Original Article

Assessment of False-Positive Rates in Ultrasonographic Detection of Echogenic Thyroid Nodules

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Abstract:

Background: Echogenic thyroid nodules are frequently evaluated using ultrasonography (USG), which, despite its non-invasive nature and diagnostic utility, has limitations in sensitivity, contributing to false-positive findings. This study assesses the diagnostic performance of USG and its false-positive rates in detecting echogenic thyroid nodules.

Methods: This cross-sectional survey was regulated in Combined Military Hospital (CMH), Dhaka, over 12 months. Fifty patients with echogenic thyroid nodules underwent ultrasonography followed by histopathological confirmation. The diagnostic characteristics of USG, encompassing sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV), were established by histopathology as the gold standard.ss

Results: Ultrasound findings revealed a specificity of 95.56%, sensitivity of 60.00%, accuracy of 92.00%, PPV of 60.00 % and NPV of 95.56%. Among histopathologically confirmed benign cases (90%), nodular goiter accounted for 74%, while follicular adenoma and thyroiditis constituted 10% and 6%, respectively. Malignant cases (10%) were exclusively papillary carcinoma. False-positive cases were identified in 2 benign nodules, while 2 malignant nodules were misclassified as benign.

Conclusion: Ultrasound is a reliable diagnostic tool with high specificity and accuracy for evaluating echogenic thyroid nodules, but its moderate sensitivity underscores the need for adjunctive diagnostic methods. Integrating advanced imaging techniques and standardized reporting systems may reduce false-positive rates and improve diagnostic precision.

Keywords: Thyroid Nodules, Ultrasonography, Diagnostic Accuracy, False-Positive Rates, Sensitivity, Specificity, Echogenic Thyroid Nodules, Histopathology

Introduction:

Thyroid nodules are a frequent clinical finding and become more common with advancing age and advances in imaging technology. Epidemiological studies reveal thyroid nodules are found in up to 60% of individuals when high-resolution ultrasonography is used, underlining their substantial involvement in thyroid disease.[1,2] While most nodules are benign and asymptomatic, the potential for malignancy necessitates accurate evaluation and risk stratification to guide management decisions.[3] Ultrasonography (USG) has evolved into the primary tool of thyroid nodule evaluation due to its non-invasive nature, ubiquitous availability and the capacity to offer precise morphological characterization.[4] Features such as echogenicity, margins and calcifications are critical for differentiating between benign and malignant lesions, making USG a valuable diagnostic modality.[5] Despite its utility, variability in interpretation and technical limitations pose challenges, particularly in the context of false-positive findings that often result in unnecessary biopsies and anxiety for patients.[6] Echogenic thyroid nodules, characterized by their increased echogenicity relative to surrounding thyroid tissue, are a focus of clinical interest due to their association with benign and malignant pathology.[7] However, the subjectivity involved in assessing echogenicity complicates the differentiation process. Studies have reported inconsistencies in USG findings, with factors such as microcalcifications, irregular margins and internal composition contributing to diagnostic uncertainty.[8] False-positive detections of echogenic nodules often lead to unwarranted fine-needle aspiration biopsies (FNA), adding to healthcare costs and patient burden without improving outcomes.[9] The American College of Radiology Thyroid Imaging Reporting and Data System (ACR-TIRADS) was established to address this issue by standardizing evaluation standards. Recent research demonstrates that recommendations like ACR-TIRADS can dramatically minimize needless biopsies while keeping excellent sensitivity for detecting cancer.[10] Fine-needle aspiration (FNA) biopsy remains the gold standard for cytological assessment of thyroid nodules, with excellent sensitivity and specificity in detecting cancer. However, the method has limits. False-positive and false-negative findings, especially in nodules with ambiguous cytology, provide important clinical problems.[11] False-positive findings may lead to overtreatment, including unnecessary surgical interventions, while false-negative results can delay cancer diagnosis, adversely affecting outcomes.[12] For example, nodules characterized as benign by FNA but later confirmed as malignant post-thyroidectomy demonstrate the inherent limitations of FNA when used as a standalone diagnostic tool.[13] Furthermore, technical artifacts, interobserver variability and the influence of co-existing conditions such as thyroiditis or calcifications exacerbate diagnostic inaccuracies.[14] The clinical implications of false-positive findings extend beyond patient management to broader systemic concerns. Increased biopsy rates strain healthcare resources and heighten the psychological and economic burden on patients.[15] Despite the advancements in molecular diagnostics and elastography, significant gaps persist in the systematic evaluation of false-positive rates, particularly in echogenic thyroid nodules.[16] This gap underscores the need for adjunctive diagnostic technologies and standardized criteria to refine risk stratification and minimize diagnostic errors. The present study aims to assess and analyze false-positive rates in ultrasonographic detection of echogenic thyroid nodules. By integrating clinical, imaging and histopathological data, this research seeks to identify factors contributing to diagnostic inaccuracies and propose strategies to enhance the precision of USG in thyroid nodule evaluation. Such insights could bridge existing gaps in the literature, inform guideline development and ultimately improve patient outcomes.

