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# Usefulness of fine-needle aspiration in the diagnosis of thyroid lesions: an institutional experience of 340 patients

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## ABSTRACT

**Objective**: To evaluate the results of fine needle aspiration cytology (FNAC) in the diagnosis, its correlation with histology, to highlight its limitations and diagnostic pitfalls as well as the impact of FNAC on the decreased rate of surgery in clinically suspect thyroid lesions.

**Study design**: FNAC was performed on 340 patients with thyroid enlargement over a period of six years. The cytological results were correlated with clinical features, thyroid function tests and histopathological examination.

**Results**: Among non- neoplastic group, the most frequently encountered lesion was colloid goiter in 231 (67.94%) cases followed by thyroiditis in 68 (20%) cases, five (1.47%) adenomatous goiter and four (1.17%) thyroglossal cysts. Among the neoplastic

group, twelve (3.52%) cases were reported as follicular neoplasm, seven (2.05%) cases as Hürthle cell neoplasm and four (1.17%) as malignant tumors. The cytological and histological concordance was determined. A false positive cytologic diagnosis of neoplasms was made in five cases. Presence of Hürthle cell metaplasia, hyperplastic nodules and papillary hyperplasia were responsible for the false positive diagnoses. For the entire series, the false negative rate was 8.57% and the false positive rate was 7.14%. FNA revealed a sensitivity of 62.5%, a specificity of 90.74%, a positive predictive value of 66.66% and a negative predictive value of 89.09%.

**Conclusion**: FNAC is thus an accurate, cost- effective, minimally invasive and reliable diagnostic tool for assessment of patients with thyroid lesions and their management.

**Key words**: aspiration cytology, fine- needle, thyroid, colloid goiter, thyroiditis.

## INTRODUCTION

Thyroid fine needle aspiration cytology (FNAC) is over 50 years old[1] and is the principle method of preoperative diagnosis in both children and adults. It has been shown to be superior to clinical, radionucleotide or thyroid ultrasound assessment alone. FNAC has now supplanted most other tests for preoperative evaluation of thyroid nodules. FNAC requires careful aspiration technique and interpretation of the cytological findings. Most practitioners rely on FNAC alone, especially for the first attempt at diagnosis.

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 stage, resulting in better outcome of patients. The routine use of FNAC in the assessment of thyroid nodules has reduced the number of patients subjected to thyroidectomy for benign diseases of the thyroid.[2] As a result, the incidence of malignancy at thyroidectomy has increased from 5-10% to 30-50% in the recent years.[3] This has assumed a dominant role in determining the management of patients with thyroid nodules.[4, 5] 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.[6, 7]

Although many studies have reported diagnostic accuracy of FNAC in detecting neoplasms, there have been few studies where the roles of FNAC in the diagnosis of goiter along with their diagnostic pitfalls have been evaluated. [8, 9, 10, 11] The present study

was undertaken to evaluate the results of thyroid FNAC, its correlation with histology, to highlight its limitations and diagnostic pitfalls as well as the impact of FNAC on the decreased rate of surgery in clinically suspect thyroid lesions.

## MATERIALS AND METHODS

This retrospective study was conducted in the department of Pathology of our tertiary care centre over a period of six years. FNAC was performed on 340 patients with thyroid enlargement. Patients' data regarding history, complete clinical examination, thyroid function tests and clinical diagnosis were retrieved from the records.

All aspirations were performed by cytopathologists as outpatient procedure without imaging. A 23 gauge needle attached to a Franzen's handle was used, either without or with aspiration by a 20 ml disposable syringe. All the conventional smears were prepared by cytotechonologists. Half of the smears were air- dried and stained with May-Grünwald-Giemsa (MGG), and the remaining half were wet fixed and stained with Papanicolaou (Pap) and Haematoxylin and Eosin (H&E) stains. All the stained smears were evaluated by trained cytopathologists. No major complications like haematoma, penetration into the trachea or, laryngeal nerve palsy were recorded.

Out of 340 patients surgery was contemplated in seventy (20.58%) patients, where aspirates had shown malignancy, follicular or Hürthle cell neoplasm, cases having cosmetically unacceptable goiters, sudden development of pressure symptoms and those not responding/ regressing to thyroid suppressive therapy. Rests were managed medically. The resected tissues were examined histologically. Cytology- histology correlations were performed, and discrepancies in the results were analyzed. The cytological results were also correlated with clinical features and thyroid function tests.

