

Cyto-histology and clinical correlation of thyroid gland lesions: A 3 year study in a tertiary hospital

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ABSTRACT

Background: Fine needle aspiration cytology (FNAC) is a cost-effective and time saving diagnostic test used to specifically distinguish between benign and malignant lesions by histocytology. The aim of this study was to study the spectrum of thyroid lesions and to correlate the FNAC findings with histopathology of excised specimens. **Materials and Methods:** A total of 300 patients with thyroid swelling were included in this study who had FNAC during 3 years study period, from July 2011 to July 2013, at a tertiary care hospital. All patients with thyroid swelling were assessed by medical history, clinical examination, biochemical tests and radiological investigations. The FNAC diagnoses were correlated with clinical features, radiological investigations, hormonal findings and subsequent histological examination of the thyroid specimens. **Results:** Out of 300 patients, females outnumbered males in thyroid diseases and revealed preponderance toward younger population (21-40 years). Nodular colloid goiter was the most common cause of thyroid swelling presented during 1 month to 1-year period. There were 104 patients (34.7%) who had surgical intervention and 86 (28.7%) patients reported for follow-up and had thyroid function tests done. The diagnostic accuracy, sensitivity and specificity for malignancy were 94.2%, 50% and 100% respectively in our study. **Conclusion:** FNAC is a reliable, safe and accurate method as an initial simple diagnostic test for thyroid nodules in decision making about surgical intervention. Our study suggested that FNAC has higher specificity than sensitivity in detecting thyroid malignancy; hence its use as a reliable diagnostic tool for evaluation of thyroid swelling cannot be overemphasized.

Key words: Cyto-histologic correlation, fine needle aspiration, thyroid lesions

INTRODUCTION

The incidence of clinically apparent thyroid nodules in the general population is 4-5%.^[1] The prevalence of goiter is more than 40 million in India with more than 2 billion globally.^[2] Some studies on goiters showed overall prevalence of hypothyroidism in 5.4% and hyperthyroidism. 1.9%. Prevalence of autoimmune thyroiditis confirmed by fine needle aspiration cytology (FNAC) was 7.5%.^[3] Accurate diagnosis of thyroid nodules is necessary for appropriate clinical management of these patients and to avoid

unnecessary surgical interventions. The majority of clinically diagnosed thyroid nodules were benign in nature and those requiring surgical intervention due to malignant lesions were 5-20%.

Over the past two decades, FNAC has become a preferred test; being a fast, safe, reliable, minimally invasive, cost effective and reaching high sensitivity and specificity in the evaluation of thyroid nodules.^[4]

However, limitations in FNAC due to scanty sample, vascularity of thyroid swelling, variation in sampling technique and skill of the performing expert as well as the experience of pathologist interpreting the aspirate do pose a problem in definitive diagnosis.^[5]

Procedures like ultrasonography and radioisotope scan have greater limitations since these tests will not differentiate benign and malignant thyroid nodules.

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The prevalence of thyroid nodules varies considerably depending on the variety of factors that include iodine intake within a given population, age, sex, diet, therapeutic and environmental radiation exposure. Small thyroid nodules are commonly found in patients with concurrent history of Hashimoto's thyroiditis.^[6]

Hence, this study is undertaken to study the spectrum of thyroid lesions with clinico-pathological and biochemical evaluation of non-neoplastic and neoplastic lesions of the thyroid.

MATERIALS AND METHODS

This was a retrospective and prospective study of 300 patients of clinically diagnosed thyroid nodules. The study was carried out at the Department of Pathology of a Tertiary Care Medical College and Hospital during the period of 3 years; July 2011 to July 2013. All patients with thyroid nodules had provisional diagnoses on the basis of history, physical examination, thyroid function tests (TFT) and ultrasound for thyroid gland.

The study was approved by the Institutional Ethics Committee and the FNAC procedure was performed after obtaining informed consent of all patients included in this study.

Careful palpation of the thyroid nodule was done to decide the location of aspiration. FNAC was done under aseptic conditions by using 10 cc or 20 cc disposable syringe with 23 gauge needle.

Two to three passes were made if the swelling was cystic or fluid was aspirated.

The smears were dried and stained with Leishman stain. Many of the smears were also fixed immediately in a fixative containing equal quantity of ether and 95% ethyl alcohol. These were stained by hematoxylin and eosin (H and E) stain and Papanicolaou stain.

A total of 104 thyroidectomy specimens were processed in an automated tissue processing units and stained with routine H and E stain for histopathological examination.

Statistical analysis was carried out using the OpenEpi, version 3 for sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of FNAC and these parameters were compared with histopathology as a gold standard.

