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# FINE NEEDLE ASPIRATION CYTOLOGY OF THYROID NODULE: DIAGNOSTIC ACCURACY AND PITFALLS

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**Objective:** To evaluate the utility of FNAC in patients with Thyroid Nodule. **Methods:** Records of all patients treated surgically for thyroid nodule(s) at Aga Khan University Hospital from January 2000 to December 2004 were reviewed. The patients who had pre operative FNAC as first line of the evaluation and the final post operative histopathology report available were included in the study. **Results:** 125 patients (90 female 35 male) had thyroid surgery. The cytological diagnosis was made according to following categories: Benign, Follicular lesion, Malignant and Inadequate sampling. Among 63 "Benign cases", 57 were benign and 6 turned out to be malignant. Among 44 cases from "Follicular group", 31 were benign and 13 were malignant. Out of 15 patients from "Malignant" group, 14 were malignant and 1 was benign. Among three patients from the "Inadequate sampling group", 2 turned out to be benign and one was malignant. The overall results showed a sensitivity of 98%, specificity of 70%, and positive predictive value of 91%, negative predictive value of 93% and diagnostic accuracy of 91%. **Conclusion:** We conclude that FNAC is an invaluable and minimally invasive procedure for pre operative assessment of patients with a thyroid nodule in our setting as well. FNAC has high sensitivity in picking up malignancy in thyroid and also has high diagnostic accuracy in the evaluation of thyroid nodules.

**Keywords:** Thyroid – FNAC - Histopathology

## INTRODUCTION

Thyroid nodules are common clinical findings and have a reported prevalence of 4% to 7% of the adult population<sup>1-3</sup>, however fewer than 5% of adult thyroid nodules are malignant<sup>4</sup>. Thyroid nodules are more common in women, and the incidence increases with age, a history of radiation exposure and a diet containing goitrogenic material<sup>3</sup>. The vast majority of these nodules are non neoplastic lesions or benign neoplasms. It is preferred to operate only on those patients with suspicion of cancer, there by avoiding unnecessary surgery and possible injury of the recurrent laryngeal nerve, hypoparathyroidism and thyroid hormone dependence in patients with benign thyroid nodule. However, the distinction of these benign lesions from a malignant nodule cannot be based reliably on the clinical presentation alone. Several diagnostic tests such as scintigraphy (with <sup>123</sup>I or <sup>99m</sup>Tc pertechnetate), transcutaneous ultrasonography and fine needle aspiration cytology (FNAC) have been used to differentiate benign from malignant thyroid nodules pre operatively. FNAC has now supplanted most other tests for pre-operative evaluation of thyroid nodules.<sup>5-7</sup>

Due to its simplicity, low cost and absence of major complications, this procedure is being performed on an increasing number of patients, which has led to the detection of thyroid cancers at earlier stages, resulting in better outcome of patients. Practice guidelines set forth by the American thyroid Association & National Comprehensive Cancer Network state that FNA should be used as the initial

diagnostic test because of its superior diagnostic reliability and cost effectiveness before both thyroid scintigraphy and ultrasonography.<sup>8</sup> Nevertheless, like any other test FNAC has its limitations. The reported pitfalls are those related to specimen adequacy, sampling techniques, the skill of the physician performing the aspiration, the experience of the pathologist interpreting the aspirate and overlapping cytological features between benign and malignant follicular neoplasm<sup>9-11</sup>.

In this study, we reviewed the cytological diagnosis of 125 FNAC of the thyroid focusing on the correlation with histological diagnosis.

## PATIENTS AND METHODS

### Patient Selection

Medical records were reviewed for all patients who had FNAC of a solitary or dominant thyroid nodule(s) during the last 5 years period between January 2000 to December 2004 and who subsequently underwent thyroid resection at Aga Khan University Hospital. The cytology reports were compared with the histological diagnosis.

