EVALUATION OF DIAGNOSTIC PERFORMANCE OF USG GUIDED FNAC OF THYROID SWELLINGS: A PROSPECTIVE STUDY.

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Abstract.

Background:

USG-guided FNAC is a good preoperative screening technique when compared to FNAC and USG done separately for the diagnosis of a thyroid lesion. However, there is little evidence in the literature that emphasizes the importance of USG-guided FNAC as the first step in the investigation of thyroid lesions.

Aim: Our study aims to see the sensitivity and specificity, adequacy, and diagnostic accuracy of USG-guided FNAC taking histopathology as the gold standard.

Methods:

This Hospital-based prospective observational study was carried out on patients who attended the OPD and/or IPD and underwent surgery in the Department of Otorhinolaryngology.

Results:

The sensitivity, specificity, and diagnostic accuracy of ultrasound-guided FNAC for thyroid lesions were 58.82%, 98.18%, and 88.89% respectively taking Bethesda categories 1 to 3 as benign and categories 4 to 6 as malignant. The positive likelihood ratio and negative likelihood ratio are 32.32 and 0.42 respectively. Positive predictive value and negative predictive value were 90.91% and 88.52%. The diagnostic accuracy of USG-guided FNAC for thyroid lesions in the present study is 88.89% and adequacy is 93.05%.

Conclusion:

Further study of a larger number of cases is desirable. US-FNAC is an expensive procedure as compared to palpable FNAC.

Recommendation:

We recommend the application of USG guide FNAC as the first step in the investigation of thyroid lesions along with a detailed interdepartmental correlation to make the diagnosis before surgery.

Keywords: USG Guided FNAC, Sensitivity, Specificity, Diagnostic Accuracy, Thyroid nodule.,
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1. INTRODUCTION.

Thyroid lesions are common worldwide. It affects all age groups and has a prevalence of 4% to 7% in the adult population1. The incidence of thyroid diseases has been increasing in recent years due to goitrogens and changing food habit 1.

Thyroid disorder has an immense impact on the physical as well as mental health of the patient. These patients not only present with thyroid swelling but also have complaints like weight gain or weight loss, fatigue, anxiety or nervousness, increased sweating or dry skin, depression, lethargy, diarrhea, palpitations, muscular weakness, heat or cold intolerance, voice change, change in menstrual pattern and muscle cramps. Various mental health problems are also related to thyroid disorders. Depression, mood disorders, and bipolar depression can be seen in people diagnosed with hyperthyroidism2.

There are different methods to investigate a thyroid gland lesion. The superficial location of the thyroid gland allows excellent visualization and evaluation of its normal anatomy and pathologic condition by sonography3. Fine Needle Aspiration Cytology (FNAC) of the thyroid gland is a well-established first-line diagnostic test for the evaluation of diffuse thyroid lesions as well as thyroid nodules4. In India, FNAC was first introduced during the early 1970s5.

It is a minimally invasive diagnostic tool that provides sufficient information thus eliminating the need for additional diagnostic studies and decreasing the number of unnecessary thyroidectomy1. It also guides the surgeon regarding the surgical procedure to be done. Hence, thyroid surgery is nowadays associated with low morbidity and extremely low mortality1.

FNAC can be repeated in those patients, whose initial attempt failed to yield enough material to make a diagnosis, using thyroid ultrasonography to guide the needle placement, if necessary. Ultrasound-guided FNAC (US-FNAC) was first introduced by Rizatto et al in 19736. Ultrasound-guided FNAC (US-FNAC) has the major advantage of real-time monitoring which helps in the accurate localization of needle tip during aspiration thus reducing the inadequacy rate than the conventional FNAC6.

The surgical excision and subsequent histopathological examination are the most accurate methods to diagnose different benign and malignant lesions of the thyroid 7,8.

As USG-guided FNAC improves the diagnosis, this study aims to see the sensitivity and specificity, adequacy, and diagnostic accuracy of USG-guided FNAC taking histopathology as the gold standard.

2. MATERIAL AND METHODS.

Study Design and Population: This hospital-based prospective observational study was carried out on patients who attended the OPD and/or IPD and underwent surgery in the Department of Otorhinolaryngology.

Criteria: Patients of age group 15 to 65 years of both genders with thyroid swelling who underwent surgery and patient ready to give consent for the study were included in the study. Patients with another neck swelling like a thyroglossal cyst, thyroid abscess, acute thyroid inflammation, physiological thyroid swelling (pubertal goiter, goiter in pregnancy), patients with contraindications to surgery, not willing to undergo surgery and who did not give consent for the study were excluded.

