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Accuracy of Diagnosis of Thyroid Lesions by Fnac With and Without Usg Mapping

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Abstract
*Introduction**:** Currently, FNAC is the preferred diagnostic method for the initial evaluation of thyroid nodules since 0.5% of cancer-related deaths accounts in relation to thyroid cancer. Early diagnosis is important for higher life expectancy due to slow progressing characteristics of thyroid gland cancers. In addition to clinical information for diagnosis and treatment of thyroid lesions, radiographic evaluation of the soft tissues of the neck and FNAC studies are essential for better diagnosis and treatment. The use of Ultrasound in the assessment of thyroid disease has greatly increased the detection of small thyroid nodules unrecognized at clinical examination.*
***Aim**: To study and correlate the cytological and histopathological observation in thyroid lesions and to assess the diagnostic accuracy of aspiration cytology as a pre-operative screening tool and to evaluate accuracy of FNAC in diagnosis of nodular lesions of thyroid without prior USG mapping in comparison with FNAC done after ultrasound mapping of thyroid .*
***Methods:** 100 patients were randomly divided into two groups of 50. To the First 50 cases FNAC was done directly by clinical examination and palpating by manual method. The other 50 cases were subjected to USG and the details of nodules were mapped in relation to surface anatomy, including the size of nodule, depth of nodule from surface, context of the nodule etc. and FNAC was done using the USG mapping, by routine procedure. Slides were stained with haematoxylin and eosin staining.*
***Results:** Out of the 50 FNAC cases done without USG mapping, sensitivity was 67% and specificity was 87%, Out of the 50 cases where FNAC was done after USG mapping, sensitivity was 80% and specificity was 96 %.*
***Conclusion**:FNAC done after US mapping is more reliable method for diagnosis of malignant lesion in the thyroid. FNAC fails to establish its supremacy in diagnosing malignant lesions. Analyzing the results, specificity and sensitivity of Ultrasound mapped FNAC is 80% AND 96% which co-relates correctly with the literature.*
***Keywords:** Thyroid lesions, Fine needle aspiration technique, Ultrasound mapping,Cytology,Histopathology*

I. Introduction

Thyroid gland is unique among endocrine organs as it is one of the largest endocrine gland in the body and first to develop in fetal life. For more than 100 years thyroid gland has been the subject of intense research and considerable attention due to vast array of developmental, inflammatory, hyperplastic and neoplastic disorders which are exceedingly common in clinical practice(1).

Most common clinical finding in the thyroid gland is either diffuse or nodular enlargement. The nodule is defined as any abnormal growth of thyroid cells resulting in a lump within thyroid**.** Thyroid nodules represent a difficult diagnostic problem.

Benign nodules can be caused by

1) Colloid nodules, cysts, infectious nodules,
2) Lymphocytic or granulomatous nodules,
3) Hyperplastic nodules,
4) Adenomas and congenital anomalies.

Malignant nodules include

1) Follicular cell origin: a) Papillary carcinoma b) Follicular carcinoma
2) C Cell origin: Medullary carcinoma
3) Undifferentiated a) Small cell b) Giant cell c) Carcino- sarcoma
4) Miscellaneous a) Lymphoma b) Squamous cell carcinoma c) Fibro sarcoma e) Metastatic tumors.

In North America, epidemiological studies showed that thyroid nodules can be detected with ultrasound in 67% of population. [2]Palpable thyroid nodules are more common in women, and male/female ratio ranged from 1.2 to 4.3. [1, 3] Thyroid nodules may cause hypothyroidism, hyperthyroidism, cosmetic

issues, and problems in other organs such as compression, and they also have the potential for malignancy. [4] Therefore, the accurate evaluation of thyroid nodules is crucial.

In recent years, the role of fine-needle aspiration cytology (FNAC) in diagnosing thyroid lesions is increasing and its role in detection of malignant potential of thyroid nodule is very helpful in management. No single diagnostic methods used for the definitive diagnosis of thyroid cancers, such as radiographs, US, scintigraphy and suppression therapy, is effective enough to make a benign/malignant differentiation .FNAC has been used since the 1950s, and is one of the effective methods in the diagnosis of thyroid nodules. [5]

In this study, the effectiveness of FNAC is assessed in association with ultrasound and was evaluated through the identification of the correlation between the cytological diagnoses of thyroid FNAC done with and without USG mapping, and the postoperative histopathologic diagnosis.

