ORIGINAL ARTICLE

DIAGNOSTIC ACCURACY OF ULTRASONOGRAPHY SCAN TO DIFFERENTIATE BENIGN VERSUS MALIGNANT NODULES OF THE THYROID GLAND USING HISTOPATHOLOGY AS GOLD STANDARD

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ABSTRACT

Introduction: Thyroid nodules are increasingly detected due to the widespread use of ultrasound imaging. While most nodules are benign, a small proportion may be malignant. Accurate and non-invasive diagnosis is essential to avoid unnecessary biopsies and reduce morbidity. The American College of Radiology (ACR) TIRADS classification system has enhanced the role of Doppler ultrasonography in stratifying the risk of malignancy in thyroid lesions.

Objective: To determine the diagnostic accuracy of Doppler ultrasonography in differentiating benign from malignant thyroid nodules, using histopathology as the gold standard.

Methods: This comparative cross-sectional study was conducted at the Radiology and Pathology Departments of Shahida Islam Medical Complex, Lodhran, from June 2023 to July 2024. A total of 60 patients aged 18–60 years with solitary thyroid nodules were enrolled. All participants underwent Doppler ultrasonography with TIRADS classification, followed by fine needle aspiration cytology and histopathological confirmation. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall diagnostic accuracy were calculated using a 2x2 contingency table.

Results: The mean age of patients was 34 years; 67% were female. Ultrasonography showed a sensitivity of 83.33%, specificity of 86.11%, PPV of 80%, and NPV of 88.97%. The overall diagnostic accuracy of ultrasonography in distinguishing benign from malignant nodules was 85%.

Conclusion: Doppler ultrasonography, when combined with TIRADS scoring, demonstrates high diagnostic accuracy for thyroid nodules. It serves as a valuable, non-invasive tool for risk stratification and guiding the need for histopathological confirmation.

Keywords: *Doppler Ultrasonography, TIRADS, Thyroid Nodules, Histopathology, Diagnostic Accuracy, Sensitivity, Specificity.*

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INTRODUCTION:

Thyroid nodules are common, and their predominance depends upon the detection strategies used.[1] On Palpation alone, there is a 3-8 % detection rate of thyroid nodules, while imaging modalities like ultrasound increase the detection rate to 20-76% and most nodules are harmless, but a small but significant percentage turn out to be cancerous.[2] The prevalence of thyroid carcinoma is increasing tremendously, accounting for 1.5 % of all tumors

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reported in the United States, and its occurrence is on the rise worldwide as well.[2,3]

Thyroid masses can be defined as a distinct lesion within the thyroid gland that is radiologically separate from the surrounding t issue and parenchyma. These tend to be cystic, solid, solitary, or multiple.1,2 Ultrasound scan has substantially increased the number of detected cases, and Papillary carcinoma of the thyroid is the most common subtype and needs to be carefully differentiated from benign entities.[4]

TI-RADS (Thyroid Imaging Reporting and Data Systems) is an ultrasound-directed risk stratification system for thyroid nodules. It is a 5-point scoring system based on shape, margins, composition, echogenicity, and echogenic foci of lesions on ultrasound for thyroid nodules, which was formulated in 2012 by the American College of Radiology (also named as ACR-TIRADS).[5] It utilizes ultrasound imaging elements to sort nodules given their probability of malignancy as benign, minimally, moderately, or highly suspicious for malignant lesion, and has helped in a significant reduction in their unnecessary fine needle aspiration cytology biopsies (FNAB) and to help in further treatment.[5-7]

study was conducted on 164 patients having thyroid nodules to find the accuracy of ultrasonography scans in diagnosing malignant masses of the thyroid gland using histopathology as a benchmark. After a detailed history, physical examination, and investigations, the ultrasonography scan was performed on all patients in the radiology department. The ultrasound scan was performed by a senior radiologist, and then an incisional biopsy was performed. The average age of patients was 34 years with a standard deviation of +- 7.318. 38% (62) were males, while 62% (102) were females among them. Ultrasound had a sensitivity of 96.58%, a specificity of 83.33%, a positive predictive value of 76.65% and a negative predictive value of 97.72%. The accuracy of USG was 88.12% in diagnosing malignant lesions of the thyroid gland using histopathology as a benchmark.[8]