## RESULTS

The age of the patients ranged from 13 to 76 years with a median age of 39 years and the female: male ratio was 5.8:1. The major presenting symptom in all the patients was diffuse and/nodular swelling of the thyroid. Other symptoms were less frequent- hoarseness of voice in eighteen patients, dysphagia in ten patients, cough in four and pain in the thyroid region in two patients. Patients gave a history of swelling being present for more than one year in 265 (77.94%) cases, less than six months in 45 (13.23%) cases and between six months and one year in 30 (8.82%) cases.

Thyroid function tests were performed in ninety patients (26.47%). Forty two patients (46.66%) were found to be euthyroid, thirty eight (42.22%) hyperthyroid and ten (11.11%) hypothyroid. The results were compared with cytological findings.

The cytologic diagnostic categories included non- neoplastic, neoplastic and inadequate as shown in Table1. The non- neoplastic diagnosis included colloid goiter, thyroiditis, adenomatous goiter and thyroglossal cyst. The neoplastic diagnosis applied to benign neoplasm and malignant neoplasm. The benign neoplasm included Hürthle cell neoplasm and follicular neoplasm and malignant neoplasm included papillary carcinoma and medullary carcinoma. Nine FNA specimens (2.64%) were deemed inadequate for the study because of insufficient cellularity or poor quality smear due to delayed or inadequate fixation.

Seventy cases had histology follow- up (20.58%), and the FNA cytology results were compared with the corresponding histological diagnosis as depicted in Table 2. There were discordant cytopathologic and histopathologic diagnosis in 11 cases. The discordant

cytologic diagnoses were categorized as false negative (six cases) and false positive (five cases), as shown in Table 3. The six false negative cases included two papillary carcinomas and four follicular adenomas. The corresponding cytologic diagnoses were colloid goiter. After cytohistologic review, these false negative diagnoses were attributed to cytologic interpretive errors. Cystic degeneration in colloid goiter was responsible for the missed diagnoses (Figure 1). Nuclear grooves and intranuclear pseudoinclusions were also missed in papillary carcinomas. The five false positive cases included one colloid goiter, one thyroiditis and three adenomatous goiters. The corresponding cytologic diagnoses of the five false positive cases were two Hürthle cell neoplasms and three follicular neoplasms. Presence of extensive oxyphilic change in goiter led to diagnosis of Hürthle cell neoplasm in one of our case. Presence of papillary hyperplasia and hyperplastic nodules were the causes of the misinterpretation in cases of adenomatous goiters. A case of Hashimoto's thyroiditis was cytologically diagnosed as Hürthle cell neoplasm (Figure 2). Extensive Hürthle cell metaplasia was attributed to interpretive error. For the entire series, the false negative rate was 8.57% and the false positive rate was 7.14%.

Statistical analysis of our data shows the diagnostic accuracy of FNAC to be 84.28%. FNA showed a sensitivity of 62.5% and a specificity of 90.74%. The negative and positive predictive values were 89.09% and 66.66% respectively.

**DISCUSSION**

Thyroid enlargement is a common occurrence in most regions of the world. India has the world's biggest goiter belt in the sub- Himalayan region. In these iodine- deficient areas,

the incidence of goiter among thyroid nodules is much higher as shown in our study (67.94%).

Thyroid enlargement, whether diffuse or in the form of a nodule, leads to a battery of investigations, mainly to rule out the possibility of a neoplasm or a thyroiditis. FNAC is usually the first line of investigation and other investigations like thyroid scan, ultrasound examination, thyroid function tests, and antibody levels are done subsequently with an aim to triage patients into those who would require surgery and those that can be managed conservatively.[12] FNAC of the thyroid has become increasingly popular as a diagnostic technique as it provides a sensitive, expedient and economical method of obtaining cytologic material for examination and its distinct advantages include accurate diagnosis, low cost, excellent patient acceptance and minimal or no morbidity.

The value of any diagnostic test lies in its ability to detect the presence of disease when it is present (sensitivity) and reliably verify the absence of disease when it is not present (specificity). The sensitivity of the thyroid FNAC ranges from 65 to 99% and its specificity from 72 to 100%.[3, 7] In our study, the sensitivity was 62.5% and specificity 90.74%. The cytohistological concordance rate in our study in colloid goiters came out to be 82.35% (42 out of 51 cases). Various studies have shown concordance between cytology and histology to vary between 80 and 100%. [8, 9, 10, 11]

Although many studies have reported diagnostic accuracy of FNAC in detecting neoplasms, there have been few studies where the role of FNAC in the diagnosis of goiter along with their diagnostic pitfalls have been evaluated.[8, 9, 10, 11] 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.[13] Since

only a small percentage of patients with benign cytological findings undergo surgery, it is difficult to state the true frequency of false negative results.[14] False negative FNA cytology results occurred in six (8.57%) of our patients. False negative rates in our series accords with the reports that suggest a range in literature from 1.5 to 9%.[15] A diagnosis of colloid goiter with cystic degeneration was rendered in six cases on FNAC which turned out to be neoplasms on histology, four being follicular adenomas while two cases were diagnosed as cystic papillary carcinomas. An accurate diagnosis could not be rendered because of sampling of areas of cystic change rather than cellular areas. Occurrence of cystic change in thyroid lesions is a common diagnostic pitfall in cytology.

