ORIGINAL ARTICLE

THE CORRELATION BETWEEN BETHESDA SYSTEM AND ULTRASOUND-BASED TIRADS FOR REPORTING THYROID CYTOPATHOLOGY

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ABSTRACT

Objectives: To correlate the screening ability of ultrasound-based TIRADS with the FNAC-based Bethesda system when the latter is kept as a gold standard.

Material and Methods: A cross-sectional study was conducted in the Histopathology department, Rehman Medical Institute, Peshawar 15th June 2022- 14th June 2023. A total of 363 patients from any age group of either gender diagnosed with thyroid nodules were included in the trial. All the participants underwent ultrasound followed by ultrasound-guided fine needle aspiration of thyroid nodules. TIRADS and Bethesda grading was done for each participant. Demographics and grading scores were recorded. Keeping Bethesda scoring as gold standard diagnostic performance of TIRADS grading was calculated.

Results: Mean age of the patients was 46.68 ± 12.28 years with a female-to-male ratio of 2.3:1. TIRADS grading revealed 210 (69.8%) from TIRADS 2 while 70(82.4%), 12(50%), and 09(23.7%) patients were from TIRADS 3, 4 and 5 categories respectively. Bethesda grades were 301(82.9%), 21(5.8%), 09(2.5%), 28(7.7%), and 04(1.1%) from Bethesda 2, 3, 4, 5, and 6 categories respectively. The sensitivity of the TIRADS was 93.8%, specificity 89.1%, positive predictive value 45%, negative predictive value 99.3%, and a diagnostic accuracy of 89.5%.

Conclusion: TIRADS grading has a high diagnostic ability when Bethesda scoring is kept as the gold standard. It can be used effectively in segregating benign from malignant nodules and is recommended for screening patients presenting with thyroid nodules.

Keywords: Biopsy, Fine-Needle, Sensitivity and Specificity, Thyroid Nodule

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INTRODUCTION

The presence of thyroid nodules is a condition that can be detected coincidently in several patients with a prevalence of 68%.[1] The primary role of a clinician in such patients is to differentiate between benign and malignant nodules. The increasing incidence of cancer throughout the globe with widespread local and systemic complications warrants early detection of malignant nodules which can be found in 5% of the patients presenting with thyroid nodules.[2]

Regional statistics from a trial conducted in Pakistan revealed 4.9% of patients with solitary nodules in the district of Dera Ismail Khan, Khyber Pakhtunkhwa. Out of 4.9% nodules, 94.4% were found benign while 5.6% were found to be malignant.[3] A previous trial performed to assess the epidemiology of thyroid nodules revealed that the prevalence increases with increasing age. Similarly, gender was an important factor as female patients of all age groups are more prone to develop thyroid nodules as compared to males. The most common histological type of thyroid cancer was papillary thyroid carcinoma, which was diagnosed in 59 (84%) patients out of 70 individuals.[4] Novel diagnostic therapies have been in use for the diagnosis of thyroid nodules which include non-invasive and invasive approaches. Patients presenting with thyroid nodules are subject to undergo ultrasonography for evaluation and it helps in differentiating a benign from a malignant nodule. Benign nodules visualized under ultrasonography are usually hyperechogenic, wider than taller, flat or oval with smooth margins, and peripheral vascularity, and resemble normal parenchymal tissue. Malignant nodules are usually hypoechogenic, solid, and taller than wider

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with nodular vascularity and irregular margins.[5,6]

Thyroid imaging reporting and data system (TI-RADS) is a scoring technique based on ultrasound findings of thyroid nodules which evaluates the composition, echogenicity, shape, margins, and echogenic foci. Based on the scoring, the nodules are classified into TIRADS 1 - TIRADS 5 categories if the nodules are benign, not suspicious, mildly suspicious, moderately suspicious, highly suspicious, and malignant respectively.[7] Such noninvasive techniques utilized for stratification of benign and malignant thyroid nodules are gaining popularity as evidenced by a high sensitivity of 94% and specificity of 67.39%.[8]

Invasive diagnostic modalities include fine needle aspiration cytology of the thyroid nodules performed by histopathologists, radiologists, surgeons, or endocrinologists. Specimens obtained after the procedure are evaluated by histopathologists using the Bethesda system for reporting thyroid cytopathology. Based on the histological characteristics of the specimen Bethesda system classifies thyroid nodules into Bethesda 1 if the nodules are not diagnostic, 2 for benign, 3 for atypia, 4 for suspicious of follicular neoplasm, 5 for suspicion of malignancy and 6 for malignant nodules.[9]