### Cytological Diagnosis

The cytology results were categorized into 4 groups benign, follicular lesion (either a follicular adenoma or follicular carcinoma which cannot be differentiated on FNAC), malignant and inadequate (unsatisfactory) sampling. Aspirates classified as "benign" included adenomatous (Colloid) nodule, Hashimoto thyroiditis and sub acute thyroiditis. The "follicular" category included follicular neoplasm

and Hurthle cell tumor and aspirates with atypical features suggestive of, but not diagnostic for malignancy. The aspirates with unequivocal cytological findings of primary or secondary malignancy were classified in the “malignant” category. Aspirates with insufficient cellularity or poor quality smear due to delayed or inadequate fixation were considered “unsatisfactory”. This group also included the aspirates consisting only of cyst fluid.

### Comparison with Final Histology

Thyroid FNAC results, grouped malignant (positive results) versus the rest of diagnoses (negative results) were compared to the results of final histological study of the excised specimen in order to calculate to values of the test.

Unsatisfactory aspirates and follicular lesion group gives no definite information, they were excluded from the calculation.

- True positive (TP): positive result in the FNA for malignancy and confirmed in the histological study.
- False positive (FP): positive result in the FNA for malignancy but not confirmed in the histological study.
- True negative (TN): negative result in the FNA for malignancy and no carcinoma in the histological study.
- False negative (FN): negative result in the FNA for malignancy but with a carcinoma in the histological study.
- Sensitivity (S): proportion of patients with associated carcinoma and a positive result in the FNA for malignancy,  $S = TP / (TP + FN)$
- Specificity (Sp): proportion of patients without associated carcinoma and with a negative results in the FNA for malignancy  $SP = TN / (TN + FP)$ .
- Positive predictive value (PPV): proportion of patients with a positive results and histological confirmation  $PPV = TP / (TP + FP)$
- Negative Predictive value (NPV): proportion of patients with negative results and without a carcinoma in the histological study.  $NPV = TN / (TN + FN)$
- Diagnostic accuracy (DA) proportion of patients diagnosed correctly by the diagnostic test,  $DA = (TP + TN) / (FP + FN + TP + TN)$

Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of FNAC relative to final histological diagnosis were analyzed by SPSS software.

## RESULTS

We included 125 patients who under went FNAC followed by Thyroidectomy (lobectomy or total

thyroidectomy) for a thyroid nodule. The 90(72%) female and 35(28%) male patients had a median age of 39 years (range 13 to 76) at the time of Thyroidectomy.

The FNA cytology results were compared with the corresponding histological diagnosis. The FNAC results were interpreted as benign in 63(50.4%), follicular 44(35.2%), malignant 15(12%) and unsatisfactory in 3 (2.4%). (Table 1)

**Table-1: Diagnosis in the 125 Thyroid Nodules with FNAC**

	Frequency	Valid Percent
Benign	63	50.4
Follicular	44	35.2
Malignant	15	12.0
Inadequate sampling	3	2.4
Total	125	100.0

The histological findings for 63 patients with a cytological diagnosis of benign, 57 were benign and 6 had malignant diagnosis. Of 44 cases with cytological diagnosis of follicular neoplasm, 31 had benign and 13 had malignant diagnosis on final histology. Among 15 patients with cytological diagnosis of malignant lesion, final histopathology revealed 1 case as benign. We had 3 patients in unsatisfactory group 2 were benign and 1 was malignant on final histopathology. (Table 2)

**Table-2: Correlation between FNAC and final histology**

HISTOPATHOLOGY				
		Benign	Malignant	Total
F	Benign	57	6	63
	Follicular	31	13	44
A	Malignant	1	14	15
	Inadequate sampling	2	1	3
Total		91	34	125

**Table-3: Distribution of Malignant Cases (n-34)**

	Frequency	Percentage
Papillary Ca	18	52.94
Follicular Ca	8	23.52
Medullary	6	17.64
Anaplastic	2	5.9
Total	34	100

We identified one false positive result from malignant group and 6 false negative results came from benign group.

Analysis of the FNAC results obtained were compared with the histological findings in order to rule out malignancy yielded a sensitivity (95% CI) of 98% (92.3% – 99%) specificity (95% CI) of 70% (53% – 75%) with positive predictive value of 91% and negative predictive value of 93% with diagnostic accuracy of 91% .

