

# Use and Accuracy of Fine Needle Aspiration Cytology in Thyroid Lesion: Our Experience in a Tertiary Teaching Hospital in North India

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## Abstract

**Background:** Thyroid lesions are one of the common lesions encountered in clinical practice now days. Fine-needle aspiration cytology (FNAC) is considered a well-established diagnostic tool for the evaluation of clinically palpable thyroid lesions. It is a safe, non-invasive, cost-effective and efficient time-saving procedure that provides specific diagnosis rapidly with minimal complications.

**Purpose:** The aim of this study was to diagnose the spectrum of thyroid lesions by fine-needle aspiration cytology and to correlate these with histopathology findings of excised specimens.

**Materials and Methods:** FNAC was performed in total 252 patients with a thyroid swelling from December 2012 to December 2014, at a tertiary care teaching hospital. Cyto-histopathological correlation was done in 121 patients.

**Results:** Out of 252 patients, with thyroid swelling (M:F = 1:3) majority were in younger age group ( $n = 106$  [42.06%] 21-40 years). In 240 adequate smears for cytological interpretations, colloid goiter was the most common diagnosis. Of these, 121 cases were surgically treated, and the tissue was submitted for a histopathological study, which showed 118 non-neoplastic lesions and 4 as neoplastic. In the present study, the cyto-histological concordance rate was 97.5%. The sensitivity, specificity, positive and negative predictive value and diagnostic accuracy are 50%, 99.14%, 66.6%, 98.3% and 97.5% respectively with significant  $P = 0.03$  and kappa value = 0.6, which shows a good cyto-histological correlation.

**Conclusion:** FNAC is an excellent safe diagnostic procedure with a high degree of diagnostic accuracy and plays a crucial role in the selection of patients for surgery thus minimizing their expenditure and hospitalization.

**Key words:** Colloid goiter, Diagnostic accuracy, Fine needle aspiration cytology, Thyroid lesions

## INTRODUCTION

Thyroid lesions are common lesions encountered in the outpatient department (OPD). Awareness and understanding of wide spectrum thyroid disorders are of

great value because most lesions are treatable by medical or surgical management. Fine needle aspiration cytology (FNAC) is a safe, non-invasive, cost-effective and efficient time-saving OPD procedure, which provides specific, rapid diagnosis with minimal complications. FNAC is a well-established diagnostic tool for the evaluation of clinically palpable thyroid lesions. Although it is not a substitute for conventional histopathology, it should be considered as an essential component of preoperative/investigative procedure of pathological process.<sup>1</sup>

The prevalence of thyroid lesions is higher in women (5%) than in men (1%).<sup>2</sup> However, most of the nodules are

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benign and depending on age, gender, radiation exposure history, family history, and other factors, malignancy can be present in 5-10% of nodules only.<sup>2-3</sup>

The routine use of this technique in the assessment of thyroid lesion has reduced the number of patients subjected to surgeries. Although FNAC is not a substitute for conventional histopathology, it is extremely valuable in categorizing the diseases. It bridges the gap between clinical evaluation and final surgical pathological diagnosis in the majority of cases and helps to reduce unwarranted surgeries. As a result, the incidence of malignancy at thyroidectomy has increased from 5-10% to 30-50%.<sup>4-5</sup>

Different imaging techniques are now days used for preoperative diagnosis of clinically palpable thyroid lesions such as radio-nuclide scanning and high-resolution ultrasonography. However, FNAC is still regarded as the most accurate, time-saving and cost effective procedure, particularly if ultrasound is used as a guide for better sample collection especially in cystic lesions.

Today this procedure is practiced all over the world as an investigation of choice. Besides thyroid, it is used in other swellings as well like salivary glands, breast lesions, soft tissue and lymph nodes.<sup>6</sup>

The aim of this study is to analyze the cytomorphology of clinically palpable thyroid lesions and correlate the findings with histopathological examination and to evaluate its sensitivity and specificity.

## MATERIALS AND METHODS

This study was carried out in the Department of Pathology, of a tertiary teaching hospital, from December 2012 to December 2014. FNA was performed in 252 patients, presenting with the thyroid swelling referred from the various departments.

