Ultrasound Evaluation of Thyroid Nodules with its Cytological Correlation- An Analytical Cross Sectional Study

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ABSTRACT

Introduction: Thyroid nodules, found in 3-7% of the global population, are mostly benign, with 4-6.5% potentially malignant. In Nepal, a hospital based study reported 16.3% malignant and 50% benign cases. Ultrasound (US) is the first-line imaging tool for assessing thyroid nodules, while fine-needle aspiration cytology (FNAC) provides a definitive diagnosis. The objective of this study was to correlate US features with cytological findings in thyroid nodule evaluation.

Methods: A prospective analytical cross-sectional study was conducted at Birat Medical College from 5th March to 28th May 2024. Data from 89 patients with thyroid nodules were collected, including baseline history, ultrasound, and FNAC results. Analysis was performed using IBM SPSS v23, with statistical significance set at $p < 0.05$.

Results: The participants had an average age of 49.45 years (±16.033)with a female predominance, though gender did not influence benign or malignant diagnoses($p = 1.000$). Statistically significant associations were found between cytological diagnosis and ultrasound features, including larger nodules (>4 cm) ($p = 0.038$), solitary nodules (40%) ($p = 0.000$), microcalcifications ($p = 0.003$), irregular margins (40%) ($p = 0.015$), and abnormal lymph nodes ($p = 0.015$). Ultrasound's sensitivity, specificity, PPV, and NPV were 60%, 96.4%, 50%, and 97.6%, respectively.

Conclusion: The study demonstrates that ultrasound features such as nodule size, composition, microcalcifications, irregular margins, and lymph node abnormalities significantly correlate with cytological findings. Ultrasound, when combined with cytology, enhances diagnostic accuracy in distinguishing between benign and malignant thyroid nodules.

Keywords: Cytology evaluation; Thyroid nodules; Ultrasonography

INTRODUCTION

Thyroid nodules affect 3-7% of the global population.[1] While over 90% of thyroid nodules are benign, a small proportion (4-6.5%) may be malignant, highlighting the importance of accurate diagnosis for proper management.[1,2] A study in Nepal by Chaudhary AK et al. (2022) found 16.3% of thyroid nodules to be malignant.[3] Ultrasound (US) is the preferred first-line imaging tool due to its non-invasive nature, cost-effectiveness and high sensitivity in detecting nodular characteristics like size, composition, echogenicity, margins as well as benign and malignant lesion.[4] Cytological evaluation, performed via fine-needle aspiration cytology (FNAC), is a key tool for further evaluation to confirm malignancy, though invasive procedures aren't always necessary.[5] Aligning ultrasound characteristics with cytological results can improve diagnostic accuracy, minimize unnecessary interventions, and refine management approaches. This study aimed to establish a correlation between ultrasound findings and cytological results in thyroid nodule evaluation.

METHODS

A hospital based prospective analytical cross sectional study was conducted in the department of radiodiagnosis and Imaging of Birat Medical College Teaching Hospital (BMCTH)from 5th March to 28th May 2024. Ethical approval was obtained from the institutional review committee (IRC-PA-373/2024)prior to conducting the research. Voluntary informed written consent was obtained before collecting data from the patients.

Patients presented to the department of radiodiagnosis and imaging for ultrasonographic evaluation of thyroid glands and detected to have thyroid nodules were included in the study and those with prior history of thyroidectomy and undetected thyroid nodules by ultrasound were excluded from the study. We enrolled 89 patients during our study period by total enumeration sampling technique. At first data was collected on the patient's age and sex. After obtaining informed written consent the Ultrasonography(USG) of the thyroid glands was performed using the Voluson S10 Expert 3D model and linear 5-12 megahertz of frequency probe. Each patient was placed in supine position with neck hyperextended for better visualization of thyroid gland. In USG the composition, echogenicity, shape, margins, sizes, calcifications and internal vascularity of the thyroid nodules were observed and recorded. Then Fine Needle Aspiration Cytology(FNAC) was performed for further evaluation under aseptic procedure using a 22 gauge needle by in-plane technique. The sample smear of thyroid nodules was obtained and sent for histopathology examination. The histopathologic findings of thyroid nodules were categorized and documented as benign and malignant. All the data was entered in Microsoft excel sheet and transferred to IBM SPSS version 23. The mean age was calculated. The USG findings of thyroid nodules were compared with the histopathology findings. Chi square test of goodness of fit(likelihood ratio) and Fishers' exact test was calculated to find the association of the USG findings with histopathology findings. P value less than 0.05 was considered statistically significant.

