

ORIGINAL RESEARCH

Correlation of Ultrasonography and Colour Doppler Findings with Cytopathological Findings in Evaluation of Thyroid Nodules

¹Dr. H M Chakit Kumar, ²Dr. Priyanka, ³Dr. Santosh P Patil, ⁴Dr. Sania Sabahi

¹Senior Resident, All India Institute of Medical Sciences(AIIMS), Bilaspur, Himachal Pradesh, India.

²Senior Resident, Department of Radiology, ESIC Medical College and Hospital, Kalaburagi, Karnataka, India

³Clinical Assistant, Department of Radio Diagnosis, P D Hinduja National Hospital & Medical Research Centre, Mahim, Mumbai, India

⁴Senior Resident, Department of Radiology, Srinivas Institute of Medical Sciences and Research Centre, Mukka, Surathkal, Mangaluru, Karnataka, India

Corresponding author

Dr. Sania Sabahi

Senior Resident, Department of Radiology, Srinivas Institute of Medical Sciences and Research Centre, Mukka, Surathkal, Mangaluru, Karnataka, India

Email: Sania.sabahi@gmail.com

Received date: 12 October, 2022 Revised date: 10 December, 2022 Acceptance date: 10 January, 2023

ABSTRACT

Background: Nodular diseases of thyroid are characterized by the disordered growth of thyroid cells. Malignancies have been found in 9% - 15% of the nodules that were evaluated with FNA. US features can provide information about the malignant potential of thyroid nodules. FNA plays a crucial role in the evaluation of the thyroid nodule, with high diagnostic accuracy of 85%-94%. The objective of this study was to assess the utility of gray scale and color Doppler US findings in characterization of benign and malignant thyroid nodules in correlation with the pathological diagnosis. **Methods:** From November 2019 to April 2021, a total of 50 patients with solitary thyroid nodule underwent thyroid US. The US characteristics of each nodule were determined and was assessed using grey scale and colour Doppler. χ^2 tests were performed. Sensitivity, specificity, positive and negative predictive values were obtained. The results were then compared to the fine needle aspiration (FNA). **Results:** Statistically significant ($P < .05$) findings of malignancy were: taller than-wide shape (sensitivity, 73.1% ; specificity, 95.5%), lobulated/poorly defined margins (sensitivity, 69.2% ; specificity, 95.5%), hypoechogenicity and marked hypoechogenicity, (sensitivity, 72.5% ; specificity, 95.5%), thick incomplete /absent halo (sensitivity, 88.5% ; specificity, 78.1%), central/ central & peripheral pattern of vascularity (sensitivity, 73.1% ; specificity, 81.8%) and associated cervical lymphadenopathy. Similarly statistically significant US findings for benign nodules were presence of wider than tall shape, well defined margins, hyperechogenicity, and presence of thin halo. Using a 5 category US classification system, the specificity and positive predictive value were high for malignant, possibly malignant, probably benign and benign US categories in the range of 93.18% to 100% and 78.57% to 100% respectively. Using multiple logistic regression, the overall diagnostic accuracy of thyroid US for differentiating a malignant lesion from a benign one in the present study was found to be 84.3%. **Interpretation And Conclusion:** Taller-than-wide shape, Lobulated/poorly defined margins, Hypoechogenicity and Marked hypoechogenicity, Microcalcifications and Central/ central & peripheral pattern of vascularity are helpful criteria for the discrimination of malignant from benign nodules. Thyroid US achieved a good overall diagnostic accuracy in the categorization of benign and malignant thyroid nodules.

Key Words: Thyroid, Nodules, Malignant, FNA.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution- Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

The thyroid gland is a large endocrine gland that can be easily examined due to its superficial location, allowing for effective evaluation of its anatomy and pathological conditions using high-resolution ultrasound. Thyroid nodules, increasingly detected in the general population, are common and found in up

to 50% of adults, with higher prevalence in females. While ultrasonography is widely used to assess these nodules, its ability to distinguish between benign and malignant nodules is sometimes questioned due to overlapping characteristics. However, combining ultrasound findings improves diagnostic accuracy. Features like hypoechogenicity, irregular margins, and

microcalcifications are strongly linked to malignancy. A high TIRADS score, along with clinical signs like hard consistency and significant lymph node involvement, further aids in predicting malignancy in nodules larger than 1 cm. Fine-needle aspiration cytology (FNAC) remains a sensitive and accurate test in diagnosing these cases

OBJECTIVES

1. To Evaluate the Grayscale Features and Color Doppler Findings Of Thyroid Nodules With High Frequency Tissue Harmonic Imaging.
2. To Determine Sensitivity and Specificity in Concluding Benign and Malignant Lesions on High Resolution Ultrasonography and Color Doppler Findings.
3. To Compare Grayscale and Color Doppler Findings with Fine Needle Aspiration Cytology Findings as Gold Standard.

