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Original Article

Radiology Section

Ultrasound and Colour Doppler Evaluation of Nodular Thyroid Masses

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ABSTRACT

Introduction: Ultrasonography (USG) of thyroid nodules is a safe, non-invasive and effective method for evaluation of nodular thyroid masses. They give a clear cut characteristic of the thyroid nodule besides their site, shape, size and number. However, its efficacy and role in differentiating nodules as benign and malignant is not well documented.

Aim: To investigate the diagnostic accuracy of USG and colour doppler in differentiating a malignant thyroid nodule from a benign lesion.

Materials and Methods: The present cross-sectional study was carried out among 52 patients clinically diagnosed with thyroid, from January 2018 to June 2019. After obtaining ethical approval and informed consent, USG and colour doppler were performed on these participants. The findings were evaluated based on hypoechogenicity, microcalcification, vascularity. The diagnostic accuracy of USG and colour doppler was evaluated in terms of sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) in comparison with the postsurgical histopathology findings.

Results: Forty two nodules were benign while 10 were malignant. It was observed that the sensitivity was 100% for detection of halo and presence of vascularity. The specificity was 97.6% for calcification and 76.2% for vascularity. Assessment of lymph node had higher sensitivity (70%) and specificity (100%) with high positive (100%) and negative (93.3%) predictive values.

Conclusion: Ultrasound and colour doppler imaging features such as inhomogeniety, presence of vascularity, halo and lymph node with malignant features had excellent histopathological correlation with malignancy.

Keywords: Diagnostic accuracy, Imaging, Malignant nodule, Microcalcification, Neoplasm, Noninvasive method, Sensitivity

INTRODUCTION

Nodular thyroid disease is a common clinical presentation. The prevalence may vary from 4-7% in clinical presentation [1,2]. The prevalence of non-palpable thyroid nodules detected either by USG or at autopsy is as high as 50% [3,4].

The most common indication for thyroid surgery is the excision of a mass or a palpable nodule. Even though most of them are benign, there is the need to detect malignancy among these with great accuracy. The risk of malignancy in thyroid nodules may vary from 4-10% [5-9].

Many diagnostic tools have been developed to identify those patients who will benefit most from surgery. So far, the gold standard test to discriminate malignant and benign thyroid nodule is Fine Needle Aspiration Cytology (FNAC), due to its high specificity and sensitivity except in cases of follicular carcinoma [10,11]. The reliability on FNAC depends on the technical skill of clinician. Hence, the search for a better diagnostic procedure is on, that yields more consistent results.

Use of USG has gained tremendous popularity in the past few years. The new high frequency transducers (7-13 MHZ) can detect nodules as small as 2 mm, increasing the sensitivity of the procedure [12-14].

Ultrasonography can detect nodules, estimate size, composition, echogenicity, calcification, and lymphadenopathy. The USG of the thyroid is a non-invasive and a widely used technique which is inexpensive in the detection and evaluation of thyroid nodules. It gives information with regard to nodule dimensions, structure, and thyroid parenchymal changes. The use of USG has changed the decision in 63% of patients in a study done by Marqusee E et al., [15]. In another study, the highest incidence of calcification was found in thyroid cancer (54%), followed by multinodular goitre (40%) by USG [16]. In the study by Kalantari S, microcalcification was the best discriminator of malignancy (sensitivity 77%, specificity 76%, PPV 41% and NPV 94%) [17]. Marked hypoechogenicity, intranodular vascularity, incomplete peripheral halo, irregular margin, central microcalcification and cervical adenopathy are categorised as high risk features [10,17,18]. The USG with colour doppler is simple, cost-effective and non-invasive investigation that can be used routinely to rule out malignancy. But there is no clear cut consensus on using it in diagnosing thyroid malignancy, as the focus is still on biopsy and Histopathological Examination (HPE) in a developing country like India, where the need for USG as diagnostic aids is higher. Hence, this study was carried out to investigate the diagnostic value of colour doppler USG in predicting malignant thyroid nodules and to fill the gaps in literature for formulating clinical recommendations. This study aimed to evaluate nodular thyroid masses with USG and colour doppler, and to correlate the findings with postoperative histopathology.

MATERIALS AND METHODS

This cross-sectional study was carried out at the Department of Radiology and Imaging of a tertiary teaching institution, from January 2018 to June 2019. Ethical Committee approval (Ref no: CMCH&RC/ME-1/2016-IEC) was obtained from the Institutional Ethics Committee prior to the commencement of the study. Each participant was explained in detail about the study and informed consent was obtained prior to the data collection.