Methods:

At CMH in Dhaka, this comprehensive investigation was conducted, in partnership with the departments of endocrinology, medicine and surgery. Patients with echogenic thyroid nodules were seen at the Departments of Medicine, Endocrinology and Surgery before being sent to the Radiology & Imaging department for B-mode ultrasonography (USG). The study was conducted over 12 months, from January 2024 to December 2024.The study comprised 50 patients utilizing a purposeful sampling strategy. Eligible individuals had echogenic thyroid nodules that met the inclusion criteria. Patients had to have echogenic thyroid nodules to be included and those with a history of any cancer or bleeding problems were excluded. A previously tested questionnaire was used to collect the data. To evaluate the morphological features and echogenicity of their thyroid nodules, each subject underwent B-mode ultrasonography. The diagnosis was verified and the accuracy of the ultrasonography was assessed using histopathological data as a reference standard. Version 25 of the Statistical Packages for Social Sciences (SPSS) was used to perform the statistical analyses. Tables, figures, and diagrams were used to present the results. Using histological confirmation of diagnosis, sensitivity, specificity, accuracy, positive predictive value

(PPV), and negative predictive value (NPV) were calculated to evaluate the dependability of ultrasonography in detecting echogenic thyroid nodules.

Study Population and Sampling:

A total of 50 patients were enrolled using a purposeful sampling technique. Patients were first evaluated in the Medicine, Endocrinology, or Surgery departments with suspected thyroid nodules and further referred to the Radiology & Imaging department for ultrasonographic examination. Onlythose diagnosed with echogenic thyroid nodules met the inclusion criteria.

- Inclusion criteria:
  Presence of radiologically identified echogenic thyroid nodules.
  Patients willing to undergo histopathological evaluation.
- Exclusion criteria:
  History of thyroid or any other cancer.
  Presence of bleeding disorders or inability to undergo histopathological testing.

Data Collection Process:

Data were collected using a pre-tested structured questionnaire, which included:

- Demographic data: Age, sex, and clinical history.
- Presenting complaints: Pain, dysphagia, hoarseness of voice.
- Local thyroid examination: Nodule consistency, tenderness, mobility, and lymph node involvement.
- Ultrasonographic findings: Nodule characteristics, including number, position, margins, microcalcifications, halo sign, and comet tail sign.
- Histopathological diagnosis: Used as the gold standard for final confirmation.

Ultrasound Examination:

B-mode ultrasonography (USG) was performed for all participants using a high-frequency linear transducer. The following characteristics were evaluated:

- Number of nodules: Single or multiple.
- Location: Right or left lobe.
- Margins: Regular or irregular.
- Other features: Presence of microcalcifications, halo sign, comet tail sign.
- Overall impression: Benign or malignant based on sonographic features and established guidelines (e.g., ACR-TIRADS).

Histopathological Confirmation:

Following ultrasonography, histopathological evaluation was conducted through either:

- Fine-Needle Aspiration Cytology (FNAC), or
- Post-surgical tissue examination, depending on clinical indications.