All the cases of thyroid swellings were included in the study and all the cases having neck swelling other than thyroid were excluded.

All the patients were carefully examined, and the procedure detail was explained to them in their language and a written consent was taken. Aspiration was done under aseptic precautions by 22-23 gauge needle, and both dry and wet smears were prepared. In cases of cystic and heterogeneous lesions or whenever cells were not retrieved by direct aspiration, guided aspiration was done. We categorized our results into inadequate/non-diagnostic, benign, follicular lesion of undetermined significance (FLUS)/atypia of undetermined significance (AUS), suspicious for

malignancy and malignant sampling according to the recent Bethesda classification.

The FNAC results were compared with the histological diagnosis which was considered as gold standard. Cases with cyto-histological disparity were re-evaluated for a probable reason. Statistical analysis of data was performed by using SPSS version 20 software. The sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of FNAC in diagnosing thyroid lesions were calculated.

## OBSERVATION AND RESULTS

Out of 252 cases with a thyroid swelling, 189 (75%) were females and 63 (25%) were males (M:F = 1:3). The age ranged from 10 years to 85 years with mean age of 37.86 years.

FNAC results were interpreted according to Bethesda classification and showed 200 benign cases (79.3%), 5 FLUS/AUS cases (1.9%), 13 cases (5.1%) of follicular neoplasm/suspicious for follicular neoplasm, 12 cases (4.5%) suspicious for malignancy, 10 cases (3.9%) malignant and 12 cases (4.7%) as Inadequate/non-diagnostic. Colloid goiter was the most common diagnosis in benign lesions. The malignant lesions showed papillary carcinoma (7 cases), medullary carcinoma (1 case) and anaplastic carcinoma (2 cases) (Table 1 and Figures 1-4).

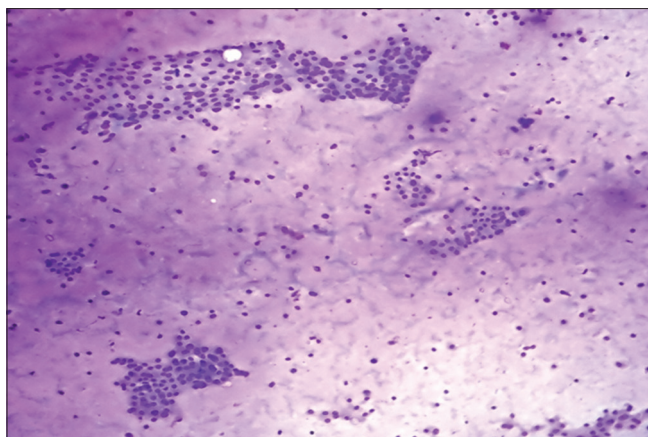
The FNAC diagnosis was compared with the corresponding histopathological diagnosis. Out of 252 cases of FNAC, 121 thyroid specimens were subjected for histopathological evaluation. Cyto-histological concordance was found in 118 cases (97.5%), whereas 3 cases were discordant. Out of 2 cases reported as benign on cytology, one case was diagnosed as papillary carcinoma and other as follicular carcinoma thyroid on histopathology. 1 case reported as malignant on cytology was nodular goiter on histopathology (Table 2).

In the present study, the sensitivity, specificity, positive and negative predictive value and diagnostic accuracy of FNAC

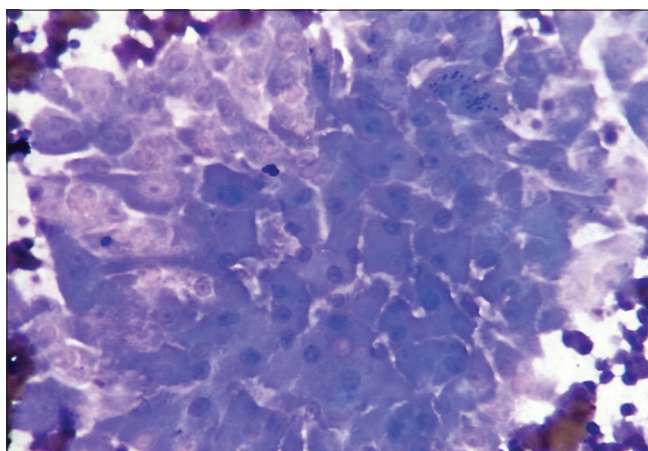
**Table 1: The cytological diagnosis distribution as per the bethesda classification**

