

## Original Research Article

# Evaluation of salivary gland tumors- clinically radiologically and pathologically: prospective study

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## ABSTRACT

**Background:** Salivary gland tumors are difficult to differentiate based solely on clinical presentation or cytological findings due to their overlapping pictures. Often inadequate samples from cytology pose a challenge in preoperative diagnosis. Histopathology is considered the gold standard in diagnosing these tumors. The purpose of this study was to determine clinical, radiological, and cytological findings of these tumors and to assess the accuracy of these results with that of histopathological diagnosis.

**Methods:** Prospectively 52 patients with salivary gland swellings were enrolled between 2007-2009. Cases with inflammatory swelling were excluded from the study. Demographic, clinical history, preoperatively ultrasonography, cytology, and histopathological data were collected and analyzed.

**Results:** Most cases (65.38%) had parotid gland involvement. Benign tumors were common (80.76%) with pleomorphic adenoma as the most common one. Malignant tumors comprised 19.23%. Mucoepidermoid carcinoma and adenoid cystic carcinoma were common malignant tumors. Local swelling was the most common clinical presentation, and no facial nerve involvement was reported. The hard palate was the most common minor salivary gland affected predominantly by benign tumors. The diagnostic accuracy of fine-needle aspiration cytology was 96.15%, followed by clinical and radiological diagnostic accuracy of 92.31% and 86.54%, respectively. Using McNemar's test, a significant agreement was found between clinical and histological diagnosis ( $p=0.1336$ ) and between FNAC and histological diagnosis ( $p=0.4975$ ).

**Conclusions:** Fine needle aspiration cytology is a highly accurate, sensitive, and specific screening technique. It is safe and reliable, though minimally invasive. Ultrasonography-guided cytology along with clinical, and radiological findings could enhance the pre-operative diagnostic accuracy in distinguishing salivary gland tumors.

**Keywords:** Salivary gland tumor, Clinical, Radiological, Fine needle aspiration cytology, Histopathological, Sensitivity

## INTRODUCTION

Salivary gland tumors have been a challenge and of great interest for clinicians, surgeons, and pathologists in predicting the prognosis.<sup>1-3</sup> Previous studies have focused on facial nerve preservation during surgery and have established a much clearer picture of histopathological

tumor types along with varied clinical attitudes and management protocols.

The sketchy clinical presentations, diagnostic limitations consisting of inadequate sampling, inexperienced pathologists pose a preoperative diagnostic challenge.<sup>4,5</sup> Surgery is the mainstay of treatment for all salivary gland

neoplasm and tumor type, localization, and stage and grade of a malignant tumor influence the extent of surgery.<sup>6</sup> Clinical and radiological (Ultrasonography, CT Scan) evaluations are not 100 % accurate. Prediction of deep lobe tumors of the parotid gland is not accurately done USG but could be better backed by CT or MRI.<sup>7</sup> Fine needle aspiration biopsy is helpful in diagnosis but is not ideal.<sup>8</sup> Unsatisfactory and inadequate aspirate of the cytological procedure is a problem.<sup>3</sup> Clinically diagnosed benign tumors are often symptomless but appear metastatic histologically. Salivary gland tumor management decisions are not based on any single diagnostic tool. Incorporation of patient history, clinical examination, cytological evaluation, and imaging studies together improves diagnostic accuracy.

Previous studies have focused on cytological and clinic-histological comparisons. In this study, a correlation study between clinical, cytological, and radiological diagnosis with that of the histological investigation was made to evaluate the preoperative diagnostic results. Histopathology was considered the gold standard screening tool.

## METHODS

The study was approved by the institutional review board of the Department of ENT and Head Neck Surgery, Jawaharlal Nehru Hospital and Research Centre, Bhilai, Chhattisgarh (India). A prospective study was conducted between March 2007 and March 2009. Fifty-two patients who either admitted or attended out-patient departments for suspected salivary gland swelling were enrolled after taking informed consent. A pre-prepared questionnaire designed for study purpose was used to collect the clinical and demographic data of all suspected patients. Clinical parameters that were collected included tumor locality, mobility, associated nodularity, enlarged lymph nodes, facial nerve, and skin involvement, and associated local pain. All patients underwent preoperative biochemical and hematological investigations and had ultrasonography followed by FNAC. Those with inflammatory swellings were excluded.

