The Research of Medical Science Review
ISSN: 3007-1208 & 3007-1216 Volume 3, Issue 7, 2025

DIAGNOSTIC ACCURACY OF THYROID ULTRASOUND IN DETECTING MALIGNANCY IN THYROID NODULE TAKING HISTOPATHOLOGY AS GOLD STANDARD

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DOI: https://doi.org/10.5281/zenodo.15861273

Keywords
thyroid nodule, ultrasonography, fine needle aspiration cytology, accuracy, sensitivity, specificity, negative predictive value, positive predictive value

Article History
Received: 15 February, 2025
Accepted: 29 June, 2025
Published: 08 July, 2025

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Abstract

Introduction: *Thyroid nodules frequently present in clinical settings. While the majority of thyroid nodules are benign, it is essential to investigate which nodules have a higher likelihood of being malignant. Ultrasound has been recognized as a non-invasive and straightforward imaging method for assessing thyroid nodules. A thyroid nodule is a distinct lesion that can be identified through ultrasound as separate from the surrounding thyroid tissue. It continues to be challenging to differentiate between benign and malignant thyroid nodules.*

Objective: *To determine the diagnostic accuracy of ultrasound for diagnosis of malignant thyroid nodule taking histopathology as gold standard.*

Methodology: *The research involved 348 patients who were selected consecutively according to age criteria between 20 and 70 years old with thyroid nodules that lasted for more than four weeks based on clinical diagnosis. The researchers obtained demographic information and clinical data. A single radiologist conducted thyroid ultrasounds with Nemio XG and 3.5–15 MHz probes for diagnosing solid, hypoechoic, calcified, and hyper-vascular nodules as USG+ve. Continuous variables within the study underwent mean ± SD analysis and categorical variables received frequency/percentage assessment through IBM-SPSS v26 software. The diagnostic metrics sensitivity, specificity as well as PPV, NPV, and accuracy was calculated from 2×2 tables. The research contained effect modifier control through stratified approaches and diagnostic accuracy evaluation after stratification.*

Results: *The female population composed a majority of 67.8% (n=236) participants. The study participants had a cumulative mean age of 42.53 ± 13.74 years. 29.6% of the total nodule diagnosed as malignant on thyroid ultrasound while 20.4% were actually malignant on histopathology. Thyroid*

ultrasound diagnoses malignant nodules with an overall 87.93% accuracy rate and 93.0% sensitivity along with 86.6% specificity and 64.1% PPV and 98.0% NPV.

Conclusion: *The sensitivity and specificity levels of thyroid ultrasound in detecting malignant thyroid nodules are high but its positive predictive value is moderate making histopathological verification essential for accurate diagnosis in positive cases. The diagnostic accuracy shows age and gender dependency while obtaining maximum precision from middle-aged groups.*

INTRODUCTION

Thyroid nodules are identified in 50–65% of healthy persons, predominantly asymptomatic and found incidentally. [i] Most are benign and do not necessitate treatment, with less than 5% being cancerous/malignant.[ii] Thyroid nodules are more prevalent in regions with iodine deficit, among females, and in those who have received neck irradiation. [iii] Factors that are correlated with an increased likelihood of malignancy encompass a familial history of medullary thyroid cancer or multiple endocrine neoplasia, age below 20 years or over 60 years, male gender, rapid growth, a firm and hard texture, and the existence of suspicious cervical lymph nodes.[iv]

While several imaging modalities such as radioactive thyroid scans, computed tomography, and magnetic resonance imaging are employed for the detection of thyroid illnesses, ultrasound (US) remains the paramount diagnostic instrument for identifying thyroid nodules.[v] Moreover, ultrasound can be utilized to ascertain the dimensions and characteristics of both palpable and nonpalpable nodules, to facilitate fine-needle aspiration (FNA), and to identify lymph node metastases. [vi]

