International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Sonographic, Cytological and Histopathological Characteristics of Spectrum of Thyroid Nodules: A Comparative Analysis

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Abstract: ***Background: Accurate characterization of thyroid nodules is crucial for appropriate management and treatment decisions. Ultrasound (USG), cytology and histopathology are widely used diagnostic modalities, but their combined utility in identifying benign and malignant thyroid nodules needs further investigation. Methods: This prospective observational study included patients with thyroid nodules detected on ultrasound, a cytological diagnosis on FNAC and histopathology. Sonographic features assessed included nodule composition, echogenicity, shape, margin characteristics, echogenic foci. Cytological specimens were classified according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC). Results: Ill-defined margins (33.3%) and solid composition (100%) were observed exclusively in malignant nodules. Hypoechoic echogenicity (50%) and "taller than wide" shape (33.3%) were more common in malignant nodules, while benign nodules exhibited anechoic (42.9%), hyperechoic (28.6%), and "wider than tall" (100%) appearances. Echogenic foci were present only in malignant cases. A significant proportion of benign nodules (42.9%) were classified as low-risk TIRADS 1, while most malignant nodules (83.3%) were higher-risk TIRADS 4. Conclusions: Certain sonographic features, including ill-defined margins, solid composition, hypoechogenicity, "taller than wide" shape, and echogenic foci, were associated with malignancy. However, some overlap with benign nodules was observed, highlighting the importance of integrating cytological and histopathological evaluation for accurate diagnosis and risk stratification.***

Keywords: Thyroid nodules, ultrasonography, fine-needle aspiration cytology, Bethesda system, Histopathology, Neoplasms, Thyroid Neoplasms.

1. Introduction

Thyroid nodules are a common clinical finding, with an estimated prevalence ranging from 3-7% in the general population based on palpation and up to 67% when detected by high-resolution ultrasound imaging.[1,2] While the majority of thyroid nodules are benign, the primary concern lies in distinguishing those with malignant potential, as thyroid cancer accounts for approximately 3.1% of all new cancer cases worldwide.[3] Accurate characterization and risk stratification of thyroid nodules are crucial for appropriate management and treatment decisions.

Ultrasound (USG) is the primary imaging modality for evaluating thyroid nodules, providing valuable information about their size, composition, echogenicity, shape, margin characteristics, vascular patterns, echogenic foci of which size and vascularity pattern are necessary for doing FNAC and biopsy.[4]

The Thyroid Imaging Reporting and Data System (TIRADS) is a standardized risk stratification system that utilizes sonographic features to categorize thyroid nodules and estimate their risk of malignancy. In this study, specific sonographic patterns observed in benign thyroid nodules could be correlated with TIRADS categories for a more comprehensive risk assessment. Incorporating TIRADS into the evaluation of thyroid nodules may enhance diagnostic accuracy and guide appropriate management decisions. However, the diagnostic accuracy of USG alone in differentiating benign from malignant nodules remains suboptimal, necessitating further evaluation through fine-needle aspiration cytology (FNAC) and histopathology.[7]

FNAC is a minimally invasive and cost-effective technique that plays a pivotal role in the evaluation of thyroid nodules. By obtaining and analysing cellular samples, FNAC can provide cytological information essential for distinguishing benign from malignant or suspicious nodules.[8] The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) has standardized the reporting and management recommendations for thyroid FNAC specimens, facilitating consistent communication and decision-making.[9]

However, histopathology is the Gold Standard for making tissue diagnosis and therefore for further management and patient care. In case of malignancy diagnosed in histopathology, Pathology Tumor-Node-Metastasis(pTNM) Staging can be done to know the size and extent of spread therefore guides in the use of adjuvant therapy. Histopathology can provide the prognosis and survival rate.