However , even FNAC has limitations because of low yield of cells, loss of histological architecture and inability to distinguish follicular adenoma and well differentiated follicular carcinoma(11-13).Many times if the nodule is deep seated or very small (particularly papillary carcinoma) , there is high chance of missing the lesion due to blind technique of FNAC. And many times if FNAC is done by Radiologist by USG guidance, pathologists never feel the aspirate is sufficient or the diagnosis is inconclusive. Hence, this study is developed to fulfill the gaps in usage of FNAC using USG mapping of thyroid lesions and to compare the results of blind FNAC with USG mapped FNAC and to increase the accuracy of diagnosis by FNAC.

II. Aims And Objectives

1) To study the cytological features in thyroid lesions
2) To correlate the cytological and histopathological observation in thyroid lesions, whenever possible
3) To assess the diagnostic accuracy of aspiration cytology as a pre-operative screening tool
4) To evaluate accuracy of FNAC in diagnosis of nodular lesions of thyroid without prior USG mapping in comparison with FNAC done after mapping thyroid USG in cases.

III. Materials And Methods

Study was carried out between MAY 2014 and JULY 2014 on 100 patients. They were randomly divided into two groups of 50. To the First 50 cases FNAC was done directly by clinical examination and palpating by manual method. The other 50 cases were subjected to USG and the details of nodules were mapped in relation to surface anatomy, including the size of nodule, depth of nodule from surface, context of the nodule etc. and FNAC was done using this USG mapping, by routine procedure.

Inclusion criteria:

Patients with thyroid enlargement coming to the cytology department for FNAC irrespective of age, sex.

Exclusion criteria:

Patients without any apparent thyroid disease.

FNAC was done with aseptic precautions by using 5cc syringe and 23 gauze needles. Material obtained is smeared on 2 glass slides. They are then wet fixed by using isopropyl alcohol and are stained with H&E method. Detailed clinical history, radiological findings and status of thyroid function test (TFT) are noted. In case of multiple nodules, more than one aspirate is done from prominent nodules. In cystic nodules, the cyst contents are aspirated centrifuged and the slides are made from sediment for microscopic examination. Aspirates are taken as adequate when cytology smears contain five or six groups of well-preserved follicular cells, with each group containing 10 or more cells, under low power view. However adequacy also depends upon the lesion being aspirated. For example in case of colloid goiter, FNAC many times yields only colloid with scanty cells but it is adequate if the lesion is taken into consideration. This is particularly important in relation to thyroid nodules since clinical management is inlarge extent decided by cytology report.

Benign nodules include multinodular goiter, hyperplastic goiter, colloid goiter, Grave's disease, autoimmune thyroiditis, granulomatous thyroiditis and thyroid cysts. Intermediate lesions suggestive/suspicious of neoplasms included follicular neoplasm and Hurthle cell neoplasms. Malignant nodules include papillary carcinoma, medullary carcinoma, poorly differentiated carcinoma, anaplastic carcinoma and lymphoma. Pre-operative FNAC results are then compared with the definitive histological diagnosis.

Comparing the results of cytological and histopathologic examinations, the sensitivity, specificity, positive and negative predictive value, and accuracy were calculated. These values were calculated by the following formulas. Patients with nondiagnostic FNAC were excluded from the calculations.

IV. Statistics

All statistical calculations were performed using IBM SPSS Statistics (IBM SPSS Statistics for Windows, Version 19.0, Company ©1989-2010, SPSS Inc. an IBM Company) program. Chi-square test was used to assess the effect of gender independent variable on the results of histopathological and cytological tests, t-test was performed to compare the mean age between genders. Significance of the statistical tests was based on 95% confidence interval.

V. Results

H&E stained cytology examination of various lesions:
(Figure 1)& (Figure 2): COLLOID GOITRE
(Figure 3)& (Figure 4): FOLLICULAR NEOPLASM
(Figure 5)& (Figure 6): HASHIMOTO THYROIDITIS
(Figure 7)& (Figure 8): PAPILLARY CARCINOMA:

Out of the 50 FNAC cases done without USG mapping,

- 44 WERE FEMALES (88%), 6 WERE MALES (12%)
- The mean age was 40(range:16-69 years)**(Figure 9)**
- P VALUE- 0.0007

Out of the 40 nonmalignant cases, 24 were reported as colloid goiter, 10 were reported nodular goiter and 6 were reported other nonmalignant cases like Hashimoto Thyroiditis, Adenomatous goiter etc.