RESULTS

A total of 300 patients were included in this study, of which 269 (89.7%) were females and 31 (10.3%) were males.

Females had more number of thyroid swellings with F:M ratio 8.6:1.

The incidence of female:male ratio was 8.6:1. The younger female patients (21-40 years) were in the majority in our study (21-40 years) and the mean age was 38.6 years. Malignant thyroid lesions were detected by FNAC in 12 patients, who were in 20-70 years old with a mean age of 45.3 years. The females outnumbered the males.

In total, 12 cases of malignant thyroid lesions in our study ranged from the age group of 20-70 years with females outnumbering males and mean age of 45.25 years.

Majority of cases presented with nodular (71%) thyroid swelling while few cases had diffuse involvement (29%). Swelling of the right lobe of thyroid (39%) was more when compared to the left lobe (31.3%). A few cases complained of pain, difficulty during swallowing or breathing. All the patients tolerated the procedure well without any complications. The aspirate was satisfactory for interpretation in majority. Of 300 patients, 50 patients had an unsatisfactory aspirate. These 50 patients (16.7%) were followed by repeat FNA. On repeat FNA of these 50 patients, a diagnostic aspirate was obtained in 48 patients (96%) and two aspirates were again unsatisfactory. The aspirate was blood mixed to frankly hemorrhagic and in some cases, either brown or dark brown fluid was aspirated, ranging from 1 to 5 ml.

TFT were performed in 200 patients (66.7%). 113 patients (56.5%) were found to be euthyroid, 46 hyperthyroid (23%) and 41 (20.5%) hypothyroid [Table 1].

The cytological diagnoses were divided into four categories: Benign, indeterminate, malignant and unsatisfactory [Table 2]. Benign category encompassed colloid goiter (CG), adenomatous goiter, different types of thyroiditis [Figure 1] and Grave's disease. All malignant lesions without any overt follicular architecture were included in the malignant category [Figure 2]. The indeterminate category encompassed diagnoses of follicular neoplasm and Hurthle cell neoplasm.

The FNAC diagnostic categories were compared with corresponding histopathological diagnose as illustrated [Table 3]. Among the benign lesions, histopathology was

Table 1: Biochemical findings in patients studied of thyroid nodules

Investigations	No. of patients	Percentage
Euthyroid	113	56.5
Hypothyroid	46	23.0
Hyperthyroid	41	20.5
Total	200	100

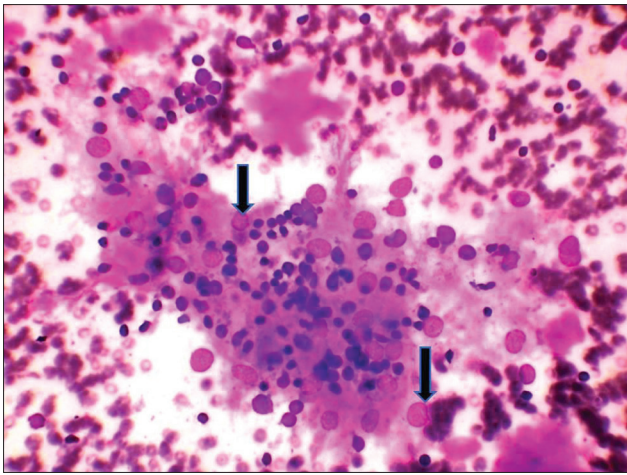


Figure 1: Fine needle aspiration cytology smear of Hashimoto's thyroiditis showing Hurthle cells (arrows) against a background of lymphocytes (Leishman, x100)

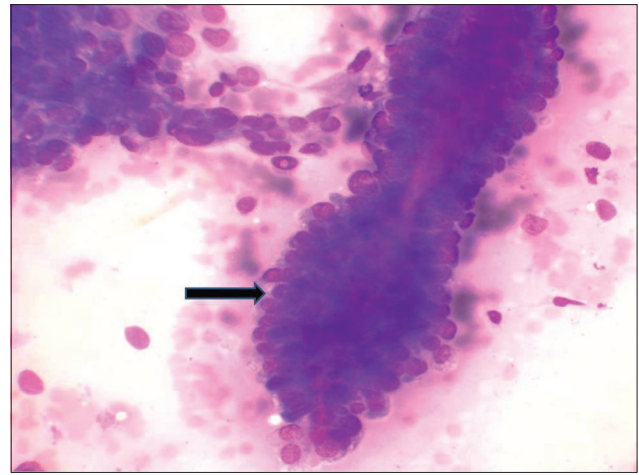


Figure 2: Fine needle aspiration cytology smear of papillary thyroid carcinoma showing papillary fragment (arrow; Leishman, x400)