Data Collection: Detail history taking, clinical examination, routine laboratory investigation, and relevant special investigations in some cases (e.g. Anti-TPO antibody) were done. All patients underwent US-FNAC for thyroid swellings under aseptic condition using a 23-gauze lumbar puncture needle fitted to a 10ml syringe with the patient in a supine posture with the neck extended. The material was collected by capillary action. In some cases, where the primary attempt failed to obtain adequate material, aspiration technique was used. The aspiration was then expressed on five clean glass slides and either fixed with 95% ethanol or kept as such for air drying. The smears were then stained with Papanicolaou

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(Pap), hematoxylin-eosin (H and E) stain, and Leishman stain.

The cytology reporting was done according to the Bethesda System of Reporting Thyroid Cytology (TBSRTC) and put into any one of the six categories (I to VI). Cat-I: Nondiagnostic; Cat-II: Benign; Cat-III: Atypia of Undetermined Significance(AUS) or Follicular Lesion of Undetermined Significance (FLUS); Cat-IV: Follicular Neoplasm or Suspicion of Follicular Neoplasm; Cat-V: Suspicious of Malignancy; Cat-VI: Malignant.

Histopathological diagnosis of all those who underwent surgery was followed up. Data was coded and entered into Microsoft Excel and analysis was done by SPSS 20 software. Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated with US-FNAC as a screening test and histopathology as the gold standard.

Diagnostic categories IV, V, and VI which were histopathologically confirmed as malignant were defined as True-positive (TP). True-negative (TN) included categories I, II, and III which were histopathologically confirmed as benign. The False-positive (FP) category included those cases which were diagnosed as follicular neoplasm (Cat-IV), suspicious for malignancy (Cat-V) and as malignant (Cat-VI) on USG-guided FNAC but later confirmed as benign on histopathology. False-negative (FN) cases included those diagnosed as benign on US-FNAC but came out to be malignant on histopathological examination.

2.1. Statistical analysis.

In the case of USG-guided FNAC, there are 6 possible results based on the TBSRTC category. A report of malignancy, suspicious for malignancy, and suspicious for a follicular neoplasm is considered as a positive test. A non-diagnostic, benign, and atypia of undetermined significance result is considered negative.

Sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated using the following formulas: -

- *Sensitivity=[TP/(TP+FN)] ×100*

- *Specificity=[TN/(TN+FP)] ×100*

- *Positive predictive value (PPV)=[TP/TP+FP)] ×100*

- *Negative predictive value (NPV)=[TN/TN+FN] ×100*

- *Diagnostic Accuracy = TP+TN/TP+TN+FP+FN*

For analysis, those lesions that belong to Category IV (follicular neoplasm) Category V (suspicious of malignancy), and Category VI (malignant) on US-FNAC were taken as positive whereas cases with cytology report of indication for surgery to rule of malignancy and those lesions which belong to Category I (inadequate/non-diagnostic) II (benign) and III (atypia of undetermined significance) were taken as negative. The analysis was performed using STATA15.1.

For adequacy of USG-guided FNAC, the percentage of adequate and inadequate samples on USG-guided FNACs was calculated excluding cystic swellings. The US-FNAC diagnosis was correlated with the histopathology diagnosis to calculate the accuracy of USG-guided FNAC and the sensitivity, specificity, and predictive values of US-FNAC were also determined. Cystic swellings and inadequate FNAC reports were included while calculating the accuracy of US-FNAC.

3. OBSERVATION.

A total of 72 patients were included in the study with an age range of 15 years to 65 years. The mean age of presentation in our study was found to be 42.2 yrs. Out of 72 patients, 56 were females constituting 77.78%, and 16 were male constituting 22.22%. As expected, there was a predominance of females with a Female: Male ratio of 3.5:1.

Clinical symptoms in cases with thyroid lesions in the present study show much variation to the other studies done. Out of 72 patients, neck swelling was present in all (100%), lymphadenopathy in only 5 (6.94%), dysphagia in 1

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(1.38%), dyspnoea in 1 (1.38%) cases, and hoarseness of voice was not seen in any patient. The reason why there is a difference between other studies and the present study is that with time, people are more concerned about their health nowadays and they prefer to visit doctors as soon as the first symptom appears 9-11. Therefore, in our study, the symptoms related to the complications of the diseases were less found. The present study shows the involvement of only the right lobe in 37.50% of cases, the left lobe in 33.33%, and both lobes in 29.17%. Involvement of the pyramidal lobe and isthmus was seen in 1.38% and 9.72% respectively in our study.

