58.75%)	44	3	Mucoepidermoid ca: 1 (False Negative), Carcinoma ex pleomorphic adenoma: 1 (False Negative), Warthin's tumor: 1	48 (60%)
Chronic sialadenitis	10 (12.5%)	8	2	Pleomorphic adenoma: 2	8 (10%)
Warthin's tumor	8 (10%)	8	0	-	9 (11.25%)
Cystic lesions	4	4	0	-	4 (5%)
Mucoepidermoid carcinoma	5 (6.25%)	4	1	Pleomorphic adenoma: 1 (False Positive)	5 (6.25%)
Acinic cell carcinoma	2 (2.5%)	2	0	-	2 (2.5%)
Adenoid cystic carcinoma	4 (5%)	3	1	Pleomorphic adenoma: 1 (False Positive)	3 (3.75%)
Carcinoma ex pleomorphic adenoma	0	0	0	-	1 (1.25%)
<b>Total</b>	<b>80</b>	<b>73</b>	<b>7</b>	-	<b>80</b>

In our study using FNAC, inflammatory swelling was seen in 10 (12.5%) cases, similar to the findings of Ashraf et al,<sup>16</sup> which reported 12% of cases. In our study, cystic lesions were seen in four (5%) cases, similar to the findings of Akhter et al, in which 7.5% of cases were reported.<sup>15</sup> In our study using FNAC, pleomorphic adenoma was the most common benign tumor, seen in 47 (58.75%) cases, and mucoepidermoid carcinoma was the most common malignant tumor in five (6.25%) cases. These results corroborate with those of a study conducted in Pakistan on 129 cases of parotid gland lesions.<sup>23</sup> In our study using FNAC, neoplastic, benign, and malignant lesions were seen in 66 (82.5%), 55 (68.75%), and 11 (13.75%) cases, respectively. Among the 66 neoplastic cases, 62 (93.9%) were benign and four (6%) were malignant; this is comparable with other studies, in which the percentages were 75.9% and 14.6%, respectively.<sup>24</sup>

In this study, histopathological analysis revealed 57 (71.25%) benign cases and 11 (13.75%) malignant cases. Among the benign cases, pleomorphic adenoma was the most common at 48 (84.21%) cases and Warthin's tumor made up nine (15.78%) cases. Among the malignant cases, mucoepidermoid carcinoma was the most common at five (45.45%) cases, followed by adenoid cystic carcinoma at three (27.27%) cases, acinic cell carcinoma at two (18.18%) cases, and carcinoma ex pleomorphic adenoma at one (9%) case. Among all the salivary gland tumors, the most common benign and malignant tumors were pleomorphic adenoma and mucoepidermoid carcinoma, respectively. These results agree with those of Pratap and Jain,<sup>25</sup> Panchal and Shah,<sup>26</sup> and Rajat et al.<sup>27</sup>

Two false-negative cases (18.18%) out of 11 malignant cases were reported in the study. False negatives have been reported in various studies, with rates ranging

between 0 and 37%.<sup>16-22</sup> In this study, there was one case of mucoepidermoid carcinoma and one case of carcinoma ex pleomorphic adenoma. Both cases were diagnosed as pleomorphic adenoma by FNAC. FNAC can quite easily diagnose pleomorphic adenoma, but occasionally, difficulty is encountered in differentiating pleomorphic adenoma from mucoepidermoid carcinoma, adenoid cystic carcinoma, and carcinoma ex pleomorphic adenoma.<sup>28</sup>

There were two occurrences of false positives. The first was a cytological diagnosis of mucoepidermoid carcinoma of the parotid gland. The patient underwent total parotidectomy, and pleomorphic adenoma was diagnosed histopathologically. A probable explanation of this is that if only pap staining was utilized, the myxoid ground substance of pleomorphic adenoma could be misinterpreted for epithelial mucus. Mucoic paucicellular fluid aspiration may indicate low-grade mucoepidermoid carcinoma or mucoepidermoid carcinoma originating in the pleomorphic adenoma.<sup>29</sup> Because the morphological patterns of epithelial components show diversity in both pleomorphic adenoma and low-grade mucoepidermoid carcinoma,

**Table 4. Statistical analysis of carcinomatous lesions (n=80)**

Test Evaluated (FNAC)	Histopathology Positive	Histopathology Negative	Total
FNAC positive	9 (True Positive)	2 (False Positive)	11
FNAC negative	2 (False Negative)	67 (True Negative)	69
<b>Total</b>	<b>11</b>	<b>69</b>	<b>80</b>

Sensitivity: 81.82%, Specificity: 97.10%, Positive predictive value: 81.82%, Negative Predictive value: 97.10%, Accuracy: 95%.