FNAC diagnosis	No. of cases	Percentage
Non diagnostic/inadequate	12	4.7
Benign	200	79.3
AUS/FLUS	5	1.9
FN/SFN	13	5.1
Suspicious for Malignancy	12	4.5
Malignant	10	3.9

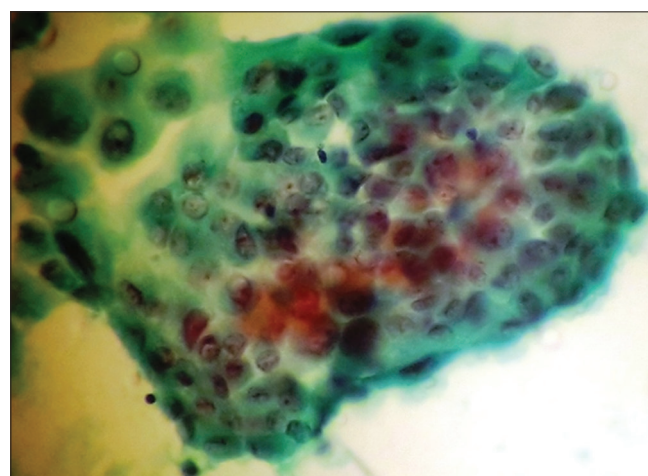
FN: Follicular Neoplasm, SFN: Suspicious for follicular Neoplasm, AUS: Atypia of undetermined significance, FNAC: Fine needle aspiration cytology, FLUS: Follicular lesion of undetermined significance



**Figure 1:** Photomicrograph of smear showing clusters of follicular epithelial cells against colloidal background (leishman giemsa,  $\times 100$ )

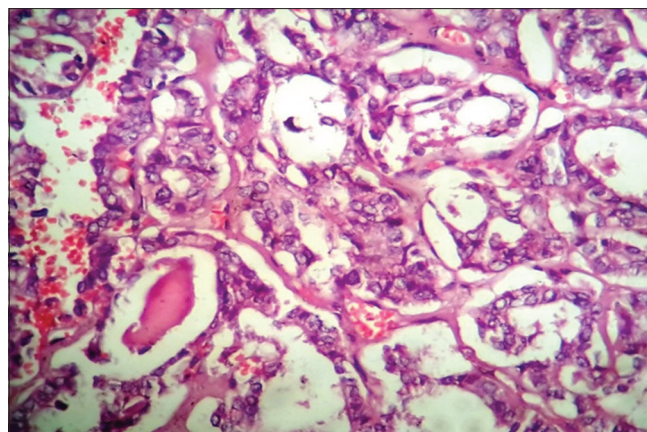


**Figure 2:** Photomicrograph showing highly cellular smear with oncocytic change in follicular epithelial cells, hurthle cell neoplasm (leishman giemsa,  $\times 400$ )



**Figure 3:** Photomicrograph of smear from papillary carcinoma thyroid showing large papillae showing nuclear overlapping, overcrowding with intracytoplasmic inclusions (Pap,  $\times 1000$ )

in diagnosing thyroid lesions were found 50%, 94.1%, 66.6%, 98.3% and 97.5%, respectively (Table 3).



**Figure 4:** Photomicrograph of papillary carcinoma thyroid showing ground glass nuclei with nuclear grooving. Tissue section (H and E,  $\times 400$ )

## DISCUSSION

Currently, FNAC of the thyroid nodule is a well-established and preferred diagnostic method for the initial evaluation of thyroid lesions as it has decreased the number of patient who underwent surgical treatment by 25-50%, thus increasing the percentage of malignant results in the operated group of patients.<sup>7</sup>

The present study was undertaken to evaluate, the type of thyroid lesion preoperatively with the help of FNAC and to correlate the observations with the histopathological examination in order to determine the usefulness and diagnostic accuracy of this technique.