The communication between a surgeon, endocrinologist, radiologist, and histopathologist is of prime importance for patients presenting with thyroid nodules. Before the availability of advanced ultrasound machines and expertise invasive procedures were commonly performed and resection was frequently employed followed by histopathological analysis in patients presenting with thyroid nodules. The application of TIRADS has led to improved diagnostics and valuable stratification of benign and malignant nodules. The objective of this paper is to evaluate the effectiveness and accuracy of TIRADS as a screening modality in correlation with FNAC FNAC-based Bethesda grading system when the results of the latter are considered the gold standard. The study can help enhance diagnostic practices in patients with thyroid nodules thus enhancing patient care and outcomes.

MATERIAL AND METHODS

This was a cross-sectional study conducted at Rehman Medical Institute, Peshawar after approval of the hospital's ethical review committee. The study period was from 15th June 2022 to 14th June 2023. Inclusion criteria were patients from any age group of either gender diagnosed with thyroid nodules were included in the trial. Patients from the TIRADS 1 category (unsatisfactory) or Bethesda 1 (non-diagnostic) after two attempts of Fine needle aspiration were excluded.

When the results of FNAC were kept as gold standard diagnostic performance of TIRADS revealed a sensitivity of 92%, specificity of 90% with expected prevalence of thyroid malignancy as 8% in patients with thyroid nodules.[10] A sample size of 363 patients was calculated using a desired precision of 10% with a confidence level of 95%.

All patients diagnosed with thyroid nodules were subject to ultrasonography of the thyroid gland by a classified radiologist. Demographic characteristics of all the participants were recorded. Based on the ultrasound findings, size, shape, texture, echogenicity, margins, and vascularity of the tissue TIRADS was employed, and a score was given to each patient. TIRADS 1 - TIRADS 5 categories were used and nodules with a score of 1 were taken as benign, 2-not suspicious, 3-mildly suspicious, 4-moderately suspicious, and 5-highly suspicious for malignancy. TIRADS scoring was recorded followed by fine needle aspiration and collection of the specimen in sterile containers. Specimens of all the patients were taken/received by the histopathology department of our hospital and reported by a specialist cytopathologist. Bethesda scoring system was employed to grade each sample. Based on the cytological characteristics, Bethesda classification was used to classify thyroid nodules into Bethesda 1 if the nodules are non-diagnostic, 2 for benign, 3 for atypia, 4 for suspicious of follicular neoplasm, 5 for suspicion of malignancy and 6 grade for malignant nodules.

The data recorded was analyzed by SPSS version 23. Frequencies and percentages were calculated for categorical variables while mean and standard deviation were calculated for continuous variables. Cross-tabulation was performed, and analysis was done to calculate sensitivity, specificity, positive predictive value, and negative predictive value. The diagnostic accuracy of TIRADS was computed with a 2 x 2 table while keeping the results of Bethesda grading as the gold standard for the segregation of benign and malignant nodules. The following formulas were used for calculation:

RESULTS

The total participants included in the study were 363 with a mean age of 46.68 ± 12.28 years out of which female participants were 256(70.5%) while male participants 107(29.5%) having a female-to-male ratio of 2.3:1. TIRADS grading was recorded for each patient which revealed 210 (69.8%) from TIRADS 2 (fig. 3&4), while 70(82.4%), 12(50%) and 09(23.7%) patients were from TIRADS 3, 4 and 5 categories respectively. After FNAC, Bethesda scoring was performed which revealed 301(82.9%), 21(5.8%), 09(2.5%), 28(7.7%), 04(1.1%) from Bethesda 2 (fig. 1&2), 3, 4, 5 and 6 (fig. 5&6) categories respectively. The results of Bethesda and TIRADS scoring are shown in Table I. For segregation of malignant from benign nodules results of Bethesda scoring were taken as the gold standard and Bethesda category 5 and 6 were taken as malignant lesions while the rest were taken as benign. TIRADS category 4 and 5 were considered malignant while 2 and 3 were taken as benign. The ability of TIRADS to predict the benign and malignant lesions was analyzed by a 2 x 2

cross table keeping the results of FNAC (Bethesda) as the gold standard and results of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy were calculated. FNAC followed by Bethesda scoring of 363 specimens revealed 32(8.8%) malignant nodules categorized as Bethesda 5 and 6 of which 30(93.8%) were accurately predicted by TIRADS. The sensitivity of the TIRADS was 93.8%, specificity 89.1%, positive predictive value 45%, negative predictive value 99.3%, and diagnostic accuracy of 89.5% as shown in Table II.