This study aims to conduct a comparative analysis of the sonographic , cytological anf histopathological features of spectrum of thyroid nodules, with the goal of identifying distinct patterns or associations that can aid in their accurate identification and differentiation from benign or malignant nodules. By integrating the complementary information

provided by USG , FNAC and histopathology, this research seeks to contribute to the development of a more robust diagnostic framework for the evaluation and management of thyroid nodules.

2. Materials and Methods

This prospective observational study was conducted at Dr. D.Y. Patil Hospital, Navi Mumbai. The study protocol was approved by the Institutional Review Board, and written informed consent was obtained from all participants.

Inclusion criteria were:

- Patients aged 18 years or older
- Presence of one or more thyroid nodules detected on ultrasound
- Cytological diagnosis on fine-needle aspiration cytology (FNAC) according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC)
- Histopathology

Patients with inadequate FNAC samples, or contraindications for FNAC were excluded from the study.

All patients underwent high-resolution thyroid ultrasound examination using a GE LOGIQ P9 R3 Ultrasound Machine with 9L liner probe. The ultrasound examinations were performed by experienced radiologists. According to TIRADS, the following sonographic features were assessed for each thyroid nodule:

1) Composition
2) Echogenicity
3) Shape
4) Margin characteristics
5) Echogenic foci

FNAC was performed under ultrasound guidance by experienced cytopathologists. Aspirated samples were smeared onto glass slides, fixed, and stained using the Papanicolaou and May-Grunwald-Giemsa techniques. The cytological specimens were examined and classified according to the TBSRTC into one of the following categories:

1) Non-diagnostic
2) Benign
3) Atypia of undetermined significance (AUS).
4) Follicular neoplasm
5) Suspicious for malignancy
6) Malignant

The sonographic and cytological findings for each thyroid nodule were recorded and analysed. However, further histopathological evaluation was done in cases suspicious for malignancy on FNAC. Descriptive statistics were used to summarize the frequency and distribution of the various sonographic, cytological and histopathological characteristics. Correlations between specific sonographic features, cytological and histological patterns were explored using appropriate statistical tests.

3. Results

The study included 13 patients with thyroid nodules, as determined by fine-needle aspiration cytology (FNAC) according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and further with histopathology. The mean age was 46.4 ± 12.2 years, and the majority (76.9%) were females.

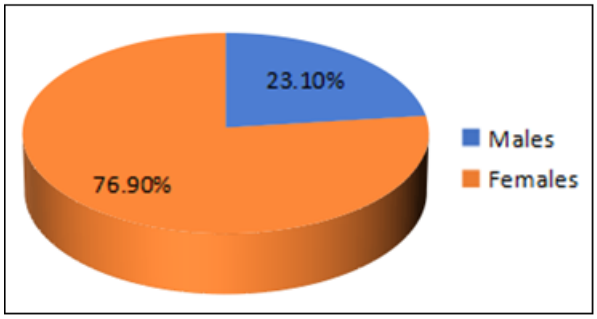

Figure 1: Pie chart showing gender distribution of thyroid nodules

The sonographic features exhibited some notable differences between benign and malignant thyroid nodules in this study. Regarding the margins, ill-defined margins were observed only in malignant nodules (33.3%), while all benign nodules had smooth margins. The composition of the nodules also varied, with solid composition seen in all malignant nodules (100%), whereas benign nodules showed a mix of solid, cystic, and mixed compositions.

Echogenicity patterns revealed that hypoechoic echogenicity was more common in malignant nodules (50%), while benign nodules had a higher prevalence of anechoic and hyperechoic appearances. Interestingly, the "taller than wide" shape was exclusively seen in malignant nodules (33.3%), whereas all benign nodules were "wider than tall." Additionally, echogenic foci, such as macrocalcifications and punctate echogenic foci, were present only in malignant cases.

When considering the TIRADS (Thyroid Imaging Reporting and Data System) classification, a significant proportion of benign nodules (42.9%) fell into the low-risk TIRADS 1 category. In contrast, the majority of malignant nodules (83.3%) were classified as higher-risk TIRADS 4 categories.