Based on the available literature, the prevalence of thyroid nodules in India has been documented as 12.2% [19]. At 95% confidence level and 10% absolute precision, the sample size was calculated as 41 using the formula 4pq/d2. Accounting for 25% of failure to respond, the minimum sample size was further rounded off to 52.

All patients with a thyroid nodule of more than 1.5 cm in size, detected on ultrasound, were included in the study. All patients with thyroid nodules suspicious of malignancy, irrespective of the size, were also included in the study. Patients with diffuse thyroid enlargement were excluded from the study.

A structured proforma was used to obtain demographic details. After clinical examination, gray scale and colour doppler sonography was performed with a 7.5 to 11 mHz linear array transducer (Ge-Logiq P9 and GE-Logiq F8). Postoperative histopathological findings were documented. This study was done by a single observer to eliminate interobserver variation.

Technique of Examination

The patients were examined in the supine position with an extended neck. As the thyroid gland is situated at anterior aspect of lower neck (C5 to T1 level), the neck was hyperextended by placing a pillow below the shoulder. As the thyroid gland is located subcutaneously in the anteroinferior aspect of neck, it was very clearly visualised with high frequency linear array transducer (7.5 to 11 mHz). The gland was examined in both longitudinal and transverse planes. The characteristics that were studied were echogenicity, homogeneity, margins of the nodule, lymph nodes and vascular pattern. Based on the colour doppler flow pattern, the vascular pattern in the nodules was divided into four types [20]:

Type 0=Nodules with no blood flow

Type I=Perinodular blood flow

Type II=Intra and perinodular blood flow

Type III=Increased blood flow

Bilateral carotid arteries, jugular veins, and supraclavicular fossa were also examined.

The main sonographic characteristics suggestive of a malignant nodule include hypoechoic texture, nonhomogenous echotexture, incomplete and irregularly thickened (more than 2 mm) peripheral halo, irregular or ill-defined margins, microcalcification, presence of type III vascularity (intra and perinodular), presence of cervical metastatic nodes with roundness index <2 and resistive index > 0.75 and presence of projections into the lumen of a cyst with blood flow signals or microcalcification [21].

Fine Needle Aspiration Cytology (FNAC) Technique

The thyroid nodule location was marked and the patient was comfortably positioned, before performing the ultrasound-guided FNAC. The anterior neck region was thoroughly cleansed with povidone iodine (betadine) solution. The transducer was also cleaned with the same solution. Sterile gel was used as a coupling agent. In the present study, 7.5 MHz linear transducer was used to perform FNAC. The needle was then held in one hand and the transducer in the other. The thyroid nodule FNACs were performed with a 25-gauge non-cutting beveled edge needle which is most commonly used in FNAC procedures. The needle was attached with 5 mL syringe and inserted obliquely within the transducer image plane at the level of the thyroid nodule. After entering the nodule under ultrasonogram guidance, the needle was moved gently back and forth within the region of interest. In case of solid thyroid nodule, gentle suction was applied in the piston while maneuvering. In case of cystic thyroid nodule, suction procedure alone was enough to collect the specimen. Once the needle was taken out from the nodule, few tiny contents of aspirated specimen were dropped over a clean slide and another clear glass slide was gently slid over the specimen slide at an oblique angle. The thin aspirate coated slide was allowed to dry for few seconds and was dipped in the jar containing absolute alcohol for fixation. The slide making procedure was repeated until satisfactory for HPE.

STATISTICAL ANALYSIS

Data was entered in Microsoft Excel and analysed using SPSS version 22.0 software. Histopathological findings and USG findings were considered as primary outcome parameters. Demographic and clinical characteristics were considered as primary explanatory parameters. With regards to tests of significance, Chi-square test was used for qualitative variables. The validity of ultrasound as a screening test was evaluated in terms of sensitivity, specificity, PPVs and NPVs.

RESULTS

A total of 52 subjects were considered for the analysis. Majority (84.6%) of the study subjects were females. 51.9% of the study subjects were aged above 40 years as shown in [Table/Fig-1]. A total of 42 had benign nodules while 10 had malignant nodules. There was no association between age groups and malignant nodules as shown in [Table/Fig-2]. Majority (50%) of the males had malignant nodules compared to females (13.6%) and this difference was statistically significant (p=0.016) as shown in [Table/Fig-2].