RESULTS

A total of 89 patients were enrolled for the study during our study period. The average age of the participants was 49.45 years, with a standard deviation of 16.033, and the ages ranged from 15 to 81 years. Female predominance was higher than male comprising 80 and 9 patients respectively out of 89. All 9 males (100%) had benign diagnoses, while 75 females (93.8%) had benign and 5 females (6.2%) had malignant diagnoses, however there was no statistically significant relationship between gender and the likelihood of a benign or malignant diagnosis (p = 1.000), Table 1.

There were statistically significant associations between US features (size, composition, calcifications, margins, abnormal lymph nodes) and the diagnosis of benign or malignant nodules via cytology findings. Larger nodules (>4 cm) were more likely to be malignant which was 9(25%) compared to smaller nodules (<2 cm), 1(3.1%) (p = 0.038). Solid nodules 4(40%) have a higher malignancy rate than cystic or mixed nodules(p= 0.000). Microcalcifications were significantly associated with malignancy 4 (28.6%) compared to no or macro-calcifications (p = 0.003). Irregular margins 4 (40%) were strongly linked to malignancy (p = 0.000). Abnormal lymph nodes were associated with a 50% malignancy rate (p = 0.015). In US-identified malignant features three out of six patients were confirmed malignant cases by cytology findings (p = 0.002).

Among 89 patients, there were 3 true positive (TP) cases where both ultrasonography and histopathology detected malignancy and 81 true negative (TN) cases where both ultrasonography and histopathology detect benign findings. Out of the 6 patients where ultrasonography detected malignancy, 3 patients had false positive(FP) findings in ultrasonography where histopathology detected benign. Two patients had false negative (FN) results where ultrasonography detected benign, but histopathology detected malignancy. The ultrasonography showed high specificity (true negative) of 96.4% and NPV of 97.6%, indicating it accurately identifies benign cases. However, its sensitivity (true positive) was 60% and PPV was 50% which is lower, indicating it may miss some malignancies and produce a moderate rate of false positives. This suggests ultrasonography is more reliable for confirming benign conditions and can be used in conjunction with cytology and histopathology examination for diagnosing malignancies (table 3).

Table 1: Prevalence of adverse impact among the participants

Variables		USG guided FNAC	Total	P value
		Benign n(%)	Malignant n(%)	
Gender	Male	9(100)	0(0)	1.000*
	Female	75(93.8)	5(6.2)	

*Fisher's exact test was applied.

Table 2: Ultrasound Evaluation of Thyroid Nodules with its Cytological Correlation(n=89)

	USG	USG Guided FNAC			P Value
		Benign n(%)	Malignant	Total	
Nodule Size in cm	<2	31(96.9)	1(3.1)	32(100)	0.038
	2-4	44(97.8)	1(2.2)	45(100)	
	>4	9(75)	3(25)	12(100)	0.000
Composition	Cystic	31(100)	0(0)	31(100)	
	Solid	6(60)	4(40)	10(100)	
	Mixed	47(97.9)	1(2.1)	48(100)	
Echogenicity	Anechoic	6(100)	0(0)	6(100)	0.782
	Hyperechoic	13(92.9)	1(7.1)	14(100)	
	Hypoechoic	56(94.9)	3(5.1)	59(100)	
	Isoechoic	9(90)	1(10)	10(100)	
Calcification	Macrocalcification	7(100)	0(0)	7(100)	0.003
	Microcalcification	10(71.4)	4(28.6)	14(100)	
	No calcification	67(98.5)	1(1.5)	68(100)	
Shape	Taller than width	5(83.3)	1(16.7)	6(100)	0.301
	Wider than tall	79(95.2)	4(4.8)	83(100)	
Vascularity	Increased	16(84.2)	3(15.8)	19(100)	0.072
	No vascularity	9(90)	1(10)	10(100)	
	Normal	59(98.3)	1(1.7)	60(100)	
Margin	Extra-thyroidal extension	3(100)	0(0)	3(100)	0.000
	Irregular	4(50)	4(50)	8(100)	
	Smooth	77(98.7)	1(1.3)	78(100)	
Abnormal Lymph nodes	No	82(96.5)	3(3.5)	85(100)	0.015
	Yes	2(50)	2(50)	4(100)	
Nature	Benign	81(97.6)	2(2.4)	83(100)	0.002
	Malignant	3(50)			