Methodology

Study Design: This prospective study was conducted over 18 months at the Khaja Bandanawaz Institute of Medical Sciences, Kalaburagi. It included all patients with visible or clinically palpable thyroid swelling referred to the Department of Radiology. Patients with non-thyroid neck swelling, ectopic thyroid, or physiological goiter were excluded. A convenient sampling technique was used, with a sample size of 50 determined by a formula based on prevalence and precision.

Study Method

A structured proforma documented patient details, clinical history, and physical exams for eligible individuals. Thyroid ultrasound, using grayscale and color Doppler modes on a GE LOGIQ F8 system, preceded Fine Needle Aspiration Cytology (FNAC). Lesions were classified as benign or malignant based on factors such as nodule shape, margins, echo texture, composition, and calcification patterns. Each nodule was categorized as malignant, possibly malignant, borderline, probably benign, or benign

RESULTS

The study on patients with thyroid swelling was completed in a period of 18 months in the Department of Radiology, Khaja Bandanawaz Institute of Medical Sciences, Kalaburagi. A total of 50 patients were taken in the study within the age group of 10 to 80 years. Both males and female patients were included in the study. Statistical analysis: The data was expressed in number and percentage. Chi square test applied to find the statistical significant. P value less than 0.05 was considered statistically significant at 95% confidence interval.

In the present study, patients of age group 10-80 years were included, with overall mean age being 43.91 ± 13.8 years. Mean age in Benign and Malignant was 41.17 ± 12.98 and 53.64 ± 13.4 years respectively. The maximum number of patients belonged to 5th decade of life (34%) followed by 4th decade (26%). Female sex was affected more compared to the male sex (84% females and 16% males). Table No 1 & Graph No 01.



Figure 1

Right lobe of thyroid was the most common location for both benign (55.55%) and malignant (85.71 %) thyroid nodules.

Out of 50 cases, 39 (78%) were of size more than 2 cm in diameter, of which 30 (83.33%) were benign nodules and 9 (64.29%) were malignant nodules.

SHAPE OF THYROID NODULE

Benign thyroid nodules were more frequently wider than tall (94.45%), while malignant nodules were typically taller than wide (73.1%). The shape classification was statistically significant.

MARGINS OF THYROID NODULE

Well-defined margins were commonly observed in benign nodules (94.45%), whereas lobulated or poorly defined margins were more frequent in malignant nodules (85.71%). Margin classification was statistically significant.

COMPOSITION OF THYROID NODULE

Cystic composition was predominant in benign nodules (21 out of 36), while solid composition was mainly seen in malignant nodules (13 out of 14). This finding was statistically significant.

ECHOTEXTURE OF THYROID NODULE

Hypoechogenicity was more common in malignant nodules (12 cases) compared to benign (4 cases). Conversely, hyperechogenicity was more frequent in benign nodules (20 cases). Anechoic shadows occurred only in benign nodules (10 cases).

HALO OF THYROID NODULE

A thin halo was found in 86% of benign nodules, while a thick or absent halo was seen in 88.5% of malignant nodules. Halo classification was statistically significant.

PATTERNS OF CALCIFICATIONS IN THYROID NODULE

No calcifications were present in 75% of benign and 64.29% of malignant nodules. Macrocalcifications

were predominant in both types but were not statistically significant.

PATTERN OF VASCULARITY IN THYROID NODULE

Benign nodules often had absent, perinodular, or perinodular > central vascularity (80.56%), while malignant nodules frequently showed central or central > perinodular patterns (78.56%). Vascularity patterns were statistically significant.

ASSOCIATION OF CERVICAL LYMPHADENOPATHY WITH THYROID NODULE

Cervical lymphadenopathy was present in 35.71% of malignant nodules and 5.55% of benign nodules, showing statistical significance in its association with malignancy.

DISTRIBUTION OF THYROID LESIONS DIAGNOSED ON ULTRASONOGRAPHY

Most common lesion that was diagnosed on USG was Adenomatoid nodule in 40% of the patients followed by colloid cyst and papillary carcinoma in 18% of the patients. The remaining lesions were follicular adenoma (12%), follicular carcinoma (8%), medullary carcinoma (2%), and hemorrhagic cyst (2%).