Figures 1&2, FNAC of a benign nodular goiter showing bland follicular epithelial cells arranged in monolayered sheet with abundant colloid (Diff quick stain 10x & 40x) Figure 3 & 4, Solid isoechoic nodule with smooth margins and specks of calcifications (blue arrow) Figure 5&6, Neoplastic cells arranged in papillae with fibrovascular core and crowded cells with intranuclear pseudo inclusion (Diff quick 10x & 40x)

DISCUSSION

The cross-sectional study was conducted to evaluate the diagnostic ability of ultrasound-based TIRADS in reporting thyroid cytopathology when FNAC based Bethesda grading system was kept as the gold standard. Gender distribution of our results revealed 256 (70.5%) females as compared to 107(29.5%) males similar to the study done by Li Y et al who concluded that females are more prone to thyroid nodules as compared to males.[12] In our study out of 363 patients presenting with thyroid nodules 32(8%) were found malignant. In a similar study conducted by Hadjisavva IS et al, the overall prevalence of thyroid malignancy in patients presenting with thyroid nodules was 14%.[13]

For all calculations in our study TIRADS category 4 and 5 while Bethesda 5 and 6 nodules were recorded as malignant. A total of 301 (83%) patients revealed benign thyroid nodules or mild suspicion of USG (TIRADS 2 and TIRADS 3) while 62(17%) were suspicious of malignancy or malignant nodules (TIRADS 4 and 5). Similarly, Bethesda grading of the tumors revealed 32 (08%) suspicious of malignancy or malignant nodules (Bethesda 5 and Bethesda 6) and 331 (92%) benign nodules (Bethesda 1,2, 3, 4). None of the benign thyroid nodules as predicted by TIRADS 2 grading in 216(59.5%) patients were (Bethesda 4, 5, or 6) malignant or suspicious of malignancy hence the risk of malignancy was 0%. Similarly, the risk of malig-

Table 1: Bethesda and TIRADS grading among patients (n=363)

	BETHESDA GRADING					
	Bethesda 2 n=%	Bethesda 3 n=%	Bethesda 4 n=%	Bethesda 5 n=%	Bethesda 6 n=%	TOTAL n=%
TIRADS 2	210 (57.85%)	06 (1.6%)	00	00	00	216 (59.5%)
TIRADS 3	70 (19.28%)	08 (2.2%)	03 (0.82%)	04 (1.1%)	00	85 (23.41%)
TIRADS 4	12 (3.31%)	05 (1.37%)	03 (0.83%)	03 (0.83%)	01 (0.27%)	24 (6.62%)
TIRADS 5	09 (2.47%)	02 (0.55%)	03 (0.83%)	21 (5.78%)	03 (0.83%)	38 (10.4%)
TOTAL	301(82.9%)	21(5.78%)	09(2.47%)	28(7.71%)	04(1.1%)	363 (100%)

Table 2: Diagnostic performance of TIRADS keeping FNAC as the gold standard (n=363)

TIRADS	FNAC (Bethesda 5, Bethesda 6)	
	Malignant	Non-Malignant
Malignant	30	36
Non-Malignant	02	295

Table 3: Comparison of our results with national and international studies

Comparison	Sensitivity	Specificity	PPV	NPV	DA
Safdar A et al	93.8%	89.1%	45%	99.3%	89.5%
Ahmed SI et al19	90.6%	87.5%	39%	99%	88.5%
Raza SH et al20	89.5%	86.8%	37%	98.9%	88.1%
Zeng L et al21	91.2%	88.7%	40%	99.1%	88.9%
Xu Y et al22	92.3%	90.5%	42%	99.2%	89.8%

