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ORIGINAL ARTICLE RESEARCH

Diagnostic Efficacy of Ultrasound (Using TI-RADS) Compared to Fine Needle Aspiration Cytology (Using Bethesda Classification) in Diagnosing Thyroid Nodule.

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ABSTRACT

Introduction: Fine-needle aspiration cytology (FNAC) is the invasive test to determine whether a nodule is malignant or may require surgery to reach a definitive diagnosis. a reliable, noninvasive method to identify which nodules warrant FNAC on the basis of a reasonable likelihood of biologically significant malignancy would be highly desirable. Hence, We compared the Thyroid Imaging Reporting and Data System (TI-RADS) of classifying thyroid nodules on ultrasound with the findings on fine-needle aspiration cytology (FNAC) reported using the Bethesda System.

Material and methods: After obtaining ethical committee clearance a prospective study was done in patients with thyroid nodules attending tertiary care hospital during April 2022 to December 2022. After obtaining informed consent from patients, 100 patients were enrolled in the study by purposive sampling method. Patients who were willing for Ultrasound and FNAC underwent bedside imaging of thyroid nodule and ultrasound guided FNAC performed by single radiologist and pathologist. Sensitivity, specificity, disease prevalence, positive and negative predictive value as well as accuracy are expressed were calculated.

Results: Mean ± SD of age was 34±12.3. Females were 74%. Based on Bethesda classification on FNAC, 23 patients have malignant lesions (which is Bethesda V and VI) and 77 patients have benign lesions (which is Bethesda < V grade). Sensitivity and specificity of ultrasound over FNAC of thyroid nodule, at 95% CI was 84.21% (60.42% to 96.62%) and 92.5% (84.39% to 97.20%) with accuracy of 90.91% at 95% CI (83.44% to 95.76%).

Conclusions: In this study, a significant association was noted between the Ultrasound (TI-RADS) and FNAC (Bethesda scores) (X2- 41.74, $p \leq 0.001$). Sensitivity and specificity of ultrasound over FNAC of thyroid nodule, at 95% CI was 84.21% (60.42% to 96.62%) and 92.5% (84.39% to 97.20%).

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INTRODUCTION

Currently, fine-needle aspiration cytology (FNAC) is the most effective, practical test to determine whether a nodule is malignant or may require surgery to reach a definitive diagnosis.[1] However, most nodules are benign, and even malignant nodules, particularly ones smaller than 1 cm, frequently exhibit indolent or nonaggressive behaviour.[2,3] Therefore, not all detected nodules require FNAC and/or surgery.

Therefore, a reliable, noninvasive method to identify which nodules warrant FNAC on the basis of a reasonable likelihood of biologically significant malignancy would be highly desirable. In 2015, committees convened by the ACR published white papers that presented an approach to incidental thyroid nodules and proposed standard terminology (lexicon) for ultrasound reporting[4,5] called Thyroid Imaging Reporting and Data System (TI-RADS) of classifying thyroid nodules on ultrasound.

We compared the Thyroid Imaging Reporting and Data System (TI-RADS) of classifying thyroid nodules on ultrasound with the findings on fine-needle aspiration cytology (FNAC) reported using the Bethesda System.

MATERIAL AND METHODS

After obtaining ethical committee clearance a prospective study was done in patients with thyroid nodules attending tertiary care hospital during April 2022 to December 2022. After obtaining informed consent from patients, 100 patients were enrolled in the study by purposive sampling method. Patients who were willing for Ultrasound and FNAC underwent bedside imaging of thyroid nodule and ultrasound guided FNAC performed by single radiologist and pathologist.

Findings were recorded in a semi-structured questionnaire which consists of patient's details, detailed history on presenting symptoms, physical examination, findings of ultrasonography of thyroid using TI-RADS score and FNAC findings as per Bethesda classification.

Procedure

All US scans of the thyroid gland and neck were performed using a linear-array transducer (5–12 MHz) on a Philips US scanner (Philips Healthcare Affiniti 70 G, USA) using an optimized gain by the same radiologist. Axial images of both thyroid lobes were obtained, with quantification and measurement of all detected TNs. Systematic exploration was then made of the lateral neck lymph node chains, submaxillary glands and parotid glands. The following ultrasound characteristics were evaluated in each Thyroid Nodule to obtain the corresponding **TI-RADS Grade**

1)Ultrasound structure
2)Echogenicity
3)Morphology
4)Anteroposterior/transverse diameter ratio
5)Contours
6)Presence/absence of a capsule
7)Calcifications
8)Hyperechogenic foci
9)Vascularization

Nodule size was not included among the evaluated ultrasound characteristics, since it is not predictive of malignancy.[6,7]

A TI-RADS score per patient was recorded, corresponding to the nodule of the highest TI-RADS grade.