Nodules reported as TIRADS 4 and 5 on USG and Bethesda V (suspicious for malignancy) on FNAC underwent post-surgical biopsy and confirmed as malignant (100%). Nodules reported as TIRADS 1, 2 and 4 on USG and Bethesda II (benign) on FNAC avoided further surgery/ biopsy (100%).

Table 1: Comparison of Sonographic features of benign and malignant thyroid disease (n=13)

Sonographic features		Benign N=7	Malignant N=6
Composition	Cystic or almost completely cystic (0 Point)	1 (14.3%)	0
	Spongiform (0 Point)	0	0
	Mixed cyctic and solid (1 point)	4 (57.1%)	0
	Solid or almost completely solid (2 points)	2 (28.6%)	6 (100%)
Echogenicity	Anechoic (0 Points)	0	2 (333.3%)
	Isoechoic (1 point)	3 (42.9%)	0
	Hyperechoic (1 point)	2 (28.6%)	3 (50%)
	Hypoechoic (2 points)	2 (28.6%)	1 (16.7%)
	Very hypoechoic (3 points)	0	0
Shape	Wider than tall (0 points)	7 (100%)	4 (66.7%)
	Taller than wide (3 points)	0	2 (33.3%)
Margins	Smooth (0 points)	7 (100%)	4 (66.7%)
	Ill-defined (0 points)	0	2 (33.3%)
	Lobulated or irregular(2 points)	0	0
	Extra thyroidal extension(3)	0	0
Echogenic foci	None or large comet-tail artifacts (0 point)	7 (100%)	4 (66.7%)
	Macrocalcification (1 point)	0	1 (16.7%)
	Peripheral (rim) calcification (2 points)	0	0
	Punctate echogenic foci (3 points)	0	1 (16.7%)
TIRADS	1 (Benign)	3 (42.9%)	0
	2 (Not suspicious)	2 (28.6%)	0
	3 (Mildly suspicious)	0	0
	4 (Moderately suspicious)	2 (28.6%)	5 (83.3%)
	5 (Highly suspicious)	0	1 (16.7%)

Table 2: Comparison of TIRADS with FNAC findings

	TBSRTC	TIRADS				
		1 (Benign)	2 (Not suspicious)	3(Mildly suspicious)	4 (Moderately suspicious)	5 (Highly suspicious)
Colloid goitre	Bethesda II	3 (100%)	2 (100%)	0	0	0
Lymphocytic thyroiditis	Bethesda II	0	0	0	2 (28.6%)	0
Anaplastic thyroid carcinoma	Bethesda V	0	0	0	1 (14.3%)	1 (100%)
Follicular thyroid carcinoma	Bethesda V	0	0	0	1 (14.3%)	0
Papillary thyroid carcinoma	Bethesda V	0	0	0	3 (42.9%)	0

Image 1: Ultrasonography of patients with colloid goitre

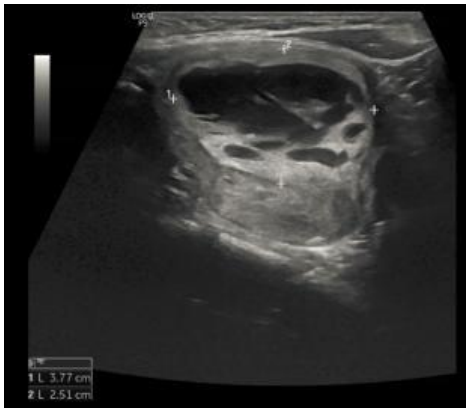

Figure 1: A smooth marginated mixed solid cystic, wider than tall nodule

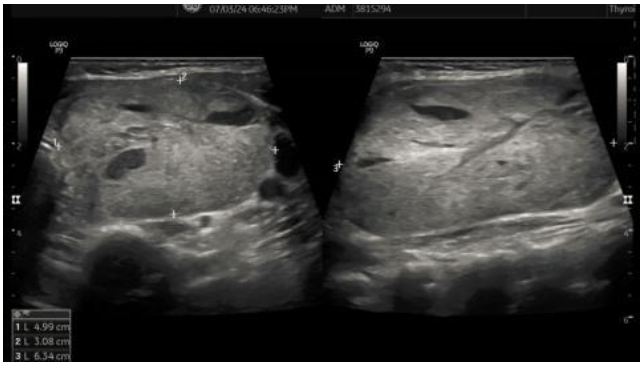

Figure 2: A smooth marginated mixed solid cystic (predominantly solid), hyperechoic, wider than tall nodule.