Out of the 10 malignant cases, 5 were reported as Papillary carcinoma, 4 were reported as Follicular neoplasm and one was reported as Medullary carcinoma by FNAC. **(Table 1)**

VI. Analysis

True Positive- Those diagnosed as malignant by FNAC with positive results on histopathology.
False Negative- Those diagnosed as benign lesions by FNAC but positive on histopathology.
True Negative- Those with nonmalignant thyroid disease on FNAC, and negative on histopathology
False Positive- Those which are positive for malignant disease on FNAC, and negative on histopathology **(Table 2)**
Sensitivity- Tp/Tp+Fn X100=8/ (8+4) X100
Sensitivity = 67%
Specificity- Tn/Tn+Fp X100=28/ (28+4) X100
Specificity= 87%
Likelihood Ratio- how likely the test result is to be found in the ratio.
Positive likelihood- Sensitivity/1-Specificity=67%/1-87% = 5.15
Negative likelihood= 1-Sensitivity/Specificity= (1-67%)/87%= 0.37
Positive Predictive Value= Tp/Tp+Fp= 8/8+4 =0.67
Negative Predictive Value= Tn/Tn+Fn= 28/28+4=0.88

Out of the 50 cases where FNAC was done after USG mapping, 45(90%), were females and 5(10%) were males. **(Figure 10),** mean age - 36.48(RANGE - 14- 69)
P Value- 0.00023

On Fnac After Usg Mapping:

Out of the 41 nonmalignant cases, 16 were nodular goiter, 15 were reported as colloid goiter, and 10 were other nonmalignant conditions.

Out of the 9 malignant lesions, 7 cases reported papillary carcinoma, 1 case reported Medullary carcinoma, 1 case reported Follicular neoplasm.**(Table 3)** ,true and false positive and negative was calculated.**(Table 4)**

Analysis
Sensitivity=Tp/Tp+Fn X100= 80%
Specificity=Tn/Tn+Fp X100 = 96%
Likelihood Ratio- how likely the test result is to be found in the ratio.
Positive likelihood- Sensitivity/1-Specificity= 80%/1-96%= 20

Negative likelihood= 1-Sensitivity/Specificity = (1-80%)/96= 0.20
Positive Predictive Value= Tp/Tp+Fp=0.89
Negative Predictive Value= Tn/Tn+Fn=0.93

VII. Discussion

Cancer of the thyroid gland accounts for 1% of all cancers and is responsible for 0.5% of cancer-related deaths.[4]Early diagnosis still maintains its importance for higher life expectancy due to the low malignant potential of thyroid nodules, and slow progressing characteristics of thyroid gland cancers.
First cytological diagnosis with FNAC was made by Martin and Ellis in 1930s. [7] Many studies have been carried out in the following years; however; the method has been widely used after 1952. [5]

Fnac is easy to apply, has a low complication rates and high diagnostic value and is a cost-effective test used in the diagnosis of thyroid nodules. [6, 8, 9] In addition to clinical information for diagnosis and treatment of thyroid lesions, Ultrasound, scintigraphy, radiographic evaluation of the soft tissues of the neck and FNAC studies are essential. The use of FNAC resulted in a decrease in the number of patients who underwent surgical treatment by 25-50%, while increasing the percentage of malignant results in the operated group of patients. [10] Currently, FNAC is the preferred diagnostic method for the initial stage of evaluation of thyroid nodules. [9]

Fnac contributes significantly to the pre-operative investigation in patients with thyroid swelling but despite its well-recognized value there are limitations to the technique. The first such drawback of FNAC is the high inadequate sample rate (3, 4). The second major limitation of thyroid cytology is its inability to distinguish follicular adenoma from follicular carcinoma (4, 5, 7, and 8). This diagnosis requires detailed histological examination for vascular or capsular invasion and cannot be reliably made on routine FNAC specimens (9, 10, 11, and 12). Hence, follicular neoplasm (lesion) is given as diagnosis in FNAC.
Among the factors that reduce the efficiency of FNAC include, inadequate sampling, inexperience of the cytopathologist and natural difficulties of differentiation of benign and malignant follicular lesions. Inadequate sampling often results from sclerotic, calcified nodules or nodules with cystic degeneration in larger areas. US guided sampling reduces the nondiagnostic test rates in such conditions. [19], [20]

Cytological evaluation errors can lead to increased rates of false negativity and false positivity. Most common lesions that contribute to false-positive results, as in our study, are the nodular hyperplasia's with dense macro papillary structures. In general, it may be difficult to establish a cytological differentiation between follicular hyperplastic nodules which are diagnosed as suspicious for malignancy or some of the follicular adenomas and well differentiated follicular carcinomas. It is reported that such conditions may lead to false-positive results. [17], [22]. In the rest of the cases the false-positive tests, as in the literature, were resulted from a very suspicious single zone in the cytological materials.
The use of US in the assessment of thyroid disease has greatly increased the detection of small thyroid nodules unrecognized at clinical examination.