The thyroid nodules were sonographically classified as TI-RADS 2 and TI-RADS 3 for benign and probably benign appearing nodules, respectively. These were compared to the Bethesda Class II for benign thyroid nodules. Nodules that were indeterminate or suspicious

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of a follicular lesion or neoplasm were classified as TI-RADS 4 and compared to the Bethesda Class III (follicular lesion of undetermined significance) and Bethesda Class IV (follicular neoplasm). We did not subclassify the TI-RADS 4 sonographic category into the different subcategories (4a, 4b and 4c) in this study. Thyroid nodules that were suspicious of malignancy (all 5 suspicious ultrasound features present) were classified as TI-RADS 5 and compared to the Bethesda Class V and Class VI FNAC Classification. Patients with TI-RADS 1 (normal thyroid gland) were excluded as there was no indication to subject them for FNAC.
After US evaluation of the thyroid gland, FNAC was done using 23 G needle attached to a 10 ml syringe which was further attached to syringe holder. In each case, haematoxylin and eosin (H&E), papanicolaou (PAP) and May-Grunwald-Giemsa (MGG) staining of smeared slides were done. Number of needle passes, nature of aspirate, cytological diagnosis was done based on Bathesda classification for cytodiagnosis of thyroid lesions. Then the slides are examined by an expert pathologist.
Operational definitions:

Definitions

- *Sensitivity*: probability that a test result will be positive when the disease is present (true positive rate).
  = ***a / (a+b)***
- *Specificity*: probability that a test result will be negative when the disease is not present (true negative rate).
  = ***d / (c+d)***
- *Positive likelihood ratio*: ratio between the probability of a positive test result given the *presence* of the disease and the probability of a positive test result given the *absence* of the disease, i.e.
  = ***True positive rate / False positive rate = Sensitivity / (1-Specificity)***
- *Negative likelihood ratio*: ratio between the probability of a negative test result given the *presence* of the disease and the probability of a negative test result given the *absence* of the disease, i.e.
  = ***False negative rate / True negative rate = (1-Sensitivity) / Specificity***
- *Positive predictive value*: probability that the disease is present when the test is positive.
  $$PPV = \frac{sensitivity \times prevalence}{sensitivity \times prevalence + (1 - specificity) \times (1 - prevalence)}$$
- *Negative predictive value*: probability that the disease is not present when the test is negative.
  $$NPV = \frac{specificity \times (1 - prevalence)}{(1 - sensitivity) \times prevalence + specificity \times (1 - prevalence)}$$
- *Accuracy*: overall probability that a patient is correctly classified.
  = ***Sensitivity × Prevalence + Specificity × (1 − Prevalence)***

Sensitivity, specificity, disease prevalence, positive and negative predictive value as well as accuracy are expressed as percentages.
Confidence intervals for sensitivity, specificity and accuracy are "exact" Clopper-Pearson confidence intervals.[8]

Statistical Analysis

Data entered in Microsoft excel 2013 and imported to SPSS version 22 package. Data represented in frequencies, mean and standard deviation (SD**).** T test and chi-square test was used for statistical analysis. $P < 0.05$ was considered to be significant statistically. Sensitivity and specificity, positive and negative predictive value as well as accuracy of TI-RADS over Bethesda system was estimated.

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RESULTS

Out of 100 patients enrolled age range was 15- 72 years with 62% of patients in the age group of 15-40 years followed by 23% and 15% in 41-60 years and >60 years respectively. Mean ± SD of age was 34±12.3. Females were 74% with female: male ration of 74:26. (Table 1)

Table 1: Distribution by Patient's characteristics

Patient Characteristic	Group	Frequency
Age	15-40 Years	62 (62%)
	41-60 Years	23 (23%)
	>60 years	15 (15%)
	Mean ±SD	34±12.3
Sex	Male	26 (26%)
	Female	74 (74%)

Based on Bethesda classification on FNAC, 23 patients have malignant lesions (which is Bethesda V and VI) and 77 patients have benign lesions (which is Bethesda < V grade). Based on TI-RADS on ultrasound showed 22 patients with TI-RADS ≥ 5 and 78 patients with TI-RADS <5. In this study, a significant association was noted between the TI-RADS and Bethesda scores (X^2- 41.74, $p \leq 0.001$). (Table 2)