*Note:P value <0.05 was considered statistically significant. *Chi Square test of Goodness of fit and ** Fishers' exact test was employed.*

Table 3: Accuracy of thyroid sonography in predicting thyroid malignancy (n=89)

USG Findings	**FNAC Findings**		**Senstivity n (%)**	**Specificity n (%)**
	Malignant	Benign	0.6 (60)	0.6 (60)
Malignant	3 (50)	3 (50)		
Benign	2 (2.4) FN	81(97.6)TN		

DISCUSSION

The objective of this study was to evaluate the diagnostic accuracy of ultrasound (USG) in the characterization of thyroid nodules, correlating the findings with cytology results obtained via fine needle aspiration cytology (FNAC). The analysis demonstrated significant associations between various USG features—such as nodule size, composition, calcifications, margins, and abnormal lymph nodes—and the final cytological diagnosis (benign or malignant). Our findings align with prior studies in the field. A study by J F Katz et al mentioned that ultrasonography patterns of thyroid disease were correlated with histopathologic findings.[6] Ultrasonography features, suggesting solid composition, taller-than-wide shape, spiculated margin, ill-defined margin, hypoechogenicity and microcalcifications were predictors for malignant nodules.[7] Among 89 (100%) patients with thyroid nodules, half of the patients 45(50.56%) had a nodular size of 2-4 cm and 12 patients had a nodular size greater than 4 cm in the USG of our study. Our results indicated that larger nodules (>4 cm) were more likely to be malignant (25%) compared to smaller nodules (<2 cm), which had only a 3.1% malignancy rate. This is consistent with studies by Choi and the team (2015), Chaoyang Meng et al(2021), which found that increasing nodule size correlates with a higher risk of malignancy.[7,8] Min Ji Hong et al (2018) also reported a similar trend, underscoring that nodules ≥ 3 cm warrant closer clinical attention due to their higher malignancy potential.[9] Contrary to our study, Uchechukwu C. Megwalu(2017) stated that Nodule size was not associated with risk of malignancy (odds ratio 1.02) after adjusting for nodule consistency, age, and sex.[10] Boonrod et al(2021)echoed a similar finding which reported that taller-than-wide shape was not a predictor of thyroid nodule malignancy.[11]

We found 31(34.8%) patients with cystic nodules, 10(11.23%) with solid nodules and mixed solid cystic nodules in 48(53.9%) patients in ultrasonography findings. Solid nodules in our study showed a significantly higher malignancy rate (40%) compared to cystic or mixed nodules (p = 0.000). This finding echoes the results of Frates et al. (2006), Islam Alatiar(2017) who identified solid composition as a significant predictor of malignancy.[12] Similarly, the study by Dong Gyu Na etal(2016) found that frequency of solid nodules was greater 730(73%), compared to minimally 6.1% and partially cystic nodules 209(20.9%),and solid nodules were more frequently associated with increased risk of malignancy thyroid cancer (P=0.013). [13]

The USG findings showed two third 59(66.3%) patients with hypoechoic, 14(15.7%) patients with hyperechoic, 10 patients with isoechoic and 6 patients with anechoic in our study. Contrary to our study, The frequency of mixed echo- texture was higher 100 (93.5%), compared to hyperechoic 3(2.8%), hypoechoic 2 (1.9%), and anechoic 2 (1.9%).[14] However the echogenicity patterns had no significant association with thyroid nodules malignancy in our study.This finding is contrast from the study done by Mondal, et al where hypoechoic nodules 13(86.7%) had the most common malignancy features.[15] Among 89 patients with thyroid nodules, 68(76.4%) patients had no calcification, 14(15.7%) patients had microcalcification and seven(7.86%) patients had macrocalcification in USG findings. Similarly, the majority 101(94.4%) had no calcification in the thyroid nodules.[14] We observed that microcalcifications were strongly associated with malignancy (28.6%) compared to no or microcalcifications (p = 0.003) in our study. Microcalcifications was a strong predictor for malignancy in other literatures.[6,7,15,14,16] Microcalcifications reflect psammoma bodies, which are commonly associated with papillary thyroid carcinoma, as highlighted by other studies.[17,18] More than two third 60(67.4%) patients had normal vascularity and 10(11.2%) had no vascularity on ultrasonographic evaluation in our study. However, there was no significant difference between vascular flow rate and occurrence of thyroid malignancy. This finding is similar to the study done by Helmi Khadra et al(2016).[19]