**Table 5. Comparison with other studies**

Authors	No. of Cases	Accuracy
Sikdar, Sriram, & Ivan (2018) <sup>31</sup>	50	87
Hayat Ullah Khan, Kamran Khalid, Imran Yousuf (2017) <sup>33</sup>	65	93.84
Naz, Hashmi, Khurshid et al. (2015) <sup>30</sup>	187	83.3
Present study	80	95

**Table 6. Diagnostic accuracy of FNAC in different studies**

Authors	Year of Study	Sensitivity (%)	Specificity (%)
Sikdar, Sriram, & Ivan <sup>31</sup>	2018	100	85
Naz, Hashmi, Khurshid et al. <sup>30</sup>	2015	77.7	86.3
Poudel, Shrestha, & Regmi <sup>32</sup>	2020	90.32	75
Present study	2017–2019	81.82	97.10

aspirated material lacking the stromal component may result in a false-positive diagnosis. This misdiagnosis can be avoided by using multiple samples.

For the second false positive, the cytological diagnosis indicated adenoid cystic carcinoma arising from the parotid gland. CT scan showed swelling arising from the superficial lobe, so the patient underwent total parotidectomy. The histopathological report showed pleomorphic adenoma. When using FNAC, the distinction between adenoid cystic carcinoma and pleomorphic adenoma may be difficult because both have myxoid acellular material and hyaline globules. The hyaline globules characteristic of adenoid cystic carcinoma may also be seen in pleomorphic adenoma.<sup>36</sup> The stromal component of pleomorphic adenoma may thus be misinterpreted as basement membrane-like material seen in adenoid cystic carcinoma.

There were two false-negative cases in the parotid gland, both of which were diagnosed as pleomorphic adenoma by cytology. The first one was mucoepidermoid carcinoma in a 35-year-old male, for which similar findings were seen in many studies. In a study by Kotwal et al, three out of four mucoepidermoid carcinomas were diagnosed as pleomorphic adenoma cytologically.<sup>37</sup>

The second false negative was carcinoma ex pleomorphic adenoma, for which the cytological diagnosis was pleomorphic adenoma. This misdiagnosis is of great clinical importance since this malignancy is very aggressive and treatment plans are different. This clinical problem was emphasized in a study by Klijanienko et

al. reported a very high false-negative rate of 35.3% in carcinoma ex pleomorphic adenoma among all malignant salivary gland swelling.<sup>38</sup>

In our study, the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were 81.82%, 97.10%, 81.82%, 97.10%, and 95%, respectively. The specificity and accuracy of our study were higher than those of most previous studies because we had a limited number of false-negative and false-positive cases (Table 5 and 6). Because this study was conducted at a teaching institution, more senior and experienced pathologists oversaw the cytology division. Additionally, more than one cytopathologist examined each slide, and multiple site aspiration and repeated aspiration are usual practices. These could be the reasons for this study's high accuracy and specificity.

Inadequate aspirate or sampling errors remain important limitations of this technique and impose a great demand for experienced histopathologists.<sup>34,35</sup> Additionally, a limitation in the number of malignant cases can contribute to the drawbacks of FNAC. This can be overcome by conducting studies with larger samples.

Ultrasound-guided FNAC is recommended by many authors to reduce non-diagnostic aspiration due to false positioning of the needle outside the tumor or in the necrotic, hemorrhage, and cystic area. According to Brennan et al,<sup>5</sup> clinically suspicious cases should be re-evaluated using appropriate imaging techniques and FNAC should be repeated under ultrasound guidance by a skillful cytotechnician and reported by an expert cytopathologist.

## Conclusion

FNAC is a sensitive, specific, and accurate diagnostic test used for the preoperative evaluation of patients with salivary gland swelling. It is a simple, safe, and cost-effective procedure with no major complications. It can be done as an outpatient procedure with good patient compliance and can be repeated if necessary. It is, therefore, of immense value in the diagnosis of benign and malignant lesions. FNAC provides a more rapid and accurate diagnosis of salivary gland swelling than any other test.

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