Table 2: Ultrasound finding versus pathological finding

Ultrasound Finding	Pathological Finding		Total	X^2/ P value
	Malignant (Bethesda V and VI)	Benign (Bethesda < V)		41.74/ <0.00001
Positive (TI-RADS≥ 5)	16 True Positive	6 False positive	22	
TI-RADS <5	7 False Negative	71 True Negative	78	
Total	23	77	100	

Sensitivity and specificity of ultrasound over FNAC of thyroid nodule, at 95% CI was 84.21% (60.42% to 96.62%) and 92.5% (84.39% to 97.20%). Positive and negative predictive value at 95% confidence intervals was 72.73% (54.66% to 85.50%) and 96.10% (89.71% to 98.59%) with accuracy of 90.91% at 95% CI (83.44% to 95.76%). (table 3)

Table 3: Diagnostic Accuracy Parameters of Ultrasound (TI-RADS) over FNAC (Bethesda Classification)

Statistic	Value	95% CI
Sensitivity	84.21%	60.42% to 96.62%
Specificity	92.50%	84.39% to 97.20%
Positive Likelihood Ratio	11.23	5.08 to 24.83
Negative Likelihood Ratio	0.17	0.06 to 0.48
Disease prevalence (*)	19.19%	11.97% to 28.34%
Positive Predictive Value (*)	72.73%	54.66% to 85.50%
Negative Predictive Value (*)	96.10%	89.71% to 98.59%
Accuracy (*)	90.91%	83.44% to 95.76%

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DISCUSSION

This study compared ultrasound findings of thyroid nodule over FNAC findings using TI-RADS and Bethesda system of classification respectively.

In the current study out of 100 patients enrolled age range was 15- 72 years with 62% of patients in the age group of 15-40 years followed by 23% and 15% in 41-60 years and >60 years respectively. Similarly in study by Banstola L et al, age of patients ranged from 16 - 70 years.[9] Where as in study by Warpe B et al The age of presentation ranged from 3 to 75 years with a mean age of 38.41 ± 14.49 years.[10] In the study by Alshahrani A S et al, 47 samples had a mean age of 44.27 (SD = ±13.5) years.[11]

In the current study, Females were 74% with female: male ration of 74:26. In study by Banstola et al, Female to male ratio was 9:1.[9] In study by Warpe et al, the thyroid lesions were more common in females than males, in the ratio of 6.02:1.[10] In study by Alshashrani et,al 85.1% were of the female gender.[11] In study by Mohamed Aya E et al, There were 15 (75%) female and five (25%) male patients, with the male to female ratio of 1 : 3.[12]

In this study based on Bethesda classification on FNAC, 23 patients have malignant lesions (which is Bethesda V and VI) and 77 patients have benign lesions (which is Bethesda < V grade). Based on TI-RADS on ultrasound showed 22 patients with TI-RADS ≥ 5 and 78 patients with TI-RADS <5. In study by Alsharani A S et al, the majority (85.1%) had multiple nodules, 38.3% were with TR4 US finding score, and the median size of the nodule on US was 3 cm with a range of 0.6 to 14 cm on average.[11] In study by Fernandez et al a total of 263 patients were included in the study. The histological results revealed 188 benign lesions and 75 malignant lesions.[13]

In this study, a significant association was noted between the TI-RADS and Bethesda scores (X2- 41.74, $p \leq 0.001$). In study by Alshaikh R et al, a significant positive correlation was noted between the TI-RADS and Bethesda scores ($r = 0.338$, $p \leq 0.001$).[14]

In this study sensitivity and specificity of ultrasound over FNAC of thyroid nodule, at 95% CI was 84.21% (60.42% to 96.62%) and 92.5% (84.39% to 97.20%). Positive and negative predictive value at 95% confidence intervals was 72.73% (54.66% to 85.50%) and 96.10% (89.71% to 98.59%) with accuracy of 90.91% at 95% CI (83.44% to 95.76%). In a retrospective study by Singaporewalla et al. involving 100 consecutive cases compared ultrasonographic TI-RADS findings to all the cytological Bethesda categories, finding a concordance rate of 83% with sensitivity (70.6%), specificity (90.4%), and NPV (93.8%) which was lower compared to the present study.[15]

CONCLUSIONS

In this study, a significant association was noted between the Ultrasound (TI-RADS) and FNAC (Bethesda scores)(X2- 41.74, $p \leq 0.001$). Sensitivity and specificity of ultrasound over FNAC of thyroid nodule, at 95% CI was 84.21% (60.42% to 96.62%) and 92.5% (84.39% to 97.20%). Positive and negative predictive value at 95% confidence intervals was 72.73% (54.66% to 85.50%) and 96.10% (89.71% to 98.59%) with accuracy of 90.91% at 95% CI (83.44% to 95.76%).

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