Out of 72 patients who underwent USG-guided FNAC excluding the two cystic swellings, 67/72 (93.05%) cytology samples were adequate and 3/72 (4.16%) were inadequate. The reason could be the factors that can improve the adequacy of thyroid FNACs which were properly applied in this study. These were the use of thinner needles, non-aspiration technique, and proper preparation of the smear7.

In our study, the US features such as hypoechogenicity, irregular margins, and microcalcification, were significant in predicting malignancy. Most of the nodules were either hyperechoic (30.5%) or isoechoic (43%). Less number of nodules were hypoechoic (26.4%). Nodules with no calcification, microcalcification, and macrocalcification were seen in 77.8%, 13.9%, and 8.33% of the cases respectively. Solid lesions, mixed lesions, and cystic lesions were found in 41.7%, 31.94%, and 2.7% of cases respectively.

Percentages of ill-defined margin and well-defined margin were 22.22% and 70.83% respectively. Similarly, 75% of the nodules are of size 1 to 4cm and 25% of the nodule are of size 4 to 6 cm 9,10.

The TBSRTC categories among the total patients were obtained as shown below in Table 1:

The largest number of cases (52) in this study was in category II (benign) whereas the smallest number (2) was in Category V. Category I, III, IV, and VI consist of 3, 6, 3, and 6 cases respectively.

In the present study of 72 patients, 3(4.16%) were in the non-diagnostic category. Total

number of patients in other categories are: II (72.22%), III (8.33%), IV (4.16%), V (2.77%), VI (8.33%). On histopathological finding, among 72 cases 44 (61.11%) were colloid goitre, 8 (11.11%) were thyroiditis, 3 (4.17%) were adenomatoid goitre, 3 (4.17%) were follicular carcinoma and 14 (19.44%) were papillary carcinoma (Table 2).

In this study of 72 patients, 3 (4.16%) were in the non-diagnostic category. Out of the 52 (72.22%) patients diagnosed as category II, 5 cases turned out to be papillary carcinoma which certainly has some overlapping cytological features with category II particularly when associated with degenerative changes or a cystic component. Of the total 72 patients in this study, only 6 cases were categorized as category III (8.33%). Of these 6 cases, one proved to be papillary carcinoma, and one follicular carcinoma. There were 3 cases in category IV (4.16%). Histopathology report revealed two cases, follicular carcinoma and one case of colloid goitre. The number of patients in category V was 2 (2.77%) and in category VI was 6 (8.33%). All of which were reported as malignant (papillary carcinoma) on histopathology. Among 72 patients, 55 patients (76.39%) had a benign histopathology, 17 patients (23.61%) were proved to be malignant.

Out of 17 malignant cases 10 cases (true positive) were diagnosed as malignant on US-FNAC while rest 7 cases (false negative) were diagnosed as benign on cytology. Similarly, out of 55 benign cases 54 cases (true negative) were diagnosed as benign on US-FNAC while only 1 case (false positive) was diagnosed as malignant on cytology.

This study shows that the sensitivity, specificity and diagnostic accuracy of ultrasound guided FNAC for thyroid lesions were 58.82%, 98.18% and 88.89% respectively taking Bethesda categories 1 to 3 as benign and categories 4 to 6 as malignant [1,3].

The positive likelihood ratio and negative likelihood ratio are 32.32 and 0.42 respectively. Positive predictive value and negative predictive value are 90.91% and 88.52%. The sensitivity (58.82%) is low in the present study. This is mostly because 5 cases of papillary carcinoma were diagnosed as TBSRTC category II. This is most probably due

Table 1: **Showing distribution of 72 cases as per TBSRTC (The Bethesda System for Reporting Thyroid Cytology) categories.**

TBSRTC category		Number of cases in each category	Percentage distribution
Category I (Non- Diagnostic)		3	4.16%
Category II (Benign)	Thyroiditis	9	12.5%
	Colloid Goitre	40	55.55%
	Adenomatoid goitre	2	2.77%
	Multinodular goitre	1	1.38%
Category III(AUS)		6	8.33%
Category IV(SFN)		3	4.16%
Category V(SM)		2	2.77%
Category VI(Malignancy)	Papillary Carcinoma	6	8.33%
Total		72	100%

(AUS- Atypia of Undetermined Significance; SFN- Suspicious for follicular neoplasm; SM- Suspicious for malignancy)

Table 2: **Showing distribution of cases in US-FNAC and ftnal histopathological examination**