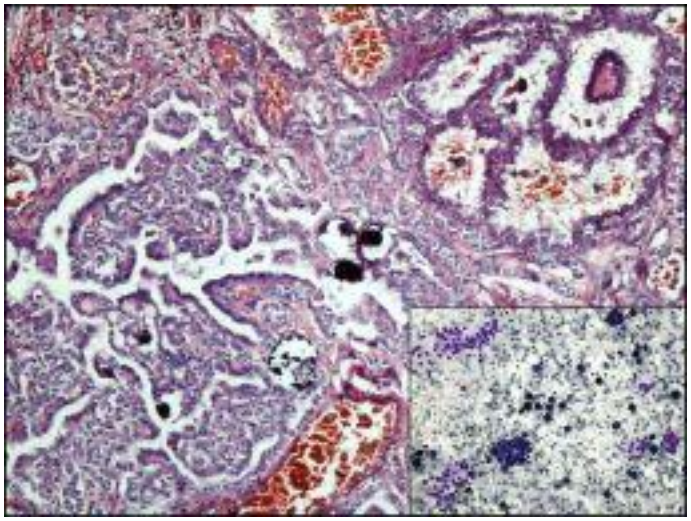
A false positive diagnosis of neoplasm was made in five cases. An erroneous diagnosis of Hürthle cell neoplasm was made in one of our case as a result of extensive oxyphilic change in a case of goiter. This is a known pitfall in diagnosis and has been reported in literature.[16] Also Hürthle cell metaplasia with nodule formation is a routine histological feature of Hashimoto's thyroiditis. Papillary hyperplasia and hyperplastic nodules are well known to occur in adenomatous goiters and could have been responsible for an erroneous diagnosis of follicular neoplasm in three cases. It may be appropriate to inform the clinician about the limitation of FNAC in such situations.

Marked cellularity of the smear is another problem inherent in thyroid FNA cytology. Increased cellularity of the smear and loss of cohesion may be present in hyperplastic/adenomatous goiter, adenoma or in carcinoma. It is difficult to differentiate follicular/ Hürthle cell adenoma from carcinoma on cytological assessment because cytology cannot evaluate the criteria of vascular or capsular invasion or, of intrathyroid spread. As in the present series, the limitations of thyroid cytology to distinguish

follicular adenoma from follicular carcinoma, was responsible for an erroneous diagnosis of follicular neoplasm in four of the cases.[14, 17]

An adequately cellular aspirate is indispensable for an accurate diagnosis. Presence of six groups of follicular cells on at least two slides from different passes recommended by Hamburger et al seems to be a fairly reasonable criterion for adequacy.[18] Inadequate FNA specimen may be results of inadequate sampling or focal lesions. Thyroid nodules that are sclerotic or, calcified and those with large areas of cystic degeneration or necrosis are extremely difficult to aspirate. The inadequacy rate of 2.64 % of the current study is comparable with those in other series, which range from 0 to 25%.[19, 20] Ultrasound guided FNAC results in better sample acquisition, especially in patients with small thyroid nodules, solid-cystic lesions or difficult-to-palpate lesions.[21]

Essential to the success of FNAC is an experienced and competent cytopathologist who is prepared to give an opinion. While interpretation is not always easy, it can always be learnt. Our surgeons find that the cytopathologic information is very useful for scheduling patients' visits and making their surgical plans. In the present study, there was a low rate of surgical intervention (20.58%) which highlighted the positive influence of FNAC on the management of thyroid disease. Surgery was avoided mainly in colloid goiter and thyroiditis. Thus, thyroid aspiration cytology directs the appropriate selection of patients for surgery, thereby reducing unnecessary surgeries. It can thus be concluded that FNAC as such is expedient, effective and safe diagnostic method for defining thyroid disorders.