Thyroid cancer is one of the most common neoplasms of the endocrine system, accounting for 1.0-1.5% of all new cancers in America, and there is a need for its accurate diagnosis for reducing morbidity and mortality associated with it.[9] The prevalence of nodules of the Thyroid gland is increasing in Pakistan in young age groups, with causes still unknown. Ultrasound is extensively used as a non-invasive, cost-effective, and readily available modality for evaluating these nodules. Histopathological examination remains the definitive diagnostic standard, but it is invasive and also not feasible for every patient. While Doppler ultrasound has shown promise in evaluating thyroid nodules, its diagnostic accuracy varies across studies. There is a need to assess it, particularly in settings where resources are limited. This study aims to assess of diagnostic accuracy of ultrasonography to differentiate benign versus malignant using histopathology as reference for reporting different categories of thyroid lesions to assess the risk of malignancy. This will help to improve our practice and local guidelines for management of such cases to reduce the morbidity and mortality associated with it.

METHODS:

This comparative cross-sectional study was conducted in the Departments of Radiology and Pathology, Shahida Islam Medical Complex, Lodhran, from June 2023 to July 2024. Ethical approval was obtained from the Institutional Review Board prior to the study. A total of 60 patients aged between 18 and 60 years, presenting with a solitary thyroid nodule, were included through non-probability consecutive sampling. Written informed consent was obtained from all participants.

Sample size: Sample size was estimated using the WHO calculator for sample size estimation with a 95% level of confidence and absolute precision required at 5% with a power of the study at 80% and was calculated as 60, with P = anticipated proportion of sensitivity of Ultrasound SCAN to differentiate benign versus malignant tumors of Thyroid gland = 96.58%.[8]

Inclusion Criteria:

- Adults aged 18-60 years and both genders with having thyroid gland nodule
- Patients who give consent

Exclusion Criteria:

- Adults <18 and > 60 years
- Patients who have a limited life expectancy
- Patients who don't give consent

Operational Definitions:

- **Histopathology:** Thyroid nodules histopathology refers to the microscopic examination of thyroid tissue to determine the nature of a thyroid nodule, whether it is benign or malignant, and to classify specific types of lesions. Nodules can be classified as BENIGN THYROID NODULE, a histopathologically confirmed benign lesion (e.g., colloid nodule, follicular adenoma), and MALIGNANT THYROID NODULE, a histopathologically verified malignancy (e.g., papillary, follicular, medullary, anaplastic carcinoma)
- **TIRADS:** It is a risk stratification system used to classify thyroid nodules based on their ultrasound characteristics. It helps guide decisions about follow-up and the need for fine needle aspiration (FNA) biopsy. There are several versions of TI-RADS, but the most commonly used is the ACR TI- RADS (developed by the American College of Radiology), which classifies based on 5 ultrasound features (Composition, Echogenicity, Shape, Margin, Echogenic foci).
- **TIRADS Scoring and categories:**

Total points	TI-RADS Category	Level of suspicion
0	TR1	Benign
2	TR2	Not Suspicious
3	TR3	Mildly Suspicious
4 - 6	TR4	Moderately Suspicious
= or >7	TR5	Highly suspicious

- **Doppler Features:** Color Doppler was used to assess vascularity. Central or intranodular vascularity was considered suspicious for malignancy.

Data Collection Procedure: All patients fulfilling the inclusion criteria after taking consent from them were included in the study. The data was collected through a pre-designed and pretested questionnaire. Complete history was taken regarding occurrence of tumor and a general physical examination was done to assess. The site of thyroid gland lesions in patients was assessed. After explaining the procedure, consent was obtained from the patients. Ultrasound scan was done in all the patients by an expert radiologist, and evidence of benign and malignant lesions was collected. After this diagnostic modality, excision biopsy was done, and the histopathology of the lesion was collected. The Diagnostic Accuracy of the Ultrasound Scan was calculated using histopathology as the gold standard.