The majority 78(87.6%) patients had a smooth/regular margin of thyroid nodules in our study which is similar to another study that represent regular margin 98(91.6%) the most common.[14] Irregular margins were significantly linked to malignancy (40%) in our study (p = 0.000), which aligns with findings from studies, who emphasized the diagnostic importance of irregular or lobulated margins in differentiating malignant from benign thyroid nodules. This feature has been consistently highlighted across multiple studies as a key sonographic indicator of thyroid malignancy.[7,16]

Four out of 89 patients had abnormal lymph nodes seen in ultrasonographic features. Abnormal lymph nodes were associated with a 50% malignancy rate in our study (p = 0.015), supporting the notion that lymph node involvement is a critical factor in diagnosing thyroid cancer. Study by Jiachen Du et al (2023) similarly found that the presence of abnormal lymph nodes as a significant risk factor for malignancy, particularly in papillary thyroid carcinoma.[20] Among 89 patients in our study, the sensitivity,specificity, NPV and PPV of USG for malignancy as compared to FNAC was 60%, 96.4%, 97.6% and 50% respectively. Conversely a study reported higher sensitivity and PPV 80% and 63.2% respectively with the

relatively similar specificity: 86% and NPV 93.4%.[15] A study done in Nigeria found sensitivity, specificity, PPV and NPV of 100% each in diagnosing benign and malignant thyroid nodules by USG as compared to FNAC.[14] Malik et al. reported a sensitivity of 70.59%, specificity of 96.39%, positive predictive value of 80%, negative predictive value of 94.12%, and accuracy of 92% when comparing sonographic findings with FNAC for diagnosing thyroid nodules.[21] Similarly, Popli et al. found sensitivity, specificity, and positive/negative predictive values of 81.8%, 87.2%, 59.0%, and 95.5%, respectively. [22] The differences in sensitivity, specificity, PPV, and NPV of ultrasound in diagnosing thyroid nodules across studies can be attributed to factors such as variations in population characteristics, operator experience, ultrasound criteria, and study design. While ultrasound remains a critical tool for initial evaluation, standardizing criteria and combining sonographic evaluation with FNAC is essential to improve diagnostic accuracy across different clinical settings. The average age of the participants was 49.45 years, with a standard deviation of 16.033, and the ages ranged from 15 to 81 years. Out of 89 patients, 80 were females and 9 were males, showing the female predominance for thyroid disease in our study. Our finding is supported by other studies where females were higher than males. [14,15] Our study has some limitations too. The small sample size of malignancies that we encountered in our study is an important limitation. In patients with multiple nodules, only the dominant nodule was evaluated and other nodules were not evaluated. We recommend further large-scale, multicenter studies may provide additional validation for these findings.Emphasizing histopathological confirmation, rather than relying solely on cytology, would improve diagnostic accuracy. In patients with multiple nodules, all significant nodules should be evaluated to prevent missing malignancies in non-dominant ones. Ultrasound protocols should focus on features like large nodules, microcalcifications, irregular margins, and abnormal lymph nodes for further FNAC or histological follow-up. Additionally, incorporating advanced techniques, such as elastography, could enhance the sensitivity of ultrasound in detecting malignant characteristics.

CONCLUSION

This study reinforces the role of USG as a highly valuable tool for evaluating thyroid nodules and predicting malignancy, with strong correlations to cytological findings. By identifying key USG features, such as nodule size, composition, calcifications, margins, and lymph node involvement, clinicians can better stratify patients for appropriate diagnostic follow-up.

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