Table 1: DISTRIBUTION OF THYROID LESIONS BASED ON FNAC DIAGNOSIS

USG Diagnosis	Number	Percentage
COLLOID CYST	9	18%
HEMORRHAGIC CYST	1	2%
CYSTCOLLOID/ADENOMATOID NODULE	20	40%
FOLLICULAR ADENOMA	6	12%
PAPILLARY CARCINOMA	9	18%
FOLLICULAR CARCINOMA	4	8%
MEDULLARY CARCINOMA	1	2%

Ultrasound and FNAC diagnoses matched in 40% of adenomatoid nodules, 18% of colloid cysts and papillary carcinoma, 12% of follicular adenomas, 8% of follicular carcinomas, and 2% each of medullary and hemorrhagic cysts.

TABLE 2: COMPARISON OF ULTRASOUND DIAGNOSIS WITH FNAC DIAGNOSIS:

TYPE	SENSITIVITY	SPECIFICITY	PPV	NPV
COLLOID CYST	88.9%	72%	94.2%	5.88%
HEMORRHAGIC CYST	100%	100%	100%	0%
CYSTCOLLOID/ADENOMATOID NODULE	85%	75%	86.6%	33.3%
FOLLICULAR ADENOMA	86.2%	90%	92.6%	7.4%
PAPILLARY CARCINOMA	88.9%	72%	94.2%	5.88%
FOLLICULAR CARCINOMA	8.5%	75%	66.6%	33.3%
MEDULLARY CARCINOMA	100%	100%	100%	0%

In this study, ultrasound had a 94.2% positive predictive value for colloid cysts, with 88.9% sensitivity and 72% specificity. It had 100% for medullary carcinoma and 94.2% for papillary carcinoma, with 86.6% for adenomatous nodules and 85% sensitivity and 75% specificity for follicular carcinoma.

TABLE 3: DIAGNOSTIC ACCURACY OF US FINDING FOR MALIGNANT NODULE

TYPE	SENSITIVITY	SPEFCITY	PPV	NPV	ACCURANCY
TALLER THAN WIDE	71.43%	94.44%	83.33%	89.44%	88%
LOBULATED/ POORLY DEFINED MARGINS	85.71%	94.44%	85.71%	94.44%	92%
SPLID/ PREDOMINANTLY SOLID	92.86%	58.33%	46.43%	95.45%	68%
HYPOECHOIC	57.14%	88.89%	66.67%	84.21%	80%
MARKEDLY HYPOECHOIC	28.57	100%	100%	78.2%	80%
THICK INCOMPLETE HALO/ABSENT	85.71%	86.11%	70.59%	93.94%	86%
MICROCALCIFICATIONS	14.29%	100%	100%	75%	76%
CENTAL AND CENTAL> PERINODULAR	78.57%	80.56%	61.11%	90.62%	80%

Sensitivities for US findings were 71.43% for taller than wide shape, 85.71% for lobulated/poorly defined margins, 57.14% for hypoechoic, 28.57% for marked hypoechogenicity, and 14.29% for microcalcifications. Specificities were 94.44%, 94.44%, 88.89%, 100%, and 100% respectively. Diagnostic accuracies were 88%, 92%, 80%, 80%, and 76%. Lobulated/poorly defined margins had the

highest diagnostic accuracy for malignant nodules at over 90%. For Solid/predominantly solid composition and thick incomplete or absent halo, sensitivities were 92.86% and 88.71%, with specificities of 58.33% and 86.11%, and diagnostic accuracies of 68% and 86%. Color Doppler findings for central vascularity had a sensitivity of 78.57%, with specificity and diagnostic accuracy at 80.56% and 80%, respectively.

TABLE 4: SIGNIFICANCE OF US CHARACTERISTICS IN DIFFERENTIATION OF BENIGN AND MALIGNANT THYROID NODULE

CHARACTERISTIC	BENIGH(36)	MALIGANT(14)	P VALUE
SHAPE			<0.0001
WIDER THAN TALL	34	04	
TALLER THAN WIDE	02	10	
MARGINS			<0.0001
WELL DEFINED	34	02	
LOBULATED/ POORLY DEFINED	02	12	
COMPOSITION			<0.001
SYSTIC/PREDOMINANTLY CYSTIC	21	01	
SOLID/ PREDOMNANTLY SOLID	15	13	
ECHOTEXTURE			
HYPERECHOIC	20	01	<0.0001
HYPOECHOIC/ MARKEDLY HYPOECHOIC	04	12	
ISOECHOIC/ANECHOIC	12	01	
HALO			<.0001
THIN	31	02	
THICK INCOMPLETE AND ABSENT	05	12	
CALCIFICATION			
MICROCALCIFICATION	00	02	0.423
MACROCALCIFICATION	09	03	
ABSENT	27	09	
VASCULARITY			0.0005
CENTRAL AND CENTRAL> PERINODULAR	07	11	
PERINODULAR AND PERINODULAR> CENTRAL	29	03	
ASSOCIATED CERVICAL	02	05	0.0143