The Society of Radiologists in Ultrasound (SRU) advises against superfluous tests and surgical procedures in individuals with benign nodules.[vii] Consequently, to diagnose clinically significant thyroid cancers, the SRU advises employing FNAC exclusively for nodules that are ≥10 mm in size with microcalcifications; ≥15 mm and solid or exhibiting coarse calcifications; ≥20 mm and mixed solid and cystic; or for nodules that have markedly increased in size since the previous ultrasound.[viii]

Despite existing literature on the topic, conducting a study to evaluate the accuracy of ultrasound (US) in detecting malignancy in thyroid nodules within the Pakistani population holds crucial significance. By incorporating advanced imaging techniques, the study aims to enhance the sensitivity and specificity of ultrasound in identifying malignant thyroid nodules. The findings will contribute to the global body of literature, providing valuable data specific to the Pakistani demographic, which may exhibit unique epidemiological and clinical characteristics. Clinically, the improved diagnostic accuracy will enable healthcare providers to make more informed decisions, potentially reducing unnecessary biopsies and surgeries for benign nodules. This will not only alleviate patient anxiety and healthcare costs but also optimize resource allocation in a healthcare system facing significant burdens from thyroid disease. Ultimately, the study's outcomes will support the integration of advanced diagnostic modalities into routine clinical practice, improving the overall management and prognosis of thyroid nodules in Pakistan.

MATERIAL AND METHODS

This six-month cross-sectional validation research took place within the PAF Hospital's Department of Radiology in Islamabad during July 2024 to December 2024 following approval from the institutional ethical committee and CPSP. A sensitivity and specificity calculator enabled the determination of a 348-participant sample type using data from previous studies with 91.7%[11] sensitivity and 78.94%[11] specificity and a 13.8%[12] preexisting rate of malignant thyroid nodules at 95% confidence along with 8% absolute precision. Analysis included consecutively selected patients from 20 to 70 years old without gender restrictions who were clinically diagnosed with thyroid nodules persisting for more than 4 weeks. This study eliminated participation from patients who had cystic nodules or watery nodules or previous cancer or thyroid surgical history or radiological

imaging reports or FNAC findings and radiation exposure or people who denied consent. All participants gave voluntary consent before researchers collected patient data including demographics along with symptom duration because the vital points involved both age and gender and records on smoking habits as well as family history of cancer and thyroid disease. The single radiologist utilized Nemio XG equipment (3.5–5 MHz curvilinear and 7.5–15 MHz linear probes) to conduct thyroid ultrasounds which produced transverse/longitudinal image results stored in PACS. Thyroid nodule was classified as USG-+ve if it exhibited a solid composition, hypoechogenicity, calcification, & hypervascularity as reported by consultant radiologist. Afterward, FNAC was performed by a blinded pathologist and reports were collected.

Clinical diagnosis of thyroid nodule defined as "a solid or fluid-filled lumps that form within thyroid as seen on physical examination"

Malignant thyroid nodule on USG defined as 'a solid nodule with calcification, hypoechoic lesion and increased vascularity are seen on USG done by a consultant radiologist blinded to the study"

Malignant thyroid nodule on histopathology defined as "follicular proliferation, variable colloid component, trabecular, solid, micro and macrofollicular architecture; vascular and capsular invasion (presence of all), as reported by a consultant pathologist blinded to the study"

Data were analyzed using IBM-SPSS v26. The study authors presented mean ± SD values for age and symptom duration variables yet described gender and USG/FNAC results data through frequencies and percentages. The diagnostic metrics were computed from 2×2 contingency tables to generate sensitivity and specificity as well as PPV, NPV and accuracy. Effect modifiers like age, gender, smoking, family history and duration of complaints were controlled by stratification and post stratification diagnostic accuracy was determined.