Data Analysis: The data obtained was entered and then analyzed using SPSS version 24. Simple frequencies as well as percentages were calculated for the qualitative variables and were presented in the form of tables and figures. A 2×2 contingency table

was used to assess the diagnostic accuracy of ultrasonography with TIRADS scoring.

The following metrics were calculated:

- **Sensitivity:** The ability of TI-RADS to correctly identify malignant thyroid lesions that are confirmed by histopathology. It was calculated by the formula: TP/ TP + FN
- **Specificity:** The ability of TI-RADS to correctly identify benign thyroid lesions that are confirmed as non-cancerous by histopathology. It was calculated by the formula: TN / TN + FP
- **Positive Predictive Value (PPV):** It is the percentage of patients with a positive TI-RADS category 4 and 5 who are diagnosed with thyroid cancer on histopathology, which is considered as gold standard. It was calculated by the formula: TP /TP + FP
- **Negative Predictive Value (NPV):** It is the probability that a patient with a negative TI-RADS 1 or 2 doesn't have thyroid cancer. It was calculated by the formula: TN / TN + FN
- **Diagnostic Accuracy:** The proportion of correctly identified cases (both true positives and true negatives) among all cases. Formula: Accuracy = TP + TN /TP + FP + FN+ TN

RESULTS:

A total of 60 patients with solitary thyroid nodules were included in the study. The mean age of participants was 34 years, with a female predominance (67%).

Doppler ultrasonography, in conjunction with ACR TIRADS classification, demonstrated high diagnostic performance in differentiating benign from malignant thyroid lesions. Histopathological analysis confirmed malignancy in 18 cases (30%) and benign pathology in 42 cases (70%).

Among the 18 histologically confirmed malignant nodules, 15 were correctly identified as suspicious or malignant on ultrasonography (true positives), while 3 were misclassified as benign (false negatives). Of the 42 benign nodules, 5 were incorrectly categorized as malignant (false positives), and 37 were accurately identified as benign (true negatives). Based on these findings, the following diagnostic metrics were calculated:

- Sensitivity: 83.33%
- Specificity: 86.11%
- Positive Predictive Value (PPV): 80%
- Negative Predictive Value (NPV): 88.09%
- Overall Diagnostic Accuracy: 85%

These results indicate that Doppler ultrasonography, when combined with TIRADS scoring, is a reliable non-invasive modality for evaluating the risk of malignancy in thyroid nodules. The high NPV suggests that a benign ultrasound finding is strongly predictive of a true negative result, supporting its role in avoiding unnecessary invasive procedures.

	Histopathology Positive	**Histopathology Negative**	**Total**
Ultrasound Positive	True Positive (TP) = 20	False Positive (FP) = 5	25
Ultrasound Negative	False Negative (FN) = 4	True Negative (TN) = 31	35
Total	24	36	60

Table 1. 2×2 Contingency Table for Diagnostic Accuracy of Doppler Ultrasonography with TIRADS Scoring

DISCUSSION:

This study, conducted at the Radiology Department of Shahida Islam Medical Complex, Lodhran, evaluated the diagnostic performance of Doppler ultrasonography using ACR TIRADS classification in differentiating benign from malignant solitary thyroid nodules. The mean age of patients was 34 years, with the majority falling within the 31–40 years age range. A clear female predominance (67%) was observed, consistent with the known higher prevalence of thyroid nodules among women.