Ultrasonography was carried out in the radiology department using the highest frequency transducer and a few patients underwent CT scans if USG findings were discordant. FNAC was performed using a 23-to-24-gauge disposable needle attached to a 10 ml disposable syringe. Repeated passes were made in different directions inside the swelling for adequate sampling. The cytological fluid was expressed on a glass slide, smeared using another glass slide, stained, and was studied under the microscope. Post-FNAC patients were observed for 15 minutes for any complications. Patients underwent surgery based on USG and cytological findings. Surgical specimens were sent to the pathology lab for gross and histopathological examination. The tissue was processed in the automatic tissue processor (Leica T.P. 1020) using different grades of alcohol, xylol, and embedded in paraffin wax. Blocks

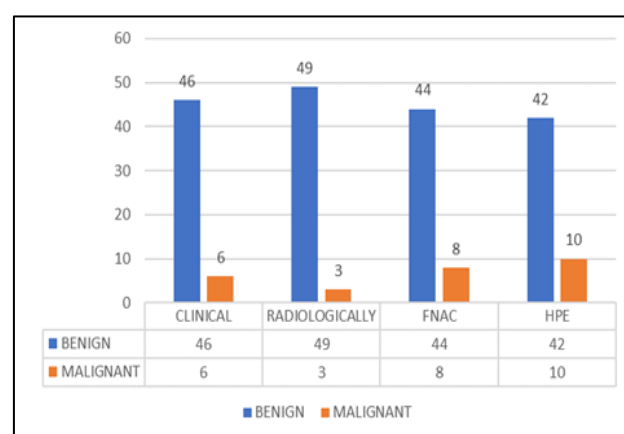
prepared using L-Moulds were sectioned into 4 to 5 mm thickness using REICHERT JUNG -1130, rotator microtome. Slides were stained using hematoxylin and Eosin stain, dried, and were microscopically evaluated. Histopathological data was collected for size, shape, consistency, and appearance of the cut surface of the tissue and morphological patterns.

## Statistical analyses

The preoperative clinical, radiological, and cytology data and postoperative data on histological diagnosis were summarized as frequency counts and percentages. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of these diagnostic modalities were examined. The histopathological diagnoses were regarded as the diagnostic standard. Clinical diagnostic accuracy was defined as the number of correct clinical predictions of malignancy divided by the total enrolled case numbers. McNemar test to examine the agreement of each of the three diagnostic modalities individually with that of histopathological diagnosis was conducted.

## RESULTS

A total of 52 patients were studied (Table 1). Overall, male to female ratio was 1.08:1. The most frequent age category reported was 31- 40 years. Benign to malignant cases were reported in the ratio of 4.2:1. Pleomorphic adenoma was the most common benign tumor while mucoepidermoid carcinoma and adenoid cystic carcinoma as malignant tumors were found to be in an equal distribution. Clinically, left-sided glands were commonly affected. In the most common age category (31- 40 years), 11/16 (68.75%) were benign cases with M: F ratio of 1.2:1 while female predominance was noticed in malignant tumors.



**Figure 1: Distribution of tumor diagnosis by diagnostic modalities.**

Presented in Table 2 and 3 are characteristics by tumor type. Those with benign tumors had a mean age of 40.79 years and there was no difference in gender distribution. Those with malignant tumors had a higher mean age in

years (47.6) and the M: F ratio was 1.5:1. The parotid gland and hard palate were the commonly affected major and minor glands, respectively. No malignant cases were observed in minor salivary glands. The swelling was the most common clinical presentation among the malignant cases. The distribution of histopathological diagnosis of tumors by gender is presented in Table 3. Among both males and females, pleomorphic adenoma was the most common benign tumor. However, as malignant tumor adenoid cystic carcinoma was common among males and mucoepidermoid carcinoma among females. The distribution of tumor diagnosis by various diagnostic modalities are presented in Figure 1.

**Table 1: Study characteristics (n=52).**

	N (%)
<b>Age categories</b>	
0 to 10	0
11 to 20	4 (7.7)
21 to 30	9 (17.3)
31 to 40	16 (30.8)
41 to 50	4 (7.7)
51 to 60	14 (26.9)
61 to 70	5 (9.6)
<b>Gender</b>	
Males	27 (51.9)
Females	25 (48.1)
<b>Location of involved salivary glands</b>	
Right	22 (42.3)
Left	30 (57.7)
<b>Histopathological type</b>	
Benign	(n=42/52)
Pleomorphic adenoma	40 (95.2)
Warthin's tumor	1 (2.4)
Myoepithelioma	1 (2.4)
Malignant	(n=10/52)
Mucoepidermoid carcinoma	4 (40)
Adenoid cystic carcinoma	4 (40)
Acinic cell carcinoma	2 (20)

Clinically 46/52 (88.4%) were diagnosed as benign cases and 42/46 were confirmed as benign by histopathology. The remaining four benign cases diagnosed clinically turned out to be malignant by histopathology. Two of the four malignant cases that were mismatched were missed on clinical palpation because of their small size and the other two were in the deep lobe of the parotid gland and were missed on sonography but showed up in CT scan.