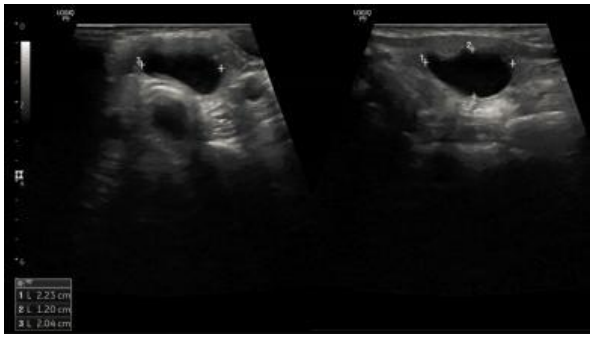

Figure 3: A smooth marginated, cystic, anechoic wider than tall nodule

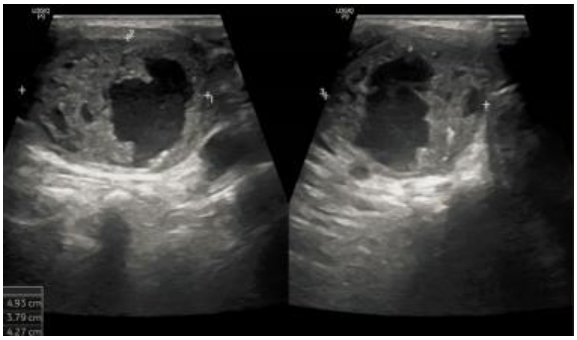

Figure 4: A smooth marginated mixed solid cystic (predominantly cystic), anechoic, wider than tall nodule

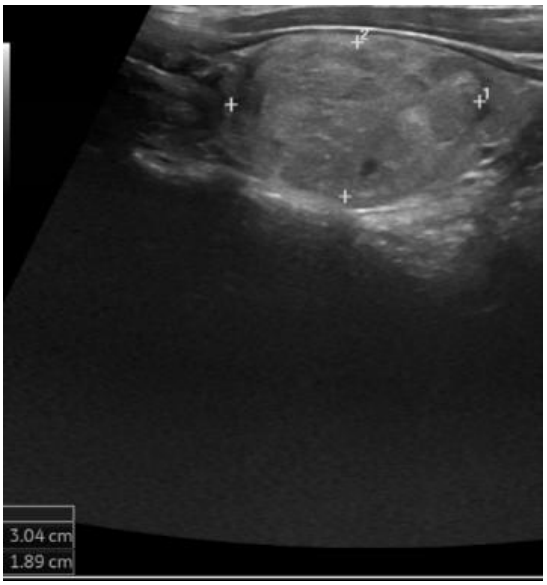

Figure 5: A smooth marginated solid, hyperechoic, wider than tall nodule

Image 2: Ultrasonography of patient with Lymphocytic thyroiditis

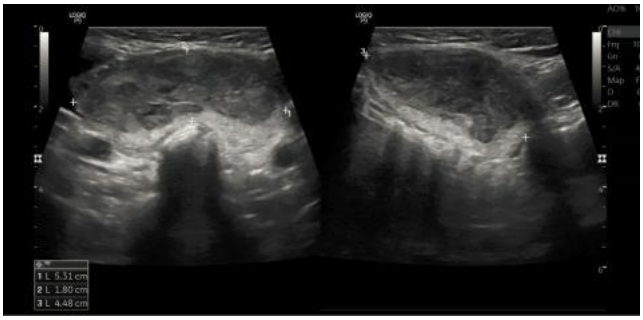

Figure 6: A smooth marginated, solid, hypoechoic, wide than tall nodule.