Cytological diagnosis	No. of patients (n=300)	Percentage
Benign		
CG	198	66
Thyroiditis	57	19
Cystic lesion	21	7
Grave's lesion	8	2.6
Indeterminate		
FN	5	1.7
HCN	4	1.4
Malignancy	5	1.6
Unsatisfactory	2	0.7
Total	300	100

CG: Colloid goiter, FN: Follicular neoplasm, HCN: Hurthle cell neoplasm

FNAC Diagnosis	No. of cases 300 (%)	Histopathology Diagnosis	No. of cases with surgical biopsy (104)	
			Consistent with FNAC 98 (%)	Not consistent with FNAC 6
Benign				
CG/AG	198 (66)	CG/AG-PTC-2, FTC-1	76 (96.2)	3
Colloid cyst lesions	21 (7)	CC-6, PTC-3, MNG with HT-1	7 (8.9)	3
Thyroiditis	57 (19)	HT-2	2 (2.6)	-
Grave's disease	8 (2.6)	Grave's disease-1	1 (1.3)	-
Indeterminate				
FN	5 (1.7)	FA-3	3 (4)	-
HCN	4 (1.6)	HCA-2	2	-
Malignant				
PTC	3 (1)	PTC-4	4	-
FTC	1 (0.3)	FTC-1	2	-
MTC	1 (0.3)	MTC-1	1	-
Unsatisfactory	2 (0.7)	-	-	-

% is shown in brackets after number. CG: Colloid goiter, AG: Adenomatous goiter, FN: Follicular neoplasm, HCN: Hurthle cell neoplasm, PTC: Papillary thyroid carcinoma, FTC: Follicular thyroid carcinoma, MTC: Medullary thyroid carcinoma, MNG: Multinodular goiter, HT: Hashimoto's thyroiditis, FA: Follicular adenoma, HCA: Hurthle cell adenoma, FNAC: Fine needle aspiration cytology

available in 92 cases. In our study, cyto-histo concordance was achieved in 86 cases (93.4%), whereas six were discordant. In malignant category, histopathology was available for seven, concordance by FNAC was (100%). Of the six discordant cases, five were diagnosed as papillary carcinoma [Figure 3] and one as follicular carcinoma [Tables 4 and 5].

False negative FNAC result was noted in six specimens but there was no false positive test in our study. Two cytological specimens (0.7%) were deemed inadequate for the study because of insufficient cellularity or poor quality smear due to hemorrhagic aspirate.

In the present study, the sensitivity, specificity and accuracy of FNAC for the detection of malignancy were 50%, 100% and 94.2% [Table 6].

DISCUSSION

Thyroid lesions are quite common, with a prevalence rate of approximately 4-7% in the adult population. In our study, the common age group with thyroid nodules was in the third and fourth decade with female preponderance, similar observations were noted in other studies.^[4,5,7]

Subclinical (non-palpable) lesions are present in up to 70% of individuals and 90-95% of these lesions have benign histology.^[7] The vast majority of clinically diagnosed thyroid nodules are benign, with carcinoma occurring in approximately 5-20% of the cases.^[7] In our study, the incidence of malignant lesion was 12%.

Currently, FNAC of the thyroid nodule is a well-established and also a reliable initial investigation. Other investigations such as ultrasonography, TFT, thyroid scan and serological

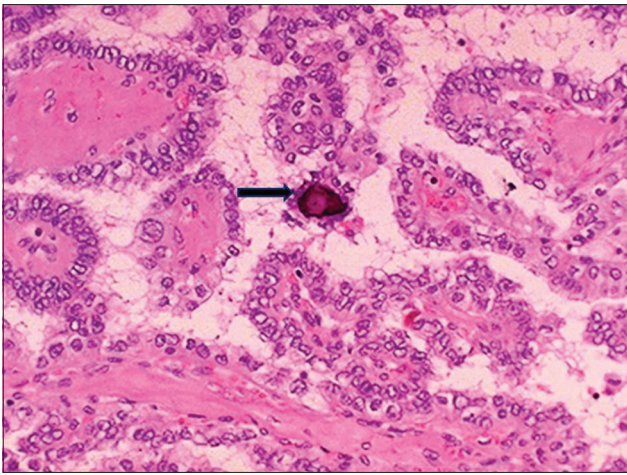


Figure 3: Histopathological examination of papillary carcinoma of thyroid showing papillary fronds with fibro vascular core and psammona body (arrow; H and E, ×100)

Table 4: Diagnostic accuracy of FNAC of thyroid lesions

FNAC diagnosis	Total no. of FNAC cases	No. of cases with surgical biopsy	Correct FNAC diagnosis	FN	FP
Benign	293	98	92 (TN)	-	0
Malignant	5	6	6 (TP)	6	-
Unsatisfactory	2	-	-	-	-
Total	300	104			