RESULTS

The research analysis involved conducting tests on 348 patients affected by thyroid nodules. The female population composed a majority of 67.8% (n=236) participants. The study participants had a cumulative mean age of 42.53 ± 13.74 years with a range between 20 and 70 years while they had a mean disease duration of 6.14 ± 2.14 months extending from 1 to 12 months. The research revealed that 11.5% of patients reported thyroid cancer in their family history while smoking existed in 21.0% of participants. The study separated its patient population into distinct age groups as well as those with complaints of different durations. The analysis of collected data showed that 29.6% of patients had malignant nodule findings on thyroid ultrasound tests while 20.4% had malignant results from histopathology testing (figure 1). Thyroid ultrasound diagnoses malignant nodules with an overall 87.93% accuracy rate and 93.0% sensitivity along with 86.6% specificity and 64.1% PPV and 98.0% NPV. The test showed greater performance in diagnosing male patients with 94.7% sensitivity but achieved better results with females at 91.8% specificity. Patients belonging to the age group of 36–50 years experienced the maximum sensitivity rating of 96.3% alongside an accuracy level of 92.31%. The detection rate of thyroid nodules through ultrasound testing proved to be better for patients with symptoms persisting under six months (94.9%) rather than greater than six months (90.6%). The detection success among individuals with a family history calculated an NPV of 100% together with a sensitivity of 100% yet PPV measured 86.4%. The patients who smoked cigarettes recorded both higher accuracy (92.5%) and specificity (92.5%) rates compared to the non-smoking subjects (specificity 84.8% and accuracy 84.8%).

Table 1: Demographic and clinical features of the study population (n=348)

Variable		Frequency (n)	Percentage (%)
Gender	Male	112	32.2
	Female	236	67.8
Age Groups	20-35 Years	122	35.1
	36-50 Years	117	33.6

Variable		Frequency (n)	Percentage (%)
Gender	Male	112	32.2
	Female	236	67.8
	>50 Years	109	31.3
Duration of Complaints	Upto 6 Months	195	56.0
	>6 Months	153	44.0
Family History of Thyroid Cancer	Yes	40	11.5
	No	308	88.5
Family History of Any Cancer	Yes	19	5.5
	No	329	94.5
History of Smoking	Yes	73	21.0
	No	275	79.0