The FNAC of the thyroid gland was performed in 252 cases, out of which histopathological specimen of 121 patients were received during the study period. Comparison of various parameters in our present study was done with previous studies.

In our study, the age of the patients ranged from 5 years to 85 years with most of the patients in the third and fourth decade (mean = 37.86) which is similar to the previous studies.<sup>5,8,9</sup>

Females were more affected than males in this study, which showed concordance with the previous studies.<sup>8-12</sup>

The inadequacy rate in the present study was 4.7%. Previous studies have shown the variable percentage of inadequate material ranging from 0% to 25%.<sup>5,13,14</sup> Ali *et al.* suggested that the rate of non-diagnostic tests should be kept below 10%.<sup>15</sup>

Inadequate FNA specimen can occur as a result of sampling error, faulty technique and in highly vascular or



**Table 2: Cyto-histo correlation of thyroid lesion**

Bethesda category	FNAC diagnosis	Histopathological diagnosis
2. Benign	90 cases of Colloid goiter  15 cases of colloid goiter with cystic change 4 cases of colloid goiter with hurthle cell change 1 case of colloid nodule 4 cases of multinodular goiter 1 case of de-quarvains thyroiditis 1 case of hyperplastic nodule 1 case of colloid goiter 1 case of colloid goiter	88 cases of colloid goiter 1 case of MNG with lymphocytic thyroiditis 1 case of benign cystic lesion 15 cases of colloid goiter 4 cases of colloid goiter 1 case of colloid goiter 3 case of colloid goiter 1 case of multinodular goiter 1 case of colloid goiter 1 case of colloid goiter Papillary carcinoma thyroid Follicular carcinoma thyroid
4. Category	1 case of hurthle cell neoplasm 1 case of FN 1 case of FN	Hurthle cell adenoma with colloid nodule Follicular adenoma Nodular goiter

FNAC: Fine needle aspiration cytology, FN: Follicular neoplasm

**Table 3: Diagnostic accuracy of FNAC in thyroid lesion**

FNAC diagnosis	Total number of FNAC cases	Number of cases with surgical biopsy	Correct FNAC diagnosis	FN	FP
Benign	200	117	116	-	1
Malignant	40	04	02	2	-
Unsatisfactory	12	-	-	-	-
Total	252	121	-	-	-

FNAC: Fine needle aspiration cytology

focal lesions. Ultra-sound guided sampling reduces the non-diagnostic test result.<sup>15,16</sup>

The reason for lower percentage in the non-diagnostic and atypical follicular lesion of undetermined significance categories can be attributed to the fact that in our institutional setting, usually an ultrasound-guided FNAC is being performed by cytopathologist himself, for small nodules and nodules that appear heterogeneous on palpation, so the aspirate are procured from the exact site with a better quality and adequacy. This led to a reduction in the non-diagnostic cases thereby allowing more specific cytological diagnosis.

Being a tertiary care center, this institute caters a large population, representative of the general population, moreover this region comes under sub-Himalayan belt or “goiter belt”, therefore proportion of benign cases is more as compared to other entities.<sup>17</sup>

The cytomorphologic interpretation of AUS is subjective. Therefore the rate of AUS diagnosis is variable among institutions and pathologists. In some studies, the diagnosis of “AUS/FLUS,” “FN/SFN” and “suspicious for malignancy” are defined as intermediate category. We grouped these lesions as neoplastic lesions.

In the present study, the cyto-histological concordance rate was achieved in 118 (97.5%) cases whereas 3 cases

showed discordance ( $n = 2$ , 1.65% false negative and  $n = 1$ , 0.80% false positive [FP]).