**Table 2: Characteristics by tumor type.**

	Benign (n=42)	Malignant (n=10)
<b>Age categories</b>		
0 to 10	0	0
11 to 20	4	0
21 to 30	9	0
31 to 40	11	5
41 to 50	4	0
51 to 60	11	3
61 to 70	3	2
<b>Gender</b>		
Males	21	6
Females	21	4
<b>Salivary gland involved</b>		
<b>Major</b>		
Parotid	25	9
Submandibular	13	1
<b>Minor</b>		
Hard palate	4	0
<b>Clinical presentation</b>		
Swelling	34	5
Pain	4	1
Skin involvement	3	0
Hard consistency	3	0
Rapid growth	2	0
Facial nerve involvement	0	0
Enlarged lymph nodes	0	0

**Table 3: Distribution of histopathological diagnosis of tumor by gender.**

Tumor type		Total (n=52)	Male (n=27)	Female (n=25)
		N (%)	N (%)	N (%)
<b>Benign</b>	Pleomorphic adenoma	40 (76.92)	20 (74.1)	20 (80)
	Warthin's tumor	1 (1.92)	0	1 (4)
	Myoepithelioma	1 (1.92)	0	1 (4)
<b>Malignant</b>	Mucoepidermoid carcinoma	4 (7.69)	2 (7.4)	2 (8)
	Adenoid cystic carcinoma	4 (7.69)	3 (11.1)	1 (4)
	Acinic cell carcinoma	2 (3.85)	2 (7.4)	0

Radiologically 49/52 (94%) cases were diagnosed as benign, and 42/49 were confirmed as benign by histopathology.

Out of the remaining seven cases diagnosed as benign by radiology, 3 cases (42.9%) were found to be discordant or diagnosed as malignant by histopathology while the remaining 4 cases (57.14%) confirmed to be concordant or

benign were missed by sonography because they were in the deep lobe of the parotid gland which was later confirmed by CT.

**Table 4: Diagnostic accuracy and sensitivity and specificity of diagnostic modalities.**

	Sensitivity (%)	Specificity (%)	Diagnostic accuracy (%)
<b>Clinical diagnosis</b>	60	100	92.31
<b>Radiological diagnosis</b>	30	100	86.54
<b>Cytological diagnosis (FNAC)</b>	80	100	96.15

**Table 5: Results of McNemar's test examining agreement between each of the three diagnostic modalities with histopathological diagnosis.**

	Histopathological diagnosis			P value
	Malignant	Benign	Total	
<b>Clinical diagnosis</b>				0.13
<b>Malignant</b>	6	0	6	
<b>Benign</b>	4	42	46	
<b>Total</b>	10	42	52	
	Histopathological diagnosis			P value
	Malignant	Benign	Total	
<b>Radiological diagnosis</b>				0.02
<b>Malignant</b>	3	0	3	
<b>Benign</b>	7	42	49	
<b>Total</b>	10	42	52	
	Histopathological diagnosis			P value
	Malignant	Benign	Total	
<b>Cytological diagnosis (FNAC)</b>				0.50
<b>Malignant</b>	8	0	8	
<b>Benign</b>	2	42	44	
<b>Total</b>	10	42	52	

Cytologically 44/52 (84.76%) cases were diagnosed as benign and 8/52 (15.38%) as malignant. Of these 44 benign cases, 42 were confirmed histopathology as benign, and the remaining 2 turned out to be malignant with one as acinic cell carcinoma and the other as adenoid cystic carcinoma of the parotid gland.

The sensitivity, specificity, and accuracy of FNAC were found to be 80%, 100%, and 96.15% respectively (Table 4). Using McNemar's test, a significant agreement was found between clinical and histological diagnosis ( $p=0.13$ ) and between FNAC and histological diagnosis ( $p=0.50$ ) (Table 5).

## DISCUSSION

Preoperative diagnosis of salivary gland tumors remains a challenge for otolaryngologists and head and neck surgeons due to overlapping clinical presentation and inadequate samples obtained from cytology often at times. This study was conducted to add to the literature the differences in histopathological presentation of salivary gland tumors and to compare the diagnostic accuracy of various diagnostic modalities with that of histopathological diagnosis, which is the gold standard.