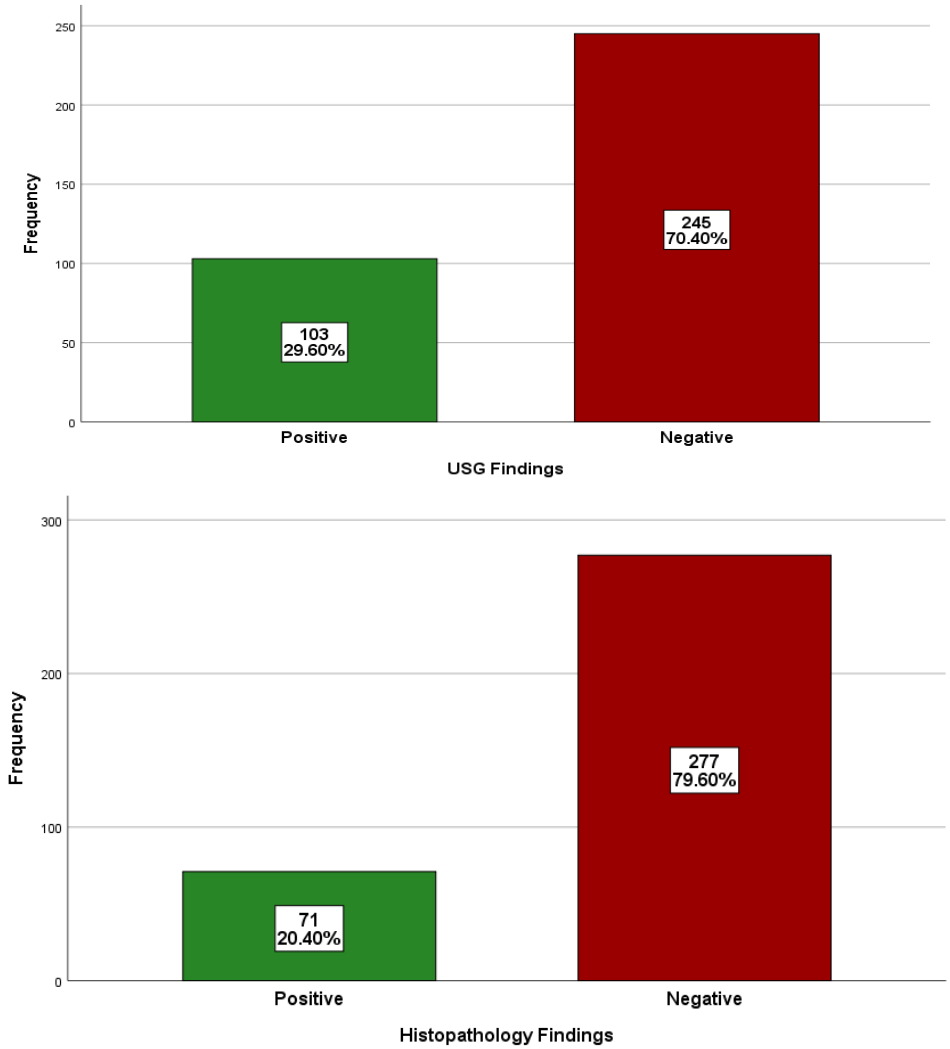

Figure 1: Findings of thyroid ultrasound and histopathology for diagnosis of malignant thyroid nodules

Table 3: Diagnostic accuracy of thyroid ultrasound for diagnosis of malignant thyroid nodules keeping histopathology findings as gold standard

Malignant Thyroid Nodules on Thyroid Ultrasound	Malignant Thyroid Nodules on Histopathology		
	POSITIVE	NEGATIVE	TOTAL
POSITIVE	66 (19.0%) (True Positives)	37 (10.6%) (False Positives)	103 (29.6%)
NEGATIVE	05 (1.4%) (False Negatives)	240 (69.0%) (True Negatives)	245 (70.4%)
Total	71 (20.4%)	277 (79.6%)	348 (100.0%)

Sensitivity	Specificity	Accuracy	PPV	NPV
93.0%	86.6%	87.93%	64.1%	98.0%

PPV: Positive Predictive Value, NPV: Negative Predictive Value

Table 4: Diagnostic accuracy of thyroid ultrasound for diagnosis of malignant thyroid nodules keeping histopathology findings as gold standard (stratification analysis for study confounders)

Study Confounders		Sensitivity (%)	Specificity (%)	Accuracy (%)	PPV (%)	NPV (%)
Gender	Male	85.7	91.8	91.07	60.0	97.8
	Female	94.7	83.8	86.44	65.1	98.0
Age Groups	20-35 Years	83.3	83.7	83.61	46.9	96.7
	36-50 Years	96.2	91.2	92.31	75.8	98.8
	>50 Years	96.3	85.4	88.07	68.4	98.6
Duration of Complaints	Upto 6 Months	94.9	86.5	88.21	63.8	98.5
	>6 Months	90.6	86.8	87.58	64.4	97.2
Family History of Thyroid Cancer	Yes	100.0	85.7	92.5	86.4	100.0
	No	90.4	86.7	87.34	58.0	97.8
Family History of Any Cancer	Yes	100.0	100.0	100.0	100.0	100.0
	No	92.5	85.9	87.23	62.6	97.8
History of Smoking	Yes	83.3	92.5	91.78	50.0	98.4
	No	93.8	84.8	86.91	65.6	97.8

PPV: Positive Predictive Value, NPV: Negative Predictive Value

DISCUSSION

The present study evaluated the diagnostic accuracy of ultrasound in detecting malignant thyroid nodules, using histopathology as the gold standard. Our findings demonstrate that ultrasound has a high sensitivity (93.0%) and specificity (86.6%), with an overall accuracy of 87.93%. These results suggest that ultrasound is a reliable initial diagnostic tool for identifying malignant thyroid nodules, particularly due to its excellent negative predictive value (NPV) of 98.0%. This implies that a negative ultrasound result strongly rules out malignancy, reducing unnecessary invasive procedures such as fine-needle aspiration biopsy (FNAB) or surgery in benign cases. However, the moderate positive predictive value (PPV) of 64.1% indicates that nearly 36% of nodules classified as malignant on ultrasound were actually benign on histopathology. This underscores the importance of confirmatory histopathological evaluation before definitive surgical intervention, as false-positive

ultrasound findings could lead to overtreatment. The high NPV, on the other hand, supports the use of ultrasound as a robust screening tool to avoid unnecessary biopsies in low-risk patients.