Sensitivity: 93.8%

Specificity: 89.1%

Positive predictive value: 45%

Negative predictive value: 99.3%

Diagnostic accuracy: 89.5%

Figure 1

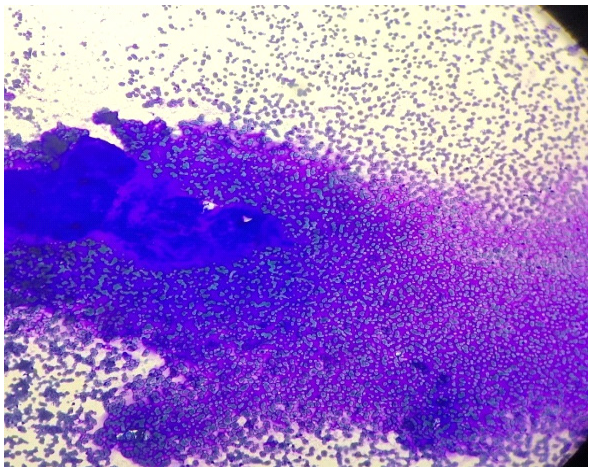


Figure 2

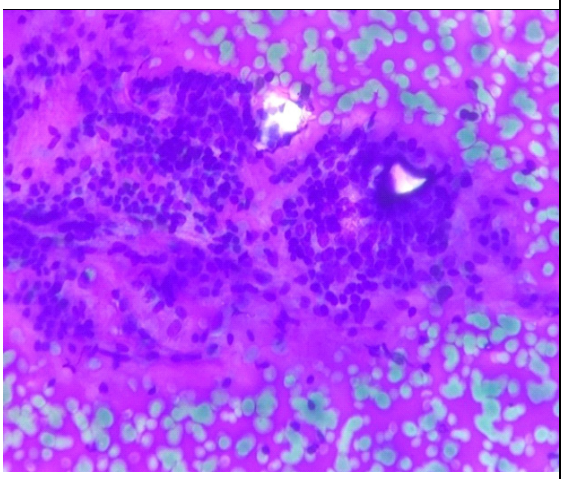


Figure 3

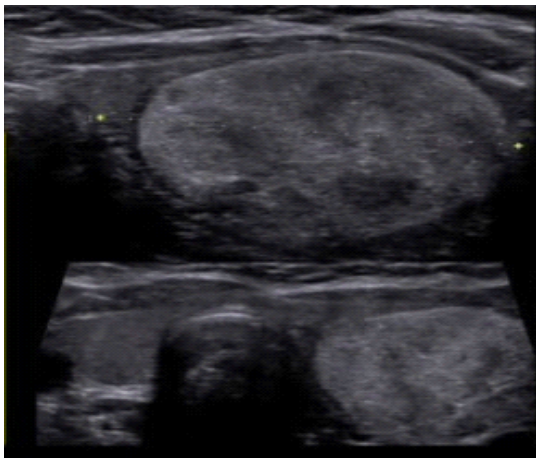


Figure 4

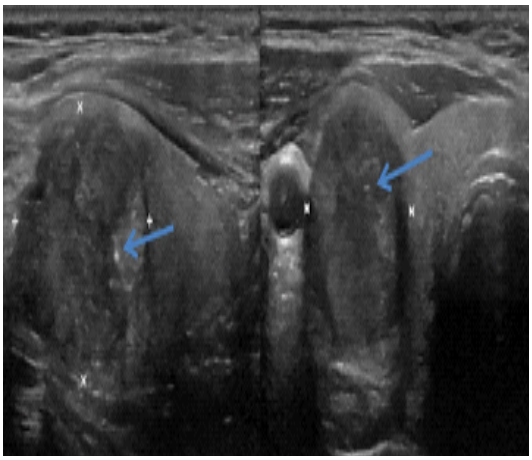


Figure 5

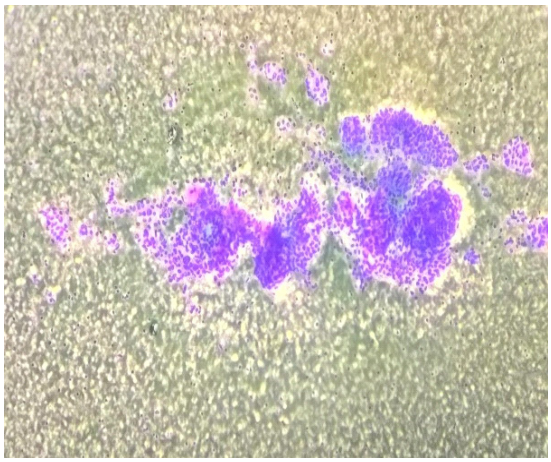
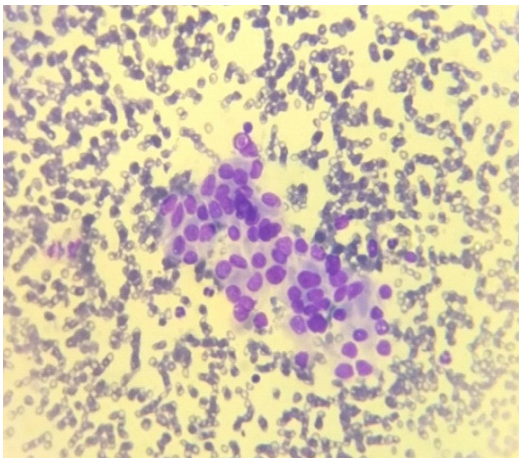


Figure 6



Figures 1&2, FNAC of a benign nodular goiter showing bland follicular epithelial cells arranged in monolayered sheet with abundant colloid (Diff quick stain 10x & 40x) Figure 3 & 4, Solid isoechoic nodule with smooth margins and specks of calcifications (blue arrow) Figure 5&6, Neoplastic cells arranged in papillae with fibrovascular core and crowded cells with intranuclear pseudo inclusion (Diff quick 10x & 40x)

nancy in TIRADS 3, TIRADS 4 and TIRADS 5 was 4.7%, 12.5% and 55.3%.

In consistency with the results of our study, a locoregional study concluded that the ultrasound and FNAC are both effective with equal sensitivity for diagnosis of malignant nodules however FNAC was more specific (90%) and had a diagnostic accuracy of 86%.[13] Similarly, another trial conducted in the region of Islamabad TIRADS was found effective in the segregation of benign and malignant thyroid nodules and TIRADS categories II, III, and IV revealed benign cytological findings.[14]

TIRADS was found a very effective technique of scoring in studies done by George NA et al[13] and Aksoy SH et al[14]. The prediction of malignancy by TIRADS 5 nodules was reported as high as 90% and a high concordance of 69% was found between the two classification systems. We concluded that the sensitivity and specificity of TIRADS were 93.8%, specificity 89.1% while Mohandas M et al found that the sensitivity and specificity of TIRADS were 85.7% and 68%.[15]