Cystic papillary carcinoma on histology shows papillae exhibiting nuclear features in the form of clearing and nuclear grooves. Numerous macrophages and psammoma bodies are also present (H&E stain, X200). Inset: cytologically misdiagnosed as coll)

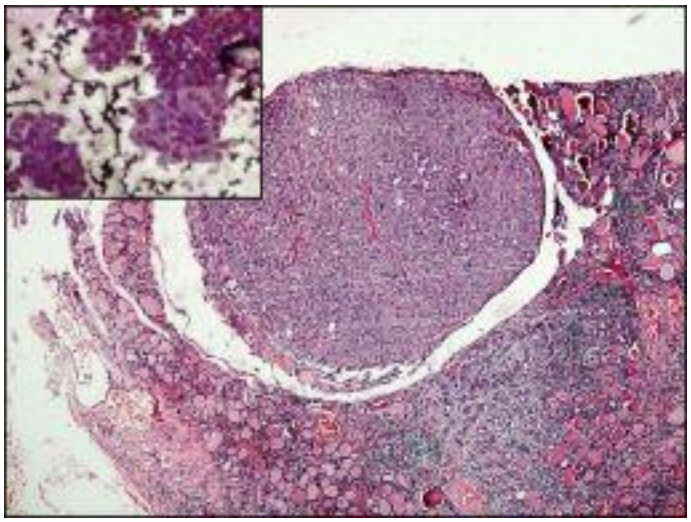


Figure 2: False positive case of Hashimoto's thyroiditis misinterpreted cytologically as Hürthle cell neoplasm. The follow up histology shows Hürthle cell nodule in Hashimoto's thyroiditis (H&E stain, X40). Inset: cytology smears demonstrates

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**LEGENDS:**

**Figure1**: Cystic papillary carcinoma on histology shows papillae exhibiting nuclear features in the form of clearing and nuclear grooves. Numerous macrophages and psammoma bodies are also present (H&E stain, X200). *Inset*: cytologically misdiagnosed as colloid goiter with cystic degeneration. The entire cytology smears demonstrates thyroid follicular cells and numerous colloidophages. (*Inset*: MGG stain, X200)

**Figure 2**: False positive case of Hashimoto's thyroiditis misinterpreted cytologically as Hürthle cell neoplasm. The follow up histology shows Hürthle cell nodule in Hashimoto's thyroiditis (H&E stain, X40). *Inset*: cytology smears demonstrates syncytial clusters of oxyphilic cells showing mild nuclear pleomorphism (*Inset*: MGG stain, X100)

**TABLES:**

**Table 1**: Cytological diagnoses of 340 patients.

| **FNAC diagnosis** | **Number of patients (%)** |
|---|---|
| **Non neoplastic** | n = 308 |
| • Colloid goiter | 231 (67.94) |
| • Adenomatous goiter | 5 (1.47) |
| • Thyroiditis | 68 (20) |
| • Thyroglossal cyst | 4 (1.17) |
| **Neoplastic** | n = 23 |
| a) Benign | |
| • Hürthle cell neoplasm | 7 (2.05) |
| • Follicular neoplasm | 12 (3.52) |
| b) Malignant | |
| • Papillary carcinoma | 3 (0.88) |
| • Medullary carcinoma | 1 (0.29) |
| **Inadequate** | 9 (2.64) |
| Total | 340 |

**Table 2**: Correlation of cytological and histopathological diagnosis (n = 70)

| **Cytological Diagnosis** | **Histopathological diagnosis** | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Colloid goiter | Adenomatous goiter | Thyroiditis | Thyroglossal cyst | Hürthle cell adenoma | Follicular adenoma | Papillary carcinoma | Total |
| Colloid goiter | 42 | — | 3 | — | — | 4 | 2 | 51 |
| Adenomatous goiter | — | — | — | — | — | — | — | — |
| Thyroiditis | — | — | — | — | — | — | — | — |
| Thyroglossal cyst | — | — | — | 4 | — | — | — | 4 |
| Hürthle cell neoplasm | 1 | — | 1 | — | 3 | — | — | 5 |
| Follicular neoplasm | — | 3 | — | — | — | 4 | — | 7 |
| Papillary carcinoma | — | — | — | — | — | — | 3 | 3 |

**Table 3**: Thyroid aspirations with interpretation errors and final diagnosis.

| Diagnosis | FNAC diagnosis | Final diagnosis |
|---|---|---|
| False positive- 5 | • Hürthle cell neoplasm- 2<br><br>• Follicular neoplasm- 3 | Colloid goiter- 1<br><br>Thyroiditis- 1<br><br>Adenomatous goiter- 3 |
| False negative- 6 | Colloid goiter- 6 | Papillary carcinoma- 2<br><br>Follicular adenoma- 4 |