Parameter	Frequency (%)
Age group (years)	
≤30	15 (28.9%)
31-40	10 (19.2%)
>40	27 (51.9%)
Gender	
Male	8 (15.4%)
Female	44 (84.6%)

[Table/Fig-1]: Baseline demographic characteristics (N=52).

Parameter	Ultrasound findings		p-value
	Benign (N=42)	Malignant (N=10)	
Age group (years)			
≤30	13 (86.7%)	2 (13.3%)	0.435
31-40	9 (90%)	1 (10%)	
>40	20 (74.1%)	7 (25.9%)	
Gender			
Male	4 (50.0%)	4 (50.0%)	0.016*
Female	38 (86.4%)	6 (13.6%)	

[Table/Fig-2]: Comparison of demographic characteristics between ultrasound findings (N=52).
p-value was determined using Chi-square test; *p<0.05 was statistically significant

There was no significant association between echogenecity and malignancy of nodules (p=0.342) in this study as shown in [Table/Fig-3]. A total of 80% of the malignant nodules were hypoechoic, 85.7% of the benign nodules had well-defined margins. There was a significant association between malignant nodules and being inhomogeneous (p=0.048), benign nodules and having well-defined margins (p=0.013). In total, 64.3% of benign nodules had no calcification compared to 30% of malignant nodules. Halo was absent in 90% of malignant nodules compared to 54.8% of benign nodules. All the malignant nodules had colour doppler flow pattern type-III compared to 23.8% of benign nodules as shown in [Table/Fig-3].

The sensitivity for diagnosing thyroid malignancies was maximum, at 100%, for detection of halo and presence of vascularity as shown in [Table/Fig-4]. Assessment of lymph node had good sensitivity (70%) and higher specificity (100%) with high positive (100%) and negative (93.3%) predictive values. The specificity was 97.6% for calcification and 76.2% for vascularity as shown in [Table/Fig-4].

In the diagnosis of malignancy, it was observed that 80% of the malignant cases had four or more positive features. The sensitivity and specificity of ultrasound diagnosis by considering more than four features was 80% and 100% respectively, with PPV of 100% and NPV of 95.5% as shown in [Table/Fig-5].

DISCUSSION

A thyroid nodule is a common medical and surgical problem. Although most are benign, 5 to 10% can turn out to be malignant. It is important to identify the reliable criteria for malignancy in a thyroid nodule on imaging. In the present study, done among 52 participants, the dichotomous division of benign and malignant thyroid nodules

Characteristics	Ultrasound findings		p-value
	Benign (N=42)	Malignant (N=10)	
Echogenicity			
Hypoechoic	25 (59.5%)	8 (80%)	0.342
Hyperechoic	14 (33.3%)	1 (10%)	
Isoechoic	3 (7.2%)	1 (10%)	
Homogeneity			
Inhomogeneous	19 (45.2%)	8 (80%)	0.048*
Homogeneous	23 (54.8%)	2 (20%)	
Margins			
Well-defined	36 (85.7%)	5 (50%)	0.013*
Ill-defined	6 (14.3%)	5 (50%)	
Calcification			
Microcalcification	1 (2.4%)	5 (50%)	#
Coarse calcification	8 (19.0%)	2 (20%)	
Egg shell calcification	6 (14.3%)	0 (0%)	
No calcification	27 (64.3%)	3 (30%)	
Cyst			
Cyst with solid components	10 (23.8%)	2 (20%)	#
Pure cyst	11 (26.2%)	0 (0%)	
No cyst	21 (50%)	8 (80%)	
Lymph node			
With malignant features	0 (0%)	7 (70%)	#
Without malignant features	42 (100%)	3 (30%)	
Halo			
Regular halo	19 (45.2%)	0 (0%)	#
Thick incomplete halo	0 (0%)	1 (10%)	
Absent	23 (54.8%)	9 (90%)	
Colour doppler flow pattern			
I	11 (26.2%)	0 (0%)	#
II	16 (38.1%)	0 (0%)	
III	10 (23.8%)	10 (100%)	
IV	5 (11.9%)	0 (0%)	

[Table/Fig-3]: Ultrasound findings among the study participants (N=52).
p-value was determined using Chi-square test; *p<0.05 was statistically significant; #Statistical test could not be applied because of 0 in one of the cells