The negative predictive value of TIRADS 99.3% in our study was very high which signifies that all the nodules that are benign on ultrasound-based TIRADS do not need any further assessment by employing the invasive procedure of FNAC. Similarly, in another study a high negative predictive value of 98.6% of TIRADS was reported by Kovatcheva RD et al.[16] By employing TIRADS in patients with thyroid nodules an early segregation of the patients can be done, and the number of invasive fine needle aspirations of thyroid nodules can be minimized. In another trial, the number of biopsies procedures in patients with thyroid nodules decreased to more than 50% after TIRADS categorization and stratification of benign and malignant nodules.[17]

With the recent advances in the field of medicine, the rapidly emerging noninvasive techniques have proven to be effective in risk stratification, early identification, and prompt therapies which can lead to decreased morbidity and mortality. Ultrasound-based TIRADS is a promising diagnostic tool with various modifications and a high degree of reliability.[18] A comparison between our results with locoregional and international research conducted on the subject is promising which is depicted in Table III. Hence this study proves that the diagnostic ability of TIRADS is highly reliable, noninvasive, and cost-effective which can be safely employed in our patients with thyroid nodules for stratification of benign from malignant nodules.

CONCLUSION

TIRADS grading has a high diagnostic ability when Bethesda scoring is kept as the gold standard. It can be used effectively in segregating benign from malignant nodules and is recommended for screening patients presenting with thyroid nodules.

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Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Safdar A	✓	×	✓	×	✓	×
Mahmood R	✓	✓	×	✓	✓	×
Khan M	✓	×	×	✓	×	×
Javaid F	✓	×	✓	×	✓	×
Sajjad A	×	✓	✓	×	×	✓
Khattak MT	✓	×	×	✓	×	×
Khan IM	×	×	✓	×	✓	×

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethical Approval:

This Manuscript was approved by the Research Ethics Committee of Rehman Medical Institute, Peshawar Vide No. RMI/REC/Article Approval/38. Dated: 16 05 2022