US features associated with malignant nodules include taller-than-wide shape, lobulated or poorly defined margins, marked hypoechogenicity, thick or absent halo, microcalcifications, central or more peripheral vascularity, and cervical lymphadenopathy. These features were statistically significant for malignancy. In contrast, benign nodules were more often wider than tall, had well-defined margins,

hyperechogenicity, and a thin halo, which were statistically significant for benignity. Solid or predominantly solid nodules were found equally in benign and malignant cases and were not statistically significant. Calcifications were more frequent in benign nodules, with macrocalcifications also more common but not statistically significant.

REPRESENTATIVE CASES

CASE 1: ADENOMATOID NODULE

Longitudinal images showing a well-defined ovoid shaped solid nodule in right lobe of the thyroid with hypoechoic halo, biopsy proved it to represent a hyperplastic nodule.

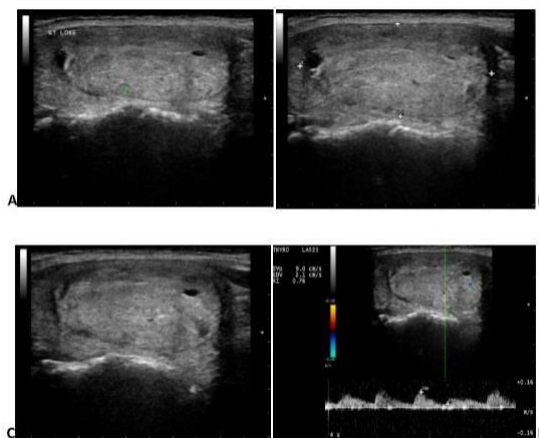


Figure 1

CASE 2: ADENOMATOID NODULE WITH HONEY COMB APPEARANCE.

Transverse and longitudinal images of right thyroid lobe shows innumerable cystic spaces within a nodule

separated by a mesh of septations. This honeycomb appearance represents a benign thyroid nodule - which was proven to be adenomatous nodule.

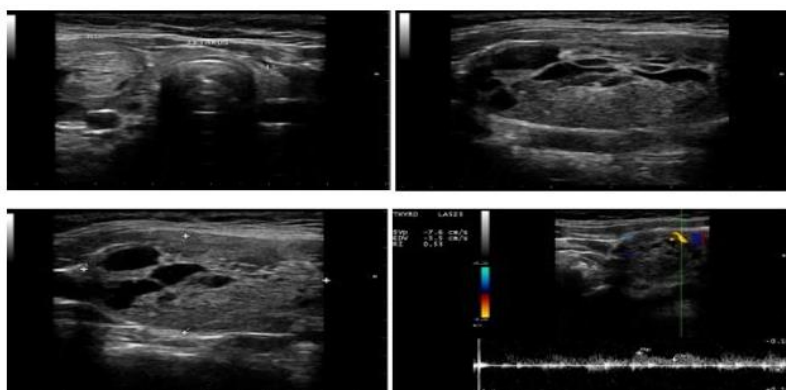


Figure 2

CASE 3: FOLLICULAR ADENOMA

FIGS 19 A-D: Longitudinal and transverse gray-scale images showing a well-defined iso to hypoechoic nodule with incomplete halo. Transverse color

Doppler image shows flow in peripheral hypoechoic capsule with an RI of 0.51. Histopathological examination confirmed follicular adenoma.

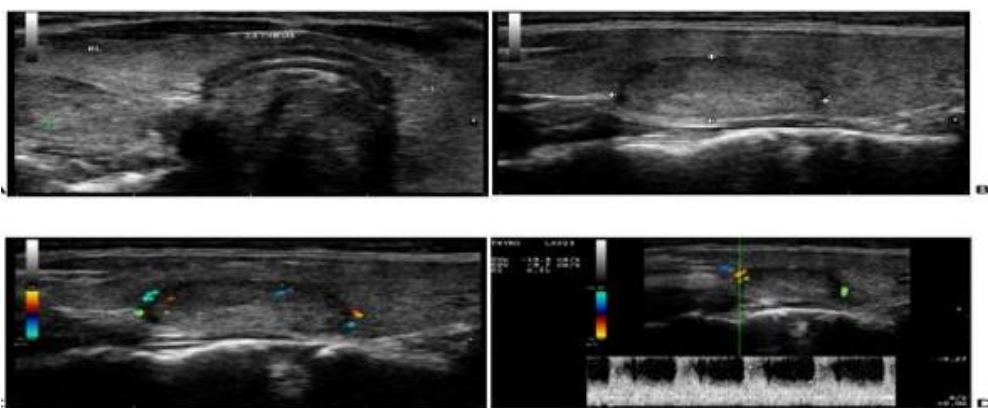


Figure 3

CASE 4: FOLLICULAR CARCINOMA

Longitudinal and transverse gray-scale images shows a taller than wide,lobulated isoechoic nodule with hypoechoic areas in the left lobe. The nodule has a thick incomplete halo with speck of calcification within. On color Doppler, central vascularity was