US findings are important in predicting malignancy in no palpable lesions. Although previous reports (15) have denied that US findings have a predictive role, in our series logistic regression analysis confirmed that irregular or blurred nodular margins, an intranodular vascular pattern and micro calcifications were closely linked to neoplastic lesions (19). On the other hand hypo echoic appearance or the presence of solitary lesions was not independent risk factors for malignancy in non-palpable thyroid nodules. The presence of micro calcifications presented a higher specificity for malignancy (95%) than the findings of irregular margins (85%) or intranodular vascular images (80.8%), but the predictive value of micro calcifications was blunted by their low sensitivity.

Recent study proved the superiority of ultrasound-guided thyroid FNA biopsies over palpation-guided FNA biopsies [7]. In clinical practice, it is recommended that ultrasound guidance should be sought after a failed manual thyroid FNA, in small nodules (less than 15 mm in diameter), in non-palpable nodules, in lesions that are located in difficult-to-access locations, in nodules with extensive cystic change, fibrosis or calcification [3,6,11,14]. Ultrasound guidance is also helpful in directing the needle to solid portions of the cystic or mixed nodules and reduces the need for repeat FNAs [14]

But it is very difficult to coordinate with Radiologist for guided FNAC and invariably Pathologist are not available in all the places while radiologist are available in all the hospitals. Hence our study is aimed to find if the FNAC done after USG mapping stands any advantage over blind FNAC.

Our results also show that there is high degree of sensitivity and specificity of FNAC results when it is done with USG mapping when compared with blind technique. **(Figure 11)**

VIII. Conclusion

After carefully observing the results and analyzing the literature we come to the conclusion that FNAC done after USG mapping is more reliable method for diagnosis of malignant lesion in the thyroid. FNAC done without USG mapping, fails to establish its supremacy in diagnosing malignant lesions. Especially if the nodule is deeply seated then many a time, FNAC done without any USG assistance leads to a wrong pre-operative diagnosis. Also, if the lesion is highly vascular it is possible that FNAC can lead to fatal damage.
Analyzing the results, specificity and sensitivity of USG mapped FNAC is 80% and 96% which co-relates correctly with the literature. Better likelihood ratio also suggests that USG mapped FNAC is a better technique than blind FNAC.

Summary

The objective of the study was to evaluate accuracy of FNAC in diagnosis of nodular lesions of thyroid without prior USG in comparison with FNAC done after mapping thyroid USG in cases.
In a study of 100 patients, 50 patients were subjected to FNAC without USG and another 50 patients underwent USG first. Then with that assistance FNAC was done in the routine method.
Results were as follows

For blind FNAC technique done in 50 patients, (p value=0.0007)
sensitivity-67%, specificity-87%, positive predictive value-0.67 negative predictive value-0.88
For FNAC done after USG mapping in 50 patients (p value = 0.00023)
sensitivity- 80%, specificity-96%, positive predictive value-0.89 negative predictive value-0.93

From the above results, we conclude that FNAC done after USG mapping is more reliable method for diagnosing thyroid lesions.