Ultrasonography demonstrated a sensitivity of 83.33% in identifying malignant nodules, which aligns closely with previously reported values. For instance, a similar study reported a sensitivity of 96%, indicating the high potential of ultrasound to detect malignant features when correlated with histopathology as the gold standard. Likewise, the specificity of 86.11% observed in our study is comparable to the 83% specificity reported in other literature, suggesting that ultrasound is also effective in ruling out malignancy in benign lesions.[8]

The positive predictive value (PPV) and negative predictive value (NPV) in our study were 80% and 88.97%, respectively. These values are in line with findings from other studies, which have reported PPVs around 76% and NPVs as high as 97%.[9] The overall diagnostic accuracy of 85% further reinforces the reliability of ultrasonography in evaluating thyroid nodules, and is comparable to the 88% accuracy reported in previous studies.[10] A recent study further supports the utility of imaging-based risk stratification tools. Their evaluation of ACR TI-RADS against the Bethesda cytology system in 224 patients found a sensitivity of 87.5% and an NPV of 86.5%, indicating a strong ability to rule out malignancy using ultrasound-based systems.[11]

In a recent cross-sectional study conducted at CMH Quetta, ultrasonography demonstrated a high diagnostic accuracy of 91.55% in differentiating benign from malignant thyroid nodules, with sensitivity and specificity of 93.15% and 89.86%, respectively. These findings strongly support the reliability of ultrasonography as a non-invasive diagnostic modality for thyroid malignancy. The authors concluded that ultrasonography is a highly effective initial screening tool and can significantly reduce the need for invasive procedures in the assessment of thyroid nodules.[12]

A study conducted by Khalil et al. demonstrated that ultrasonography had a sensitivity of 90.62% and specificity of 88.37% in differentiating benign from malignant thyroid nodules, which closely aligns with the findings of our study. Their results support the reliability of USG as a non-invasive and accurate tool in the initial evaluation of thyroid lesions.[13]

In the study by Al-Ghanimi et al., ultrasonography demonstrated a high specificity (94.9%) in diagnosing benign thyroid nodules when compared to fine-needle aspiration cytology. The authors concluded that ultrasound is a reliable, non-invasive modality that can guide biopsy decisions and help avoid unnecessary invasive procedures.[14]

A recent review article stated that although the pooled sensitivity and specificity of ultrasonography in distinguishing benign from malignant thyroid nodules were high, they remain insufficient to replace histopathological confirmation as the definitive diagnostic standard.[15]

The diagnostic performance of ultrasonography is largely attributed to its ability to assess multiple features, such as echogenicity, margins, shape, calcifications, and vascularity, which are systematically evaluated using the ACR TIRADS classification. This approach improves risk stratification and helps reduce unnecessary biopsies, especially in low-risk cases.

These findings support the role of Doppler ultrasonography, particularly when combined with

standardized scoring systems like TIRADS, as a non-invasive, accessible, and cost-effective first-line imaging modality for thyroid nodule assessment. Given the growing use of ultrasound in thyroid screening, consistent application of risk stratification protocols is critical in guiding clinical decisions and optimizing patient outcomes.

Strengths and Limitations: A key strength of this study is the use of histopathology as the definitive gold standard for confirming the nature of thyroid nodules, which allowed accurate evaluation of the diagnostic metrics. Additionally, the use of Doppler and standardized TIRADS classification enhanced the reproducibility and clinical relevance of the findings.

However, the study is limited by its small sample size (n=60) and single-center design, which may restrict generalizability. Inter-observer variability in ultrasound interpretation and FNAC sampling was not assessed, and follow-up data were not included to evaluate long-term outcomes. Future multi-center studies with larger sample sizes and inter-rater reliability assessments are recommended to validate and extend these findings.

CONCLUSION:

Doppler ultrasonography, when combined with the ACR TI-RADS scoring system, demonstrated high diagnostic accuracy in differentiating benign from malignant thyroid nodules. With its strong sensitivity, specificity, and predictive values, it serves as a reliable, non-invasive tool to guide clinical decision-making and reduce unnecessary biopsies. While histopathology remains the gold standard, ultrasound offers substantial utility as an initial diagnostic modality in thyroid nodule evaluation.

DECLARATION OF INTEREST: The authors declare no conflict of interest.

AUTHOR'S CONTRIBUTIONS:

N.M: Conceptualization, data collection, and write-up

A.M: Data analysis and final editing of manuscript.

A.Z: Proofreading, literature review, and references

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