US-FNAC Report (TBSRTC category)	No. of cases (n=72)	Final HPE (n=72) Benign	Malignant
Category I	3	Colloid Goitre-3	
Category II	52	Colloid Goitre-36 Thyroiditis-8 Adenomatoid Goitre-3	Papillary carcinoma 5
Category III	6	Colloid Goitre-4	Follicular Carcinoma-1 Papillary carcinoma 1
Category IV	3	Colloid Goitre-1	Follicular Carcinoma-2
Category V	2		Papillary carcinoma 2
Category VI	6		Papillary carcinoma 6

to cystic or degenerative change within the neoplasm leading to difficulty in sampling the more cellular part of the lesion. Also, two cases of TBSRTC category III (taken as benign in the study) came out to be follicular carcinoma on histology [4,6]. The specificity in the present study is high reflecting a very rare chance of false positive diagnosis on FNAC thus avoiding unnecessary radical surgery.

Also, the diagnostic accuracy (88.89%) of US-FNAC in the present study. It can be improved by multiple sampling particularly from any solid /cellular foci within the lesion and correlating the clinical and radiological findings during cytological reporting.

4. DISCUSSION.

Fine needle aspiration cytology is a simple, quick, cost effective and patient friendly procedure which can be done on outpatient basis in cases of thyroid lesions. High resolution grey scale ultrasound (USG) has emerged as the initial imaging modality of choice for the evaluation of patients with thyroid lesions. When both FNAC

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and USG are studied together as USG guided FNAC, it becomes a safe and reliable diagnostic approach for thyroid lesions. The present study analysed the usefulness of USG guided FNAC and TBSRTC (The Bethesda System for Reporting Thyroid Cytology) method of thyroid cytology reporting in different types of thyroid lesions.

A total of 72 patients of thyroid swelling were included in our study with an age range of 15yrs to 65yrs. Female:Male ratio was 3.5:1. The sensitivity, specificity, positive predictive value, negative predictive value and diagnostic accuracy of US-FNAC were found to be 58.82%, 98.18%, 90.91%, 88.52%, and 88.89% respectively.

The adequacy rate (93.05%) in the present study is quite high. This signifies that the use of ultrasound guidance for doing fine needle aspiration cytology in thyroid lesions significantly reduces the rates of inadequate samples thus decreasing the chance of repeat FNAC. The specificity is also very good (98.18%) indicating that the chance of over diagnosis is very rare. With the use of US-FNAC, the accuracy of diagnosing the malignant lesions is very high as proved by the 100% correlation between category V and VI lesions and histopathology outcome. So, over treatment like unnecessary radical surgery can be avoided.

The diagnostic accuracy of present study is also good (88.89%) which reflects the efficacy of the procedure. The proportion of indeterminate lesions can also be reduced by image‑guided aspiration of the thyroid lesions by obtaining adequate material. In present study, only 4.16% lesions belong to Category III (indeterminate lesions).

The low sensitivity for diagnosis of malignant lesions can be improved by considering the possibility of malignancy in some cases of category III depending on the clinical and radiological feature. Also sampling from more representative sites like solid/cellular area in cases of lesions with cystic/degenerative changes can minimize the under diagnosis in some cases particularly papillary carcinoma of thyroid.

5. CONCLUSION.

US-FNAC is an expensive procedure as compared to palpable FNAC. This procedure depends on coordination between multiple departments like otorhinolaryngology, pathology and radiology. Hence, sometimes it is difficult to find a common time slot for all. Manipulation during the procedure make the FNAC sample haemorrhagic in few cases making the cytological interpretation difficult.

6. LIMITATIONS.

The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

7. RECOMMENDATION.

We recommend the application of USG guide FNAC as the first step in the investigation of thyroid lesions along with a detail interdepartmental correlation to make the diagnosis before surgery.

8. ACKNOWLEDGEMENT.

9. LIST OF ABBREVIATIONS.

USG- Ultrasonography
FNAC- Fine Needle Aspiration Cytology
US- Ultrasound
OPD- Outpatient Department
IPD- Inpatient Department
TPO- Thyroid peroxidase
H nd E- hematoxylin and eosin
TBSRTC- The Bethesda System of Reporting Thyroid Cytology
SPSS- Statistical Package for Social Sciences

TP- true positive

TN- true negative

FP- false positive

FN- False negative

AUS- Atypia of Undetermined Significance

SFN- Suspicious for follicular neoplasm

SM- Suspicious for malignancy

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The study was not funded.

11. Conflict of interest.

The authors report no conflicts of interest in this work.

12. PUBLISHER DETAILS:

13. REFERENCES.

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