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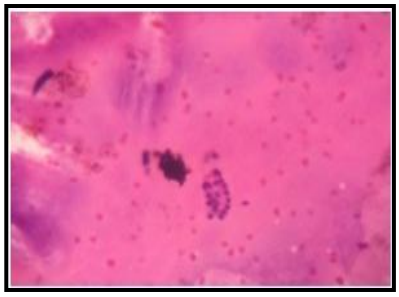
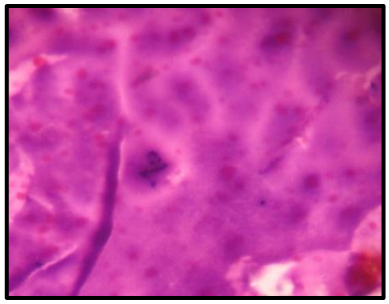
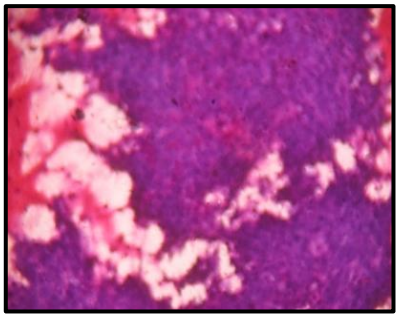
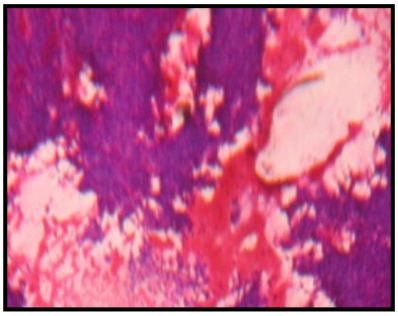
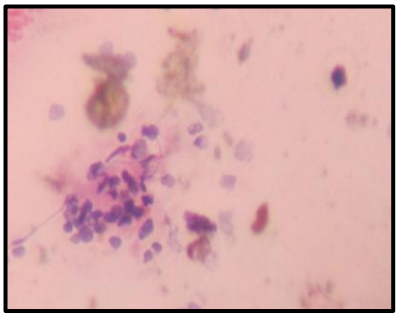
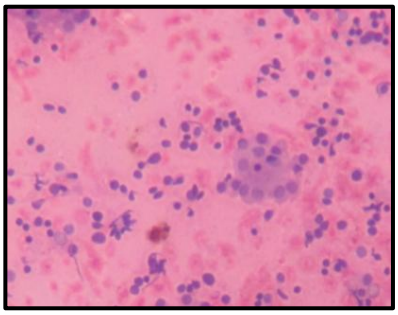
(Figure 1)&(Figure 2): Colloid Goitre

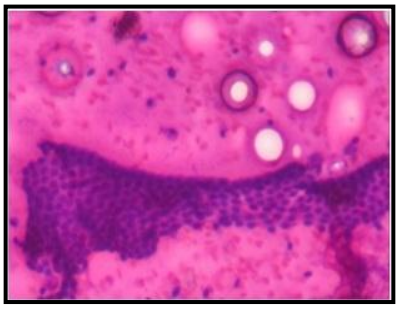
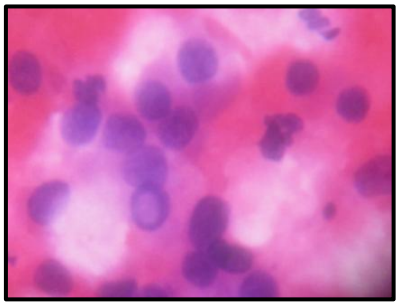
(Figure 3)&(Figure 4): Follicular Neoplasm

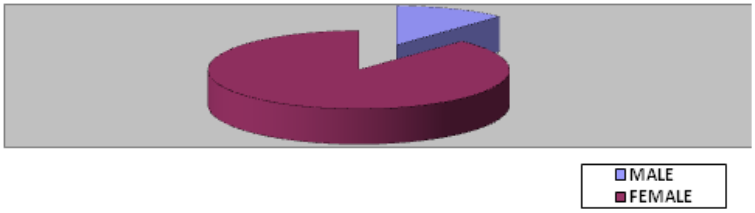
(Figure 5)&(Figure 6): HASHIMOTO THYROIDITIS

(Figure 7)&(Figure 8): Papillary Carcinoma

(Figure 9): Percentage of male to female without USG investigation



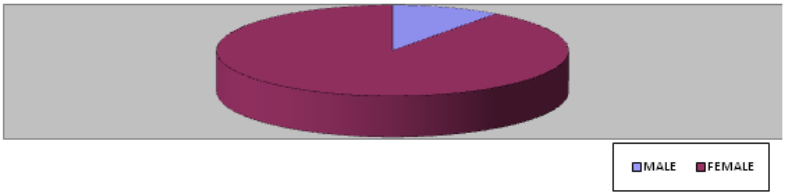
(Table 1): Comparison of number of malignant and non malignant lesions without USG mapping.

	FNAC	HISTOPATHOLOGY
NON MALIGNANT	40	37
MALIGNANT	10	13

(Table 2): Number of true and false positive and negative cases without USG mapping

True Positive-8	False Negative-4
True Negative-28	False Positive- 4

(Figure 10): Percentage of male to female after USG investigation



(Table 3): Comparison of number of malignant and non malignant lesions after USG

	FNAC AFTER USG MAPPING	HISTOPATHOLOGY
NON MALIGNANT	41	39
MALIGNANT	9	11

(Table 4): Number of true and false positive and negative cases after USG mapping

True Positive-8	False Negative-2
True Negative-30	False Positive-1

(Figure 11) –Comparison of sensitivity and specificity of FNAC results when it is done with USG mapping and when compared with blind technique.