noted with an RI of 0.68. CT axial images of the brain in head and bone windows showing expansile lytic lesion with enhancing soft tissue component suggestive of metastasis. HPR proved to be follicular carcinoma

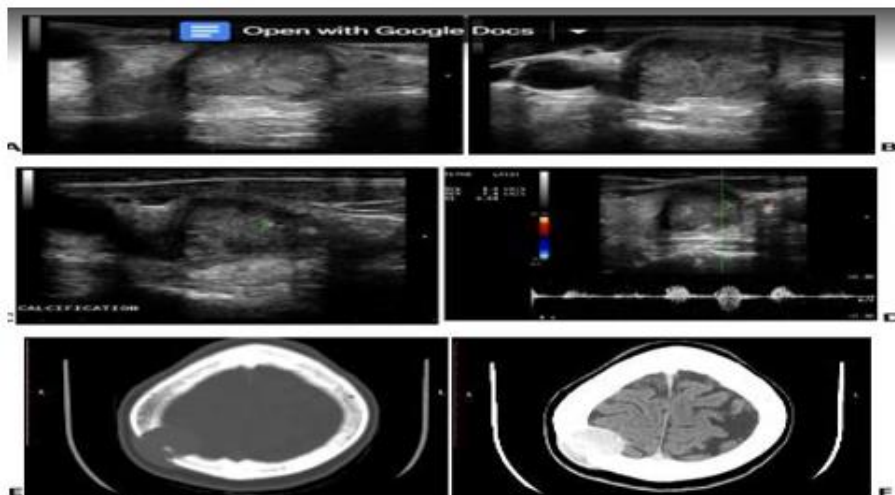


Figure 4

CASE 5: PAPILLARY CARCINOMA WITH LYMPH NODAL METASTASIS

Longitudinal gray-scale images showing an ill-defined hypoechoic nodule with microcalcifications and internal vascularity in right lobe of thyroid.

Transverse images showing cystic changes and microcalcifications in Level III cervicallymph nodes on right side. Elastography showing score of 4.

FNAproved to be papillary carcinoma of thyroid with lymph node metastasis.