Figure 7: A smooth marginated, almost completely solid, hypoechoic, wider than tall nodule.

Image 3: Ultrasonography of patient with Papillary thyroid carcinoma

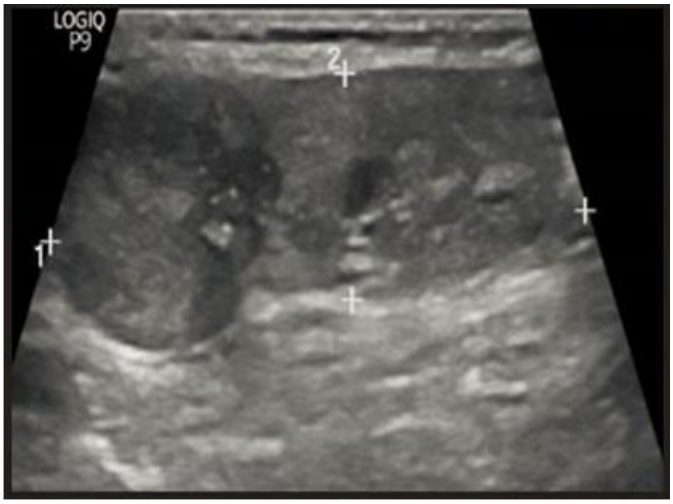

Figure 8: A smooth marginated, solid, isoechoic, wider than tall thyroid nodule with punctate echogenic foci

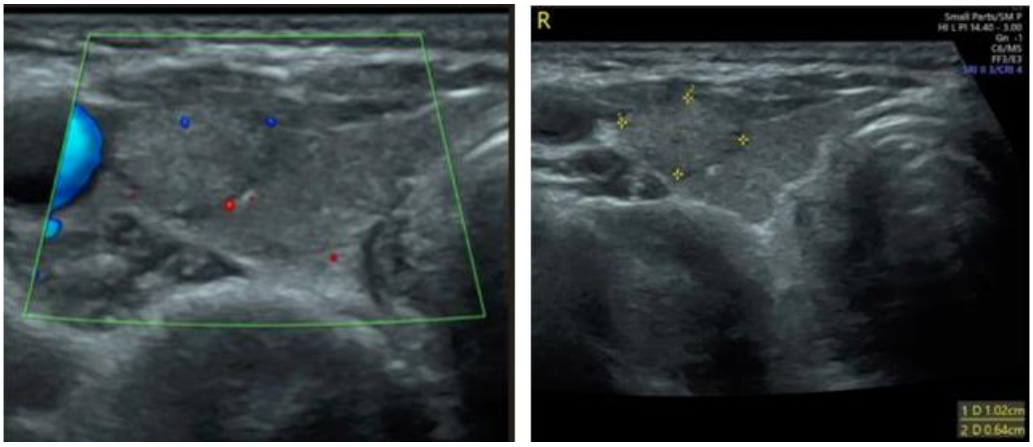

Figure 9: An ill-defined, solid, isoechoic, wider than tall thyroid nodule.

Figure 10: Thyroid nodule with macrocalcification

Figure 11: A smooth marginated, solid, hyperechoic, taller than wide thyroid nodule.