Parameter	Validity parameters			
	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
Echogenicity	80%	40.5%	24.2%	89.5%
Homogeneity	80%	54.8%	29.6%	92%
Margins	50%	85.7%	45.5%	87.8%
Calcification	50%	97.6%	83.3%	89.1%
Cyst	20%	76.2%	16.7%	80%
Halo	100%	45.2%	30.3%	100%
Lymph node	70%	100%	100%	93.3%
Vascularity	100%	76.2%	50%	100%

[Table/Fig-4]: Validity of USG in diagnosing thyroid malignancies.
Validity parameters were determined using formulas for Sensitivity, Specificity, PPV, NPV

Parameter	Validity parameters			
	Sensitivity	Specificity	Positive Predictive Value (PPV)	Negative Predictive Value (NPV)
≥2	100%	45.2%	30.3%	100%
≥3	100%	73.8%	47.6%	100%
≥4	80%	100%	100%	95.5%

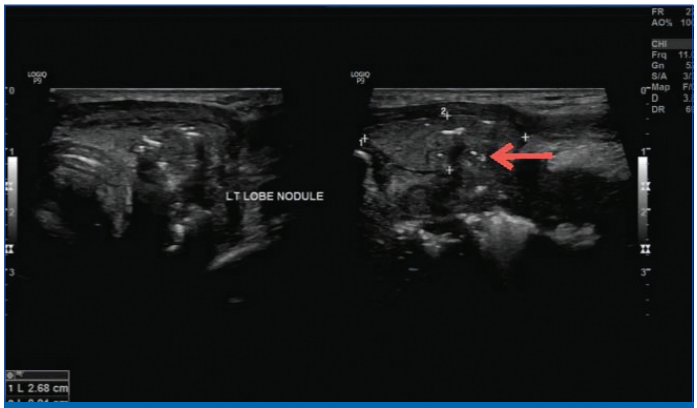
[Table/Fig-5]: Comparison of number of sonographic patterns with histopathology findings.
Validity parameters were determined using formulas for Sensitivity, Specificity, PPV, NPV

using hypoechogenicity alone showed a moderate sensitivity of 80% and a low specificity of 40.5%. However, the PPV was low (24.2%) as some of the benign lesions could present as hypoechoic thyroid nodules. In the present study, 80% of the malignant cases were hypoechoic which was comparable to a study done by Papini E et al., which reported 87% [9].

A study done by Peccin S et al., has shown that a parallel combination of hypoechogencity with microcalcification or absent halo sign to be highly specific and sensitive in diagnosing malignancy [22]. Inhomogeneity is a feature that favours malignancy as suggested by Vorenetskii B et al., [23]. The current study demonstrated that 80% of malignant lesions appeared inhomogeneous. Its specificity and PPVs were low at 54.8% and 29.6%, respectively although the sensitivity and NPVs were high (80% and 92.0%, respectively).

Ill-defined margins, a feature suggestive of malignancy, were seen in 50% of malignant lesions in the present study. But the specificity was relatively high (85.7%) since most of the benign lesions do not have this sign. This was comparable to that of a study done by Papini E et al., wherein irregular margins in a thyroid nodule showed a specificity of 85% [9]. But the sensitivity was 77.4% compared to 50% in this study. Presence of irregular ill-defined margins had PPV and NPV of 45.5% and 87.8% respectively in this study with a p-value 0<0.04 which was significant.

Microcalcification had a low sensitivity (50%) and a high specificity of 97.6%. This denoted that in the presence of microcalcification, the lesion is most likely to be malignant as shown in [Table/Fig-6]. These findings were comparable to a study done by Takashima S et al., which showed specificity of 93%, PPV of 70% and sensitivity of 36% [24]. Similar findings were seen in studies done by Kakkos SK et al., and Samghabadi MAS et al., [16,25]. Peccin S et al., in a series of 284 patients with thyroid nodules, observed that the combination of hypoechogenicity or microcalcification or absent halo is highly sensitive and specific in diagnosing malignancy [22].