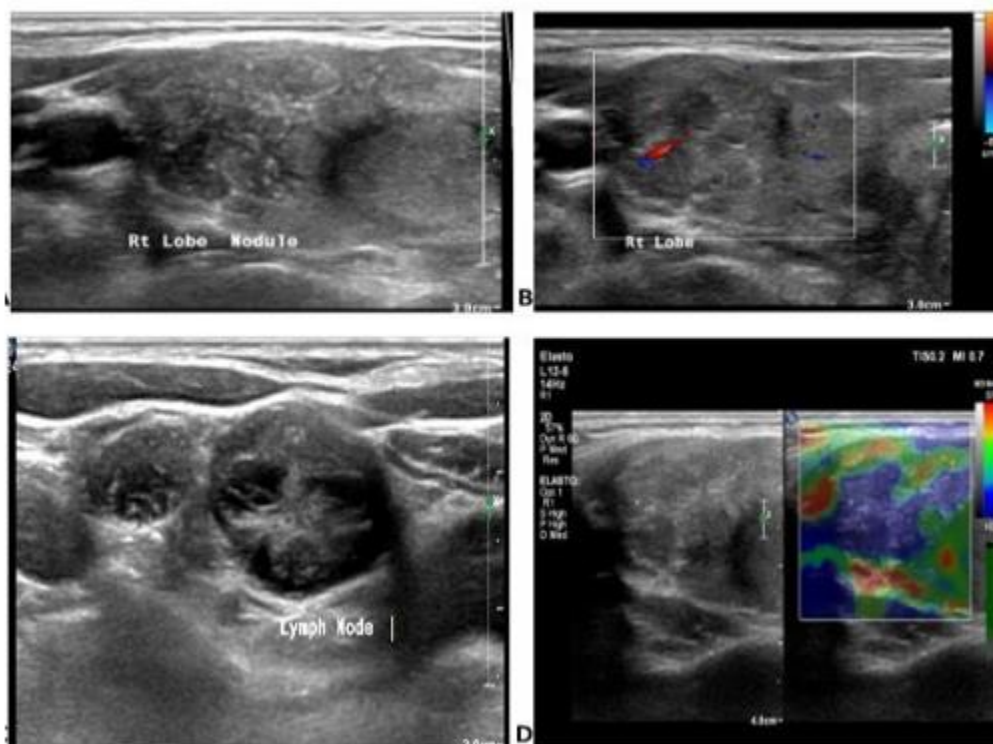


Figure 5

CASE 6: ANAPLASTIC CARCINOMA

Transverse and longitudinal gray-scale images

showing an irregular, heterogeneous thyroid mass with coarse internal calcifications involving right lobe.

Color Doppler images showing central vascularity. Cystic changes and internal vascularity in Level II cervical lymph nodes on right side. Elastography

showed a score of 4. Histopathology proved to be anaplastic carcinoma of thyroid.

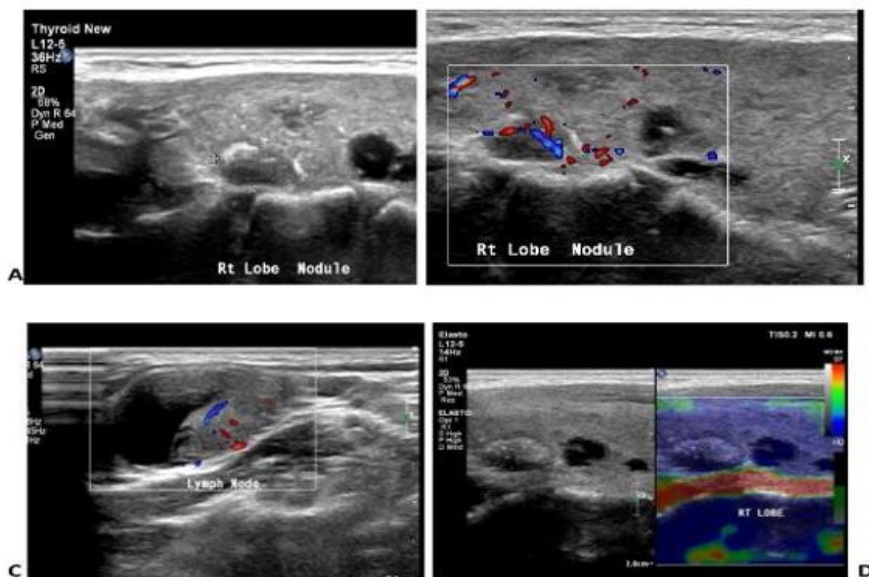


Figure 6

CASE 7: MEDULLARY CARCINOMA OF THYROID

Longitudinal images showing hypoechoic nodule in the right lobe of thyroid with specks of calcifications. Color Doppler images showing central vascularity with an Rlof of 0.63. Histopathological examination proved it to be medullary carcinoma of thyroid.

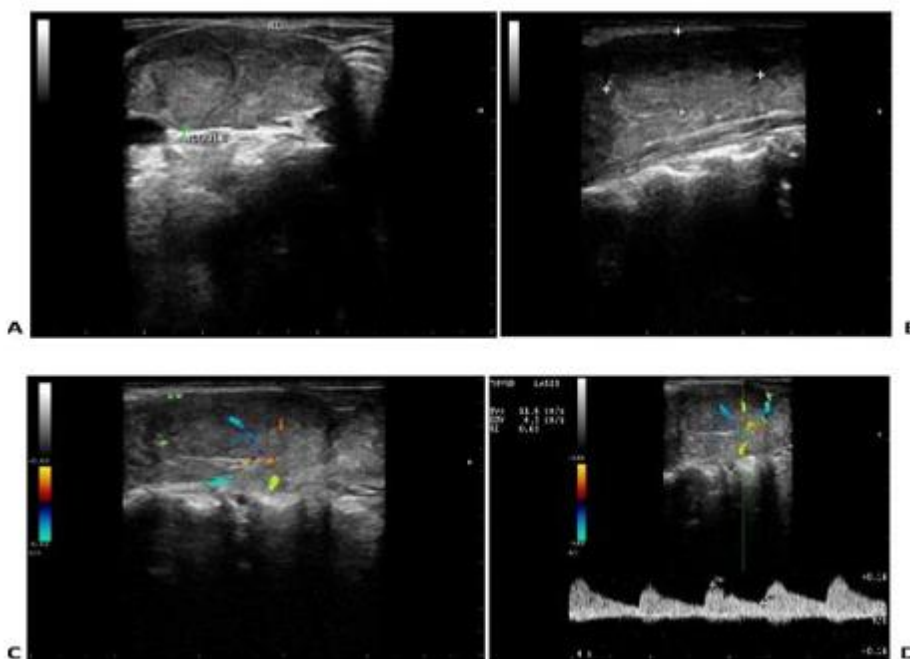


Figure 7

DISCUSSION

Thyroid ultrasound (US) is the major imaging modality for evaluating thyroid nodules. Using US, a thyroid nodule appears as a nodular lesion within the thyroid gland that is distinguishable from the adjacent parenchyma. Several gray scale and Doppler US