FNAC: Fine needle aspiration cytology, TN: True negative, TP: True positive, FN: False negative, FP: False positive

Table 5: Patients with TFT and/or surgical follow-up

Diagnosis	Total number of FNAC diagnosis cases	TFT follow-up	Surgical follow-up
Thyroiditis	57	29	2
Cystic lesion	21	5	10
Goiter	198	45	79
Grave's disease	8	6	1
Follicular/Hurthle cell adenoma	9	1	5
Malignancy	5	0	7
Unsatisfactory	2	0	0
Total (%)	300	86 (28.6)	104 (34.6)

TFT: Thyroid function test, FNAC: Fine needle aspiration cytology

Table 6: The statistical values for histological diagnosis in thyroid malignant lesions

Statistical parameter	Formula	Value %
Sensitivity	$TP / (TP + FN) \times 100$	50
Specificity	$TN / (TN + FP) \times 100$	100
Positive predictive value	$TP / (TP + FP) \times 100$	100
Negative predictive value	$TN / (TN + FN) \times 100$	93.8
Diagnostic accuracy	$(TN + TP) / (TP + FN + TN + FP) \times 100$	94.2

TP: True positive, FN: False negative, TN: True negative, FP: False positive

studies can be helpful in the evaluation of diffuse thyroid lesions.^[4,8]

FNAC is also widely accepted as an accurate and cost-effective diagnostic modality in the pre-operative

diagnosis of various thyroid lesions. The sensitivity of the thyroid FNAC ranges from 43% to 99% and its specificity from 72% to 100% respectively.^[5,9,10] In our study, findings were comparable with those reported in other series. The inadequacy rate in this study was only 0.7%. Previous studies have shown the percentage of inadequate material ranges from 0% to 25%.^[4,11,12]

In the present study, the cyto-histological concordance rate was achieved in 98 (94.3%) cases and the discordant cases of cyto-histology, false negative were 5.7%. The false negative FNAC results may occur due to error in sampling or misinterpretation of cytology; these are of great concern because it indicates the potential to miss malignant lesion.^[13] This rate of failure to diagnose cancer could be attributed to the failure of aspiration from precise location. False negative cytology results may cause delay in treatment and hence adversely affects the outcome in patient with thyroid cancer.^[14]

A false negative cytological diagnosis of CG was rendered in three cases where two cases turned out to be papillary thyroid carcinoma and one case was follicular carcinoma on histology. Out of the two cases of papillary carcinoma, one was micro papillary variant and the other was papillary carcinoma with secondary deposits to lymph nodes.

Poor cellularity of the aspirated samples in cystic lesions and suboptimal preparations has been often misinterpreted as benign lesions. These sampling errors may be responsible for the under diagnosis of papillary carcinoma. In our study, we missed three cases owing to the cystic changes observed in the cytological smears. Occurrence of cystic change in thyroid lesions is a common diagnostic pitfall in cytology. Therefore, aspiration from multiple sites and from solid areas is advisable. In such cases, ultrasound guided FNAC in cystic thyroid nodule results in better sample with high overall accuracy.

In the present study, there were 50 cases of unsatisfactory smears, for which repeat fine needle aspiration was done; 48 patients had a diagnostic repeat FNA that permitted appropriate follow-up while the remaining two cases were again unsatisfactory. Out of these 48 cases, 29 cases underwent surgical resection of thyroid; of which five cases were proven to be neoplastic lesions by histological diagnosis and the remaining 24 cases were non-neoplastic lesions.

FNAC is a valuable diagnostic tool for distinguishing between benign and malignant thyroid lesions. In this study, the sensitivity, specificity and accuracy of FNAC for the detection of malignancy were 50%, 100% and 94.2%, respectively.

CONCLUSION

FNAC of the thyroid is simpler and accurate preoperative diagnostic test compared with other diagnostic modalities. It is minimally invasive, safe outpatient procedure and can be repeated due to patient acceptance. FNAC was found to be well correlated to the clinical and other methods of assessment of thyroid swellings. Successful FNAC depends on certain contributing features such as experienced aspirator, skillful cytological interpretation, rational analysis based on clinical and cytological information in the context of an individual patient.

FNAC can significantly reduce mortality as well as morbidity of patients by making early and accurate differentiation of benign and malignant thyroid nodules due to its high accuracy, sensitivity and specificity. A benign FNAC diagnosis should be viewed with caution as false negative results do occur and these patients should be followed-up with thorough investigation and at times with surgical intervention.

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