Histopathology classified nodules into:

- Benign: Nodular goiter, follicular adenoma, thyroiditis.
- Malignant: Papillary carcinoma.

Statistical Analysis:

Statistical analysis was performed using SPSS version 25.

The following diagnostic metrics were calculated:

Sensitivity=TP/(TP+FN)

Specificity=TN/(TN+FP)

Accuracy=(TP+TN)/Total

Positive Predictive Value (PPV)=TP/(TP+FP)

Negative Predictive Value (NPV)=TN/(TN+FN)

Where: TP=True Positive, TN=True Negative, FP=False Positive, FN=False Negative.

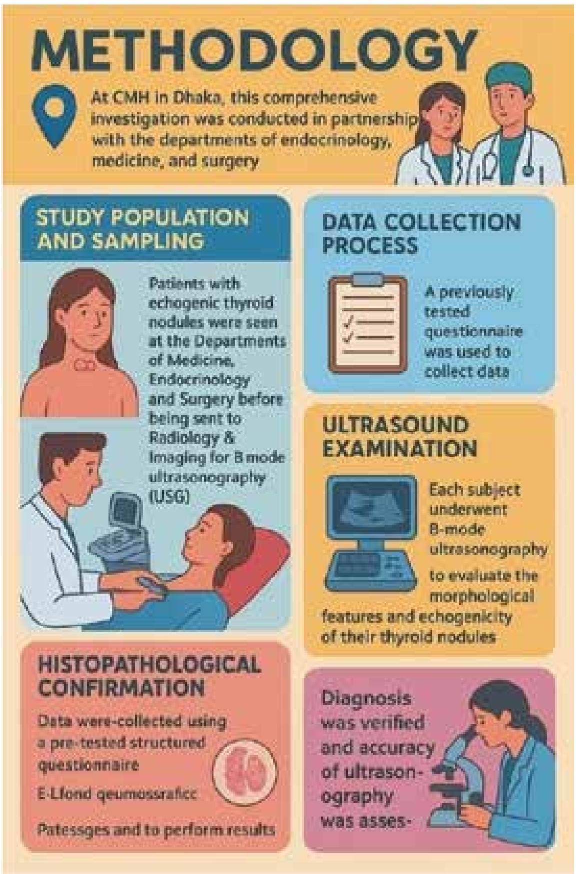

Figure-1: Flowchart of study methodology for evaluation of echogenic thyroid nodules.

Results:

This table-I summarizes the demographic and clinical presentation of the 50 participants. The majority (50%) were aged 31–40 years, showing a peak incidence in middle age, while only 4% were ≤20 or >60 years, indicating lower prevalence at extremes of age. A striking female predominance (86%) was observed, consistent with the known higher prevalence of thyroid disorders among women. Regarding clinical symptoms, dysphagia was the most frequent complaint (62%), followed by pain (22%) and hoarseness of voice (6%), reflecting typical presentations of thyroid nodules affecting swallowing or causing local discomfort.

Table-I: Participants were distributed according to their baseline features (N=50)

Variable	Frequency	Percentage
Age		
≤20	2	4
21-30	7	14
31-40	25	50
41-50	10	20
51-60	4	8
>60	2	4
Gender		
Male	7	14
Female	43	86
Presenting Complaints		
Pain	11	22
Dysphagia	31	62
Hoarseness of the voice	3	6

Table-II: Respondents' allocation of the local assessment (N=50)

Variable	Frequency	Percentage
Number of nodules		
Single	15	30
Multiple	35	70
Consistency		
Soft	15	30
Firm	30	60
Hard	5	10
Tenderness		
Tender	20	40
Non-tender	30	60
Other characteristics		
Deglutition induced movement	50	100
Palpable cervical lymph nodes	5	10
Enlarged thyroid gland	50	100

The findings from the local examination of the participants are presented in Table-II. Local examination revealed that multiple nodules (70%) were more common than single nodules (30%), suggesting a predominance of multinodular thyroid disease. Most nodules were firm (60%), while soft (30%) or hard (10%) nodules were less common, the latter often raising suspicion for malignancy. Tenderness was present in 40% of cases, possibly due to inflammatory causes. Importantly, all nodules exhibited deglutition-induced movement, confirming thyroid origin, and 10% had palpable cervical lymph nodes, indicating possible regional involvement in suspected malignancies.