## DISCUSSION

FNAC contributes significantly to the pre operative investigation in patients with a solitary or dominant thyroid nodule but despite its well recognized value there are limitations to the technique.

The aim of this study was to evaluate the diagnostic accuracy in 125 patients with thyroid nodules submitted to FNAC and afterwards to surgery.

The false negative FNAC results may occur because of sampling error or misinterpretation of cytology, and are of great concern because they indicate the potential to miss malignant lesion.<sup>12</sup> However, it is difficult to calculate the true frequency of false negative results because only a small percentage (approx 10%) of patients with benign cytological findings under go surgery.<sup>13</sup> Most authorities agree that the true false negative rate is below 5% if all patients with thyroid FNAC also have a histological examination.<sup>13</sup>

False negative FNA cytology results occurred in 6(3.78%) of our patients. This is also consistent with recent reports in the literature that suggest a false negative rate of 2% to 7%<sup>14-19</sup> and other reported range from 1% to 16% in different series.<sup>2,9,11</sup>

A false positive cytology result may in retrospect have resulted in surgical over treatment for an individual patient. False positive FNA cytology results are uncommon and were found in only 1(0.15%) patient in this series. This finding is consistent with other recent reports that cited an incidence of false positive FNA cytology results ranging from 0% to 9%.<sup>14-19</sup>

We categorized cytological results into Benign, Follicular, Malignant and Indeterminate. Such categorization of FNA cytology results is necessary to allow clinicians to use cytology results to guide patient management with specific reference to the need for Thyroidectomy.

In the follicular group 13(5.72%) were malignant, which was due to limitations of thyroid cytology to distinguish follicular adenoma from follicular carcinoma.<sup>20-23</sup> This diagnosis require detailed histological examination for vascular and capsular invasion and cannot be reliably made on routine FNAC specimens.<sup>24-28</sup>

The sensitivity of thyroid FNAC ranges from 65% to 99% and its specificity from 72% to 100%.<sup>29-32</sup> In this study, the sensitivity for cytological diagnosis of neoplasia was 98%, specificity of 70%, positive predictive value of 91%, negative predictive value of 93% and diagnostic accuracy of 91% which is similar to the experience of others.<sup>24,25,33</sup> Ikram et al has reported sensitivity and specificity for malignancy as 100% which is slightly higher then our results as they do not have false

positive results in their study due to small number of patients.<sup>34</sup> Our study also testifies the results of previously done study at Aga Khan University by Afroze N et al, where they have reported sensitivity of 61.9%, the specificity of 99.31%, positive predictive value 92.86%, negative predictive value of 94.74% and accuracy index of 94.58%. This is slightly different then our results and this may be due to the fact that they had considered suspicious cases alternatively as positives and negatives.<sup>35</sup> Our results also coincides with results of Safirullah et al, where they have reported a sensitivity of 94.2%.<sup>36</sup>

Inadequate FNA specimen may be results of inadequate sampling or focal lesion. Thyroid nodules that are sclerotic or calcified and those with large areas of cystic degeneration or necrosis are extremely difficult to aspirate. In our series 3(2.4%) patients have inadequate sampling which again corresponds to results of international studies in which the inadequate sampling has been reported from 1% to 5%.<sup>4</sup> The advent of ultrasound guided FNA biopsy improved specimen acquisition, especially in patients with small thyroid nodules or nodule that are difficult or impossible to detect on physical examination<sup>36-38</sup>.

## CONCLUSION

The assessment of the patient with a thyroid nodule(s) includes the triple modalities of clinical examination, cytology and imaging investigations. The result of thyroid aspiration cytology is therefore only one factor governing the management decision. Indeterminate FNAC results and cytodiagnostic errors are unavoidable due to overlapping cytological features particularly among hyperplastic adenomatoid nodules, follicular neoplasms and follicular variants of papillary carcinomas.

Ongoing correlation of cytology and histology is an important quality assurance measure and it allows laboratories to calculate their false positive and false negative rates.

We conclude that FNAC is an invaluable and minimally invasive procedure for pre operative assessment of patients with a thyroid nodule. FNAC has high accuracy in the diagnostic evaluation of thyroid nodule.

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