Our study reported male preponderance. The most common age category reported was 31-40 years. The mean age of females was higher in comparison to males which is in line with other studies.<sup>9,10</sup> In our study, the benign tumors comprised 80.76% which is compatible with that of 11, though differences in the distribution of benign and malignant tumors have been reported, with equal distribution reported by 12 or higher prevalence of malignancy reported by 13, 14. The parotid gland was the most common major salivary gland involved in our study and it has been reported by other studies as well.<sup>10,15,16</sup> however, they found involvement of the oral cavity as the most common site (70.1%) for minor salivary gland tumors and with lower frequency for laryngeal and tracheal minor salivary gland tumors. None of our patients had laryngeal or tracheal minor salivary gland involvement as seen by others.<sup>16</sup> The most common malignant tumor observed in our study was mucoepidermoid and adenoid cystic carcinoma which is in alignment with that of others.<sup>14,10,40,27</sup>

It is difficult to differentiate benign from malignant tumors based solely on clinical findings. (11,13). Four out of six cases that presented with pain in our study were diagnosed as malignant by histopathology and similar presentations had been reported by others.<sup>17</sup> A good clinical concordance observed in our study supports a strong clinical history. Other studies had also reported clinical accuracy of 100% and 57% for diagnosing benign and malignant cases respectively 17 though others had reported that no single feature or group of features led to clinical diagnosis of a specific tumor type.<sup>18</sup> This indicates that it is difficult to diagnose malignant tumors based on clinical findings alone unless it reaches an advanced stage and presents with other findings such as facial nerve involvement. The 19% of tumors diagnosed as malignant by histology in our study is comparable to other studies.<sup>19,14</sup> However, an equal prevalence had been reported in others.<sup>12</sup> The mucoepidermoid and adenoid cystic carcinoma diagnosed as the most common malignant tumors in our study is comparable to other studies.<sup>14,10,28,29</sup> Morphologically



diagnosed pleomorphic adenoma being the predominant benign salivary gland tumor in our study had been reported by several studies.<sup>11,21,30,27</sup>

Cytologically 15.38% of cases were diagnosed as malignant in our study and a few studies reported 18% tumors as malignant. However, in another study, 42.5% of tumors were found to be malignant.<sup>13,15,16</sup> It had been highlighted that the pathologists' face difficulty in reaching the correct diagnosis for salivary gland tumors just based on morphology.<sup>20</sup> The accuracy of FNAC in our study was 96.15% compared to other studies.<sup>21,22</sup> To characterize salivary gland mass FNAC is very useful, with a sensitivity of 96% and specificity of 91% given the sufficient cell count in the specimen and had shown a higher accuracy in detecting salivary gland neoplasms.<sup>23,22</sup> Zajicek was the first pathologist who embraced FNAC for precise diagnosis and to determine accuracy in a variety of conditions.<sup>24</sup> However, false-negative results can lead to disease progression and delayed surgery. Imaging evaluations are considered as important investigational methods in diagnosing salivary gland tumors, especially when FNAC is difficult to perform due to the unusual tumor location or if the patient is unwilling to undergo FNAC (5). In the current study, the sensitivity of FNAC alone was 80% and could have been increased further if USG guided FNAC was performed on our patients. Fine-needle aspiration cytology is usually performed pre-operatively and experts consider that USG may supplant CT in detecting superficial salivary gland tumors, especially in suspected malignancy cases, to see the extent and the stage of the tumors. Good knowledge about a precise location for proper sampling by FNAC and the correct technique does influence the rate of clinicopathological concordance, which might have resulted in higher diagnostic accuracy in our study.

According to Yousem et al sonographies are underused in various medical conditions but emphasizes that an experienced hands-on US could supplant both CT and MRI in predicting superficial salivary gland tumors.<sup>25</sup> USG features of malignant salivary neoplasms usually include an irregular shape, irregular borders, blurred margins, and a hypoechoic homogeneous structure. In our study, based on the radiological diagnosis, the proportion of benign and malignant tumors was 94 % and 6 % respectively, and had been shown by others.<sup>26</sup> The radiological accuracy of 86.54% noticed in our study is higher than 60%–70% as reported by other studies.<sup>27</sup> However, the present study recorded malignant tumors as homogeneous and well-defined except in 1-2 cases. The internal structure of a malignant tumor reported by ultrasonography showed solid but cystic or cystic with the mural solid nodules in a few of our patients.

A few of the limitations in our study were the small sample size due to a single-center study. The FNAC was not USG guided in our study, yet our results showed high accuracy with FNAC. One of the limitations of FNAC is getting insufficient sample fluid occasionally, which we did not

experience. USG has its limitations in diagnosing bone-deep and deep-lobe infiltrations which can be taken care of by performing a preoperative CT scan and we experienced these difficulties. To avoid diagnostic pitfalls, to determine the exact anatomical location, and to predict histologic tumor type we emphasize a preoperative diagnostic approach based on cell type, clinical settings, and radiological imaging.

## CONCLUSION

FNAC is a safe, reliable, cost-effective, highly accurate, and minimally invasive diagnostic tool. When screening patients for salivary gland swellings, clinical diagnosis reduces the substantial number of benign tumors from undergoing surgical procedures such that undetected malignant cases remain low. USG guided FNAC should be used extensively with clinical suspicion because the synergistic role of these two modalities plays a significant role in differentiating solid from cystic lesions, and in enhancing the accuracy of FNAC to detect salivary gland tumors.

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