features are evaluated as potential predictors for the presence of thyroid malignancies. However, there is a considerable overlap in the appearance for distinction between benign and malignant thyroid nodules, regardless of whether it has a solid or cystic US configuration.

PRESENT STUDY

In a study of 50 thyroid nodules, 36 were benign and 14 were malignant. The median age for benign nodules was 41 years, while for malignant nodules, it was 53 years. The sample comprised 42 females (84%) and 8 males (16%), with a male-to-female ratio of 1:5.25. The right lobe was the most common site for both types of nodules. Most nodules, benign (30/36) and malignant (9/14), were larger than 2 cm. Benign nodules included colloid/adenomatoid (20), colloid cysts (9), and follicular adenomas (6).

Malignant types were papillary thyroid carcinoma (9), follicular carcinoma (4), and medullary thyroid carcinoma (1). Ultrasound features such as a taller-than-wide shape, lobulated margins, and microcalcifications were significant for malignancy. In contrast, a wider-than-tall shape and well-defined margins indicated benignity. The study found solid nodules and thick incomplete or absent halos in both groups, with diagnostic accuracy ranging from 76% to 92%.

TABLE 23: COMPARISON OF DIAGNOSIS INDICES FOR GRAY SCALE US CHARACTERISTICS OF MALIGNANT THYROID NODULE

CHARACTERISTIC	MOON ET AL ⁵⁹					POPLI ET AL ⁵¹					PRESENT STUDY				
	SE N%	SP E%	PP V %	NP V%	AC C%	SE N%	SP E%	PP V %	NP V%	AC C%	SE N%	SP E%	PP V %	NP V%	AC C%
TALLER THAN WIDE	40	91.4	77.4	67.4	69.6	77.2	80.1	46.5	94	79.5	71.4	94.4	83.3	89.4	88
LOBULATED/POORLY DEFINED MARGINS	48.3	91.8	81.3	70.7	73.4	84	88.7	62.7	96.1	87.9	85.7	94.4	85.7	94.4	92
SOLID/PREDOMINANTLY SOLID	-	-	-	-	-	88.6	53.5	30	95.4	60	92.8	58.3	46.4	95.5	68
HYPOECHOIC	87.2	58.5	60.7	86.1	70.7	-	-	-	-	-	57.1	88.9	66.7	84.2	80
MARKEDLY HYPHOCCHOIC/POECHOIC	41.4	92.2	79.7	68.1	70.7	65.9	87.2	53.7	91.9	83.3	28.6	100	78.2	80	
THICK INCOMPLETE HALO/ ABSENT	-	-	-	-	-	70.4	65.8	31.6	90.8	66.6	85.7	86.1	70.6	93.9	86
MICROCALCIFICATION	44.2	90.8	77.9	68.8	71	65.9	97.9	87.8	92.7	92	78.6	80.6	61.1	90.6	80

COMPARISON OF DOPPLER PARAMETERS IN DETERMINATION OF MALIGNANCY IN THYROID NODULES

The Central/central > peripheral vascularity pattern had 78.5% sensitivity and 80.5% specificity for malignant nodules, consistent with Chammas *et al.* and Moon *et al.*'s findings.

COMPARISON OF ULTRASOUND DIAGNOSIS WITH FNAC DIAGNOSIS

This study found that ultrasound had a 92.5% positive predictive value for detecting colloid cysts, with 88.9% sensitivity and 72% specificity. Yeh *et al.* reported a 94.2% predictive value for micronodulation. FNAC showed 81.3% sensitivity for benign lesions. Ultrasound had 100% predictive value for medullary carcinoma, 94.2% for papillary carcinoma, and 85% for adenomatous nodules. Chaudhary *et al.* noted an 83.3% sensitivity for malignant nodules.