Our findings align with several prior studies evaluating ultrasound in thyroid nodule diagnosis:

A meta-analysis by Brito et al.[ix] reported pooled sensitivity and specificity of 93% and 98% for calcification, while, 94% and 98% for hypoechoic feature respectively, that are closely matching our overall results (93.0% and 86.6%). But our study found a cumulative sensitivity and sensitivity unlike this analysis.

Similarly, Kundi S et al.[x] found that ultrasound had a sensitivity of 90% and specificity of 91.1% in detecting malignant nodules, reinforcing its role as a first-line diagnostic tool. In a study by Alam T, et al. has shown that sensitivity and specificity of ultrasound in differentiating malignant thyroid nodule from benign thyroid nodule calculated to be 91.7% and 78.94% respectively.[xi] In another study by Al-Sharafi BA, et al. has shown that prevalence of malignant thyroid nodule was 13.8%.[xii]

Our PPV (64.1%) was slightly lower than that reported by Kundi S et al,[10] and Wahid G et al.[xiii], possibly due to differences in malignancy prevalence or ultrasound criteria used. However, our NPV (98.0%) was consistent with previous studies, confirming ultrasound's reliability in ruling out malignancy.[10,11,13] Higher sensitivity in females as showed by our findings, possibly due to hormonal influences on nodule vascularity.[xiv] Older age groups (>50 years) showed reduced specificity in our study, which is likely due to increased degenerative changes in elderly patients.[xv]

Our finding of 100% sensitivity in patients with a family history of thyroid cancer aligns with studies by Mazeh et al,[xvi] emphasizing the need for rigorous screening in high-risk populations. The lower sensitivity in smokers has also been noted by few past researches, who suggested that smoking-induced fibrosis may obscure malignant features.[xvii] While ultrasound remains the cornerstone of thyroid nodule evaluation, some studies suggest complementary roles for elastography and contrast-enhanced ultrasound. However, these techniques were not assessed in our study.[xviii]

Some studies, such as those by Jung HJ et al, reported higher PPV (93.3%), likely due to stricter sonographic criteria for malignancy. Our false-positive rate was slightly higher than few past researches, possibly due to differences in radiologist interpretation or nodule characteristics in our population.[xix,xx]

Our research demonstrates robustness through its sample of 348 patients which enables accurate sensitivity and specificity evaluation. The histopathological confirmation method surpasses diagnostic methods that depend solely on histopathology analysis because it decreases verification bias while providing greater diagnostic reliability. The study provides important clinical knowledge about individual treatment approaches through its analysis of diagnosis effectiveness within distinct age ranges and genders as well as smoking status groups. The NPV of 98.0% indicates that ultrasound has proved successful in eliminating cancerous tumors while lowering the need for invasive medical procedures.

Limitations of study:

Being a single institutional study, it prevents full applicability of these findings across different groups whose thyroid malignancy prevalence rates differ. The radiologic evaluation of thyroid ultrasound directly hinges on individual professional abilities which could lead to inconsistent test outcomes between different examiners. The sensitivity evaluation could have been falsely elevated because all patients submitted to histopathology examination might have had nodules perceived as sufficiently concerning for surgical intervention. The study contained a limitation because histopathology reporting of benign nodules based on initial exams could have been affected by sampling errors though surgical samples decreased this risk. Although the study contains these noted limitations it contributes significant practical observations regarding the performance of ultrasound in thyroid nodule evaluation.

CONCLUSION

The research demonstrates that ultrasound imaging of the thyroid represents an excellent tool for cancer detection since it provides great accuracy and negative predictive strength and avoids invasive procedures. Histological confirmation establishes a

definite diagnosis but it stands as the most important step for obtaining a certain diagnosis. Analysis of our gathered data validate current research views on ultrasound while verifying its key position for thyroid nodule assessment. Nonetheless the research suffers from selection bias and operator dependency constraints.

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