Misinterpretation of aspirate from a non-neoplastic lesion of the thyroid as neoplastic (FP) occurred in 1 case in our study where a follicular neoplasm reported on FNAC was found to be colloid goiter on histopathology, as aspiration was probably done from the hypercellular areas of colloid nodules which led to over-diagnosis. A possible remedy is multiple aspirates from different parts of the swelling that could demonstrate colloid - rich areas and monolayered sheets of epithelial cells representing macrofollicles and degenerative changes, which would suggest the possibility of non-neoplastic lesions.<sup>18</sup>

False negative cases (misinterpretation of aspirates from neoplastic lesions of thyroid as non-neoplastic) may also occur due to error in the sampling or misinterpretation of cytological material because of overlapping features of different lesions, these are of great concern because it indicates potential to miss malignant lesion.<sup>19</sup> Since only a small percentage of patients with benign cytological findings undergo surgery, it is difficult to state the exact frequency of false negative results.<sup>20</sup> In our study, a false negative diagnosis of colloid goiter was rendered in 2 cases, which turned out to be neoplasm on histopathological examination, one papillary carcinoma and other follicular carcinoma. False negative results in our series accords with the reports that suggest a range in literature from 1% to 11%.<sup>20,21</sup> False negative cytology results delays in treatment and hence adversely affects the outcome in patients with malignancy.<sup>22</sup>

Cytological examination in the first false negative case showed abundant colloid with low cellularity of follicular cells and cystic macrophages, which led to misinterpretation as a benign lesion. An accurate diagnosis could not render because of sampling from cystic areas and aspirating abundant colloid rather than cellular area. The occurrence

of cystic change in thyroid lesions is a common diagnostic pitfall in cytology.<sup>6</sup> Most authors recommend preparation of 4-6 smears from different areas of the nodule. Strict criteria for specimen adequacy could help to reduce markedly the erroneous diagnosis in such cases.<sup>6,22</sup> Ultrasound guided FNAC results in better sample acquisition leading to low rate of non-diagnostic smears and high overall accuracy.<sup>23</sup>

Cytological examination in the second case show moderate cellularity with small clumps of thyroid follicular cells arranged in poorly cohesive groups and a moderate amount of colloid favoring a diagnosis of colloid goiter. Histological features were consistent with follicular carcinoma showing vascular and capsular invasion. Cytological differentiation between follicular neoplasm and nodular goiter is often difficult.<sup>1</sup> Aspiration, in this case, was probably done from colloid - a rich macrofollicular area of the neoplasm.<sup>1</sup> As possible remedial measures, cytological features like increased cellularity with nuclear crowding and overlapping, repetitive uniform follicular cell patterns, syncytial clusters, microfollicular structure, scanty or no colloid may help in distinguishing follicular neoplasm from colloid goiter, although none of them is conclusive.<sup>24</sup>

Sometimes marked cellularity is another problem in thyroid cytology. Increased cellularity of the smear and loss of cohesion may be present in the hyperplastic nodule, adenoma or in carcinoma. It is also, difficult to differentiate follicular adenoma from carcinoma on the cytological assessment because cytology cannot evaluate the criteria of vascular or capsular invasion or of intrathyroid spread.

So, it is concluded that proper sampling from representative sites is utmost importance for an accurate diagnosis. Most authors recommend preparation of 4-6 smears from different areas of the nodule. Strict criteria for specimen adequacy could help to reduce markedly the erroneous diagnosis in such cases.<sup>6,22</sup> Ultrasound-guided FNAC results in better sample acquisition leading to a low rate of non-diagnostic smears, and high overall accuracy and pathologist should be aware of standard pitfalls thus facilitating the correct diagnosis.<sup>23</sup> As reported earlier, the sensitivity of the thyroid FNAC ranges from 43% to 99% and its specificity was found 72-100% respectively.<sup>12,20,25</sup> In our study, findings were comparable with the results in these series.

In our study, we find the diagnostic accuracy 97.5%, specificity 99.14%, sensitivity 50%, Positive predictive value 66.6% and negative predictive value 98.3%. Other statistical indices like Chi-square value = 4.7117E-12,  $P = 0.03$  which is significant and kappa value = 0.6 (kappa value > 0.75 shows excellent correlation between two studies). The overall diagnostic accuracy in our series is also comparable with previous studies.<sup>12,20</sup>

## CONCLUSION

Thus, we conclude from this that FNAC is an excellent, safe diagnostic procedure with a high degree of accuracy and less invasive procedure than a tissue biopsy. The yield on FNAC can be increased by USG guided aspiration. It plays a crucial role in the selection of patients in surgical management thus minimizing the surgical burden.

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