CONCLUSION

Our results demonstrated that the presence of gray scale features - Taller-than-wide shape, Lobulated/poorly defined margins, Hypoechoogenicity and Marked hypoechoogenicity, Thick incomplete/absent halo, Microcalcifications, Central/central > peripheral pattern of vascularity and associated cervical lymphadenopathy suggests malignancy. Likewise the presence of Wider than tall shape, Well defined margins, Hyperechogenicity, and Thin halo suggests benignity. A solid/ predominantly solid component alone cannot be a useful criterion for the differentiation of malignant from benign nodules. The presence of calcification or macrocalcification showed no statistical significance in the differentiation of a malignant nodule from a benign nodule. Using a 5-category US classification system, the specificity and positive predictive value were high for distinguishing benign and malignant nodules. But the diagnostic accuracy did not cross 75% for any of the ultrasound categories. However the overall

diagnostic accuracy of thyroid US for differentiating a malignant lesion from a benign one in the present study was found to be 84.3 % which is in correlation with previous studies.

Thus Ultrasound and Colour Doppler study is an easy, non-invasive and rapid technique that can be routinely used as an additional tool in the work-up of thyroid nodules to select cases for FNAC, avoid unnecessary biopsies, and consequently decrease the hazards and costs. It also increases confidence in the decision for benign versus malignant when assessing thyroid nodules.

REFERENCES

- Lee JH, Anzai Y. Imaging of thyroid and parathyroid glands. *Semin Roentgenol.* 2013;48(1):87-104.
- Desser TS, Kamaya A. Ultrasound of thyroid nodules. *Ultrasound Clin.* 2009;4(2):87-103.
- Sholosh B, Borhani AA. Thyroid ultrasound part 1: technique and diffuse disease. *Radiol Clin North Am.* 2011;49(3):391-416.
- Nachiappan AC, Metwalli ZA, Hailey BS, Patel RA, Ostrowski ML, Wynne DM. The thyroid: review of imaging features and biopsy techniques with radiologic-pathologic correlation. *Radiographics.* 2014;34(2):276-93.
- Rago T, Scutari M, Santini F, Loiacono V, Piaggi P, Di Coscio G, et al. Real-time elastosonography: useful tool for refining the presurgical diagnosis in thyroid nodules with indeterminate or nondiagnostic cytology. *J Clin Endocrinol Metab.* 2010;95(12):5274-80.
- Loevner LA. Imaging of the thyroid gland. *Semin Ultrasound CT MR.* 1996;17(6):539-62.
- Weber AL, Randolph G, Aksoy FG. The thyroid and parathyroid glands: CT and MR imaging and correlation with pathology and clinical findings. *Radiol Clin North Am.* 2000;38(5):1105-29.
- Kabala JE. Computed tomography and magnetic resonance imaging in diseases of the thyroid and parathyroid. *Eur J Radiol.* 2008;66(3):480-92.
- Langer JE, Baloch ZW, McGrath C, Loevner LA, Mandel SJ. Thyroid nodule fine-needle aspiration. *Semin Ultrasound CT MR.* 2012;33(2):158-65.
- Lew JI, Solorzano CC. Use of ultrasound in the management of thyroid cancer. *Oncologist.* 2010;15(3):253-8.
- Sandler MP, Patton JA, McCook BM. Multimodality imaging of the thyroid gland. *Best Pract Res Clin Endocrinol Metab.* 1989;3(1):89-119.
- Intenzo CM, Dam HQ, Manzone TA, Kim SM. Imaging of the thyroid in benign and malignant disease. *Semin Nucl Med.* 2012;42(1):49-61.
- Joyce JM, Swihart A. Thyroid: nuclear medicine update. *Radiol Clin North Am.* 2011;49(3):425-34.
- Solbiati L, Osti V, Cova L, Tonolini M. Ultrasound of thyroid, parathyroid glands and neck lymph nodes. *Eur Radiol.* 2001;11(12):2411-24.
- Gharib H, Papini E, Paschke R, Duick D, Valcavi R, Hegedüs L, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *Endocr Pract.* 2010;16(Suppl 1):1-43.
- Tuttle RM, Haddad RI, Ball DW, Byrd D, Dickson P, Duh QY, et al. Thyroid carcinoma, version 2.2014. *J Natl Compr Canc Netw.* 2014;12(12):1671-80.
- Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. *Am J Clin Pathol.* 2009;132(5):658-65.
- Reading CC, Charboneau JW, Hay ID, Sebo TJ. Sonography of thyroid nodules: a "classic pattern" diagnostic approach. *Ultrasound Q.* 2005;21(3):157-65.
- Tessler FN, Tublin ME. Thyroid sonography: current applications and future directions. *AJR Am J Roentgenol.* 1999;173(2):437-43.
- Sacks W, Braunstein GD. Papillary thyroid carcinoma. In: *Thyroid Cancer.* Springer; 2012.p. 133-53.