Table-III: Distribution of ultrasound findingsof thyroid gland (N=50)

Variable	Frequency	Percentage
Number of nodules		
Single	16	32
Multiple	34	68
Position of the nodule		
Right lobe	34	68
Left lobe	16	32
Margins of nodule		
Regular	45	90
Irregular	5	10
Micro calcification	9	18
Presence of Halo	9	18
Comet tail sign	4	8
Ultrasound findings consistent with		
Benign	45	90
Malignant	5	10

Ultrasound findings revealed that multiple nodules were predominant (68%), with the right lobe being the most frequent site (68%) which is shown in Table-III. Most nodules had regular margin (90%), suggesting benignity, while irregular margin (10%) were linked to malignancy suspicion. Microcalcifications (18%) and halo signs (18%) were seen in a subset, both features being diagnostically significant—microcalcifications often indicate malignancy, while a halo sign suggests benignity. Comet tail artifacts (8%) were associated with benign colloid nodules. Overall, ultrasonography categorized 90% of nodules as benign and 10% as malignant, aligning closely with histopathology findings.

Table-IV: Distribution of the patients by histopathological findings (N=50)

Histopathology findings	Frequency	Percentage
Benign	45	90
Follicular adenoma	5	10
Thyroiditis	3	6
Nodular goiter	37	74
Malignant	5	10
Papillary	5	10

The majority of nodules (90%) were benign, with nodular goiter accounting for 74% of all cases. Follicular adenoma was identified in 10%, while thyroiditis was observed in 6% of participants. Malignant nodules were found in 10% of cases, all of which were classified as papillary carcinoma.

Table-V: Distribution of ultrasound findings by histopathological findings of the benign thyroid nodule (N=50)

Ultrasound findings	Histopathologically benign n=45	Histopathologically malignant n=5	Total
Benign (n=45)	43 (TN)	2 (FN)	45
Malignant (n=5)	2 (FP)	3 (TP)	5
Total	45	5	50

Table-V presents the comparison between ultrasound findings and histopathological results for the 50 thyroid nodules analyzed. Among the 45 nodules histopathologically confirmed as benign, 43 were accurately identified as benign by ultrasound (true negative), while 2 were misclassified as malignant (false positive). Conversely, of the 5 histopathologically confirmed malignant nodules, 3 were correctly identified as malignant by ultrasound (true negatives), while 2 were incorrectly classified as benign (false negative).

Table-VI: Diagnostic criteria of Ultrasound findings with histopathological findings as the gold standard

Criteria	Formula	Value
Sensitivity	TP/(TP+FN)	60.00%
Specificity	TN/(TN+FP)	95.56%
Accuracy	(TP+TN)/Total	92.00%
Positive Predictive Value	TP/(TP+FP)	60.00%
Negative Predictive Value	TN/(TN+FN)	95.56%

The specificity of ultrasound for detecting histopathologically benign nodules was 95.56%, indicating its high ability to correctly identify true negative. Sensitivity was calculated at 60.00%. The overall accuracy of ultrasound findings was 92.00%, demonstrating a strong agreement with histopathological results. The positive predictive value (PPV) was 60.00%, indicating moderate reliability in ruling out malignancy when a nodule was classified as malignant by ultrasound. However, the negative predictive value (NPV) was 95.56%, suggesting a high likelihood of benignity when ultrasound classified a nodule as benign

Discussion:

The present investigation aimed to evaluate the diagnostic reliability of ultrasonography in differentiating between benign and malignant cases, in addition to the false-positive rates in the ultrasonographic identification of echogenic thyroid nodules. Our results are in line with an increasing amount of research that highlights the benefits and limitations of using ultrasonography as the main method of thyroid nodule diagnosis. Our findings demonstrated that, though two benign nodules were incorrectly identified as malignant (false positive), ultrasonography correctly identified 43 of 45 benign nodules (true negative). Three cancer nodules were accurately detected by ultrasound (true positive), while two were mistakenly categorized as benign (false negative). This corresponds to a positive predictive value (PPV) of 60.00%, a negative predictive value (NPV) of 95.56%, a sensitivity of 60.00%, a specificity of 95.56%, and an accuracy of 92.00%.These results align with previous research, including the Sui et al. (2019) research who observed high specificity (96.4%) but emphasized the problem of reaching high specificity in ultrasound-based evaluations.[17] The moderate sensitivity observed in our study suggests that ultrasound is prone to over-diagnosing malignancy in benign nodules, a limitation that contributes to false-positive rates.The clinical implications of false-positive findings are significant. Misclassifying benign nodules as malignant often leads to unnecessary fine-needle aspiration biopsies (FNAB) or surgical interventions, increasing patient anxiety and healthcare costs. Studies by Kundi et al. and Lee et al. emphasize similar concerns, noting that false-positive rates in ultrasound diagnostics can exacerbate resource utilization and patient burden.[18,19] Additionally, the relatively low PPV (60.00%) in our study highlights the need for caution when ruling out malignancy based solely on ultrasound findings, a limitation that has been echoed by Khan et al. in their analysis of papillary carcinoma detection.[20] Histopathological confirmation in this study revealed that 90% of nodules were benign, with nodular goiter (74%) being the most common finding, followed by follicular adenoma (10%) and thyroiditis (6%). Malignancy was confirmed in 10% of cases, all classified as papillary carcinoma. These findings are consistent with those of Mihai et al. and Elsabah et al., who also observed nodular goiter as the predominant benign pathology and papillary carcinoma as the most frequent malignancy.[21,22] However, the misclassification of benign nodules as malignant remains a persistent challenge, contributing to unnecessary interventions.Ultrasound findings in our study revealed that echogenic thyroid nodules predominantly exhibited benign characteristics such as regular margins (90%), absence of microcalcifications (82%) and absence of irregular features. These features are commonly associated with benignity, as corroborated by Wang et al., who reported similar associations with benign nodules.[23] However, the 18% prevalence of microcalcifications in our cohort reflects their dual diagnostic role, as they are often seen in both benign and malignant nodules, complicating ultrasonographic differentiation.To address the limitations of ultrasound, advanced diagnostic techniques and standardized reporting systems have been proposed. Studies by Zhu et al. and Lin et al. have shown that integrating ultrasound with contrast-enhanced ultrasound (CEUSG) or elastography can significantly enhance diagnostic accuracy and reduce false-positive rates.[24,25] Furthermore, classification systems such as ACR-TIRADS have been instrumental in reducing observer variability and standardizing malignancy risk assessment, as reported by multiple studies.[26,27] In conclusion, while ultrasonography remains a valuable tool for evaluating echogenic thyroid nodules, its susceptibility to false-positive findings requires adjunctive diagnostic approaches. Future research should focus on refining ultrasound criteria, integrating molecular and imaging technologies and adopting standardized risk stratification systems to improve specificity and reduce false-positive rates. These efforts will enhance diagnostic precision, minimize unnecessary interventions and optimize patient outcomes.

Limitations of The Study:

The investigation had a small number of participants and was conducted in a single hospital. Consequently, the results might not be representative of the community at large.

Conclusion:

Our investigated research assessed the false-positive rates and diagnostic accuracy of ultrasonography in detecting echogenic thyroid nodules. In this study, USG showed very high specificity (95.56%) and negative predictive value (95.56%)and overall accuracy (92.00%) in detecting benign cases, its modest sensitivity (60.00%) and positive predictive value (60.00%)indicated limits in properly diagnosing malignant nodules. The findings highlight the importance of adjunctive diagnostic methods like contrast-enhanced ultrasonography or elastography, as well as standardized reporting systems like ACR-TIRADS in improving specificity and lowering false-positive rates. Future research should focus on combining these sophisticated diagnostic technologies with ultrasonography to improve diagnosis accuracy, reduce wasteful procedures and improve patient outcomes.

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Ethical approval: The study was approved by the Institutional Ethics Committee.

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