Figure 12: A smooth marginated, solid, hypoechoic, taller than wide thyroid nodule

Image 4: Ultrasonography of patient with Follicular thyroid carcinoma

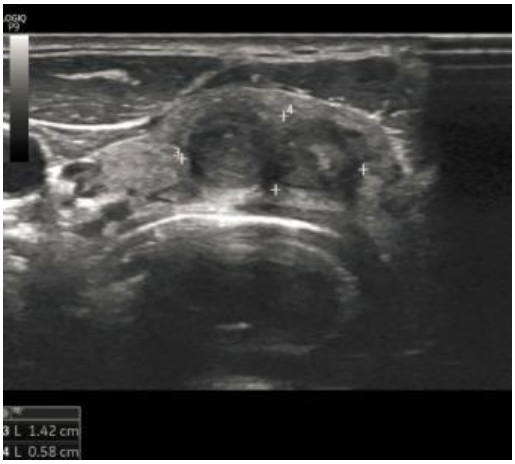

Figure 3: A smooth marginated, solid, hypoechoic, wider than tall thyroid nodule.

Figure 3: Ultrasonography of patient with Anaplastic thyroid carcinoma

Figure 4: An ill-defined, solid, hypoechoic, wider than tall thyroid nodule

4. Discussion

The present study evaluated the sonographic features of benign and malignant thyroid nodules and correlated them with cytological findings according to the Bethesda System for Reporting Thyroid Cytopathology (TBSRTC) and histopathology. The results revealed some notable differences in the sonographic appearances of benign and malignant nodules, consistent with previous literature.

Regarding margins, ill-defined margins were observed exclusively in malignant nodules (33.3%), aligning with the findings of Russ et al., who reported that irregular margins were associated with an increased risk of malignancy.[10] Similarly, Remonti et al.'s meta-analysis identified irregular margins as a significant predictor of thyroid cancer.[11]

The solid composition observed in all malignant nodules (100%) in our study is consistent with the findings of Harshvardhan et al., who reported a higher frequency of solid composition in malignant thyroid nodules.[1] However, it is important to note that some benign nodules in our study also exhibited a solid appearance, highlighting the need for cytological correlation.

Echogenicity patterns revealed that hypoechoic echogenicity was more common in malignant nodules (50%), which is in line with previous studies. Park et al. found that hypoechoic echogenicity was associated with a higher risk of malignancy, particularly in the presence of underlying heterogeneous thyroid parenchyma.[12]

The "taller than wide" shape, observed exclusively in malignant nodules (33.3%) in our study, has been reported as a concerning feature for malignancy in previous literature. Chung et al. found that this shape was more common in papillary thyroid carcinoma, particularly in patients with Graves' disease.[13]

The presence of echogenic foci, such as macrocalcifications and punctate echogenic foci, observed only in malignant cases in our study, is consistent with the findings of Kim et al., who reported a significant association between calcification patterns and histopathological diagnoses of thyroid nodules.[14]

Regarding the TIRADS classification, a significant proportion of benign nodules (42.9%) fell into the low-risk TIRADS 1 category, while the majority of malignant nodules (83.3%) were classified as higher-risk TIRADS 4 category. These findings align with the purpose of TIRADS, which is to stratify thyroid nodules based on their sonographic features and estimate their risk of malignancy.

It is noteworthy that some overlap in sonographic features between benign and malignant nodules was observed in our study, emphasizing the importance of integrating cytological evaluation. This observation is consistent with the findings of Brito et al., who conducted a systematic review and meta-analysis, concluding that the diagnostic accuracy of thyroid nodule ultrasound alone for predicting malignancy is suboptimal, necessitating cytological or histological confirmation.[7]

While our study provides valuable insights into the sonographic, cytological and histological characteristics of thyroid nodules, it is important to acknowledge its limitations. The relatively small sample size may limit the generalizability of the findings, and future studies with larger sample sizes are warranted.

5. Conclusion

In conclusion, the present study highlights the importance of combining sonographic, cytological and histopathological assessments for the accurate evaluation of thyroid nodules. While certain sonographic features, such as ill-defined margins, solid composition, hypoechogenicity, "taller than wide" shape, and the presence of echogenic foci, were more associated with malignancy, some overlap with benign nodules was observed. The integration of TIRADS classification, cytological findings from FNAC and histopathology can provide a more comprehensive risk stratification and guide appropriate management decisions for thyroid nodules.

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