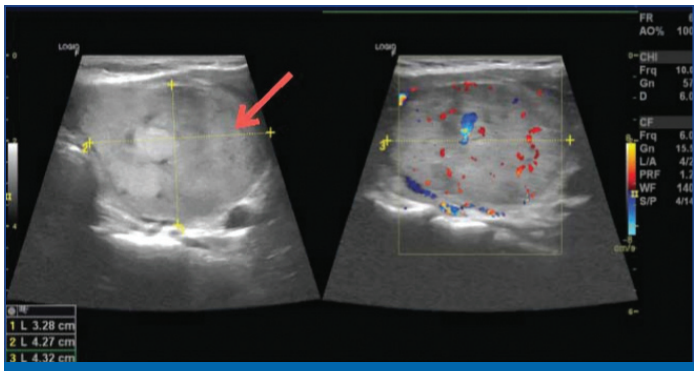


[Table/Fig-6]: Hypoechoic inhomogeneous thyroid nodule with microcalcification consistent with ultrasound diagnosis of papillary carcinoma (HPE- papillary carcinoma).

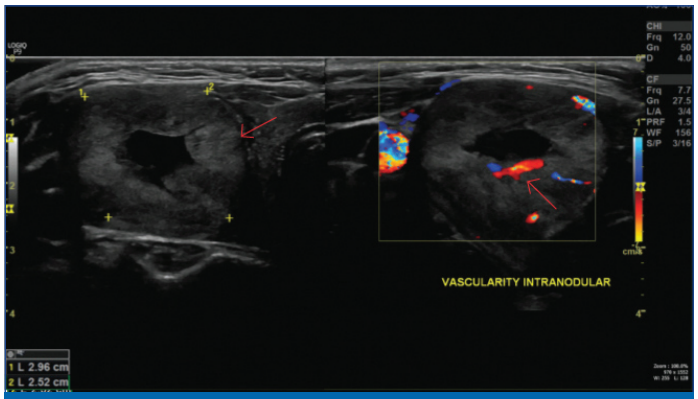
A thick irregular incomplete halo is a specific sign for follicular carcinoma and was present in the only follicular carcinoma in this study. When absent, it showed a sensitivity, specificity, PPV and NPV of 100%, 45.2%, 30.3% and 100%, respectively. Similar findings were seen in studies done by Samghabadi MAS et al., and Summaria V et al., [25,26]. Lymph node enlargement is a clinical sign highly suggestive of malignancy and USG shows the round bulging nature of lymph node involved in thyroid cancer with loss of hilar echoes. These findings were suggested in a study done by Haber RS [27]. In the present study, 70% malignant lesions showed these changes. Cervical lymphadenopathy was associated with lower sensitivity (70%) and higher specificity (100%). Similar findings were seen in a study conducted by Summaria V et al., [26].

The predominant finding of colour doppler, which is suggestive of malignancy, is increased vascularity in both intranodular and perinodular regions (Type III flow pattern) while type II flow pattern was consistent with a benign lesion such as colloid goitre as shown

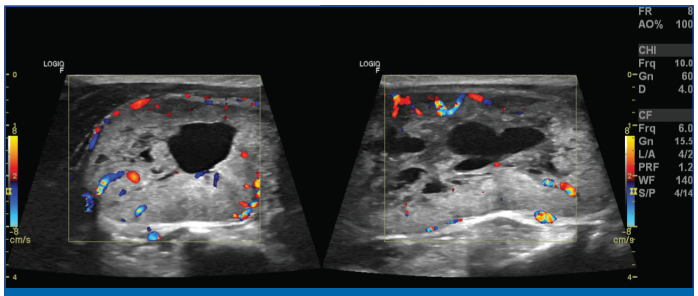
in [Table/Fig-7-9]. This sign showed a maximum sensitivity of 100% in the present study. The specificity, PPV and NPV were 76.2%, 50% and 100%, respectively. Giammanco M et al., showed that by combining this feature with the B-mode USG, a decrease in false positive and false negative diagnosis could be recorded [28]. In the present study, all the 10 cases showed type III vascularity, with a significant p-value <0.001. Summaria V et al., and Fukunari N et al., also observed similar findings [26,29].



[Table/Fig-7]: Isoechoic nodule with cystic areas and thin regular halo. Doppler shows type II intranodular flow (HPE- Colloid goiter).



[Table/Fig-8]: Isoechoic nodule with central cystic area and type II intranodular flow (HPE-colloid nodule).



[Table/Fig-9]: Isoechoic nodule in right lobe of thyroid with cystic changes and type II flow (HPE-colloid nodule).

Type III blood flow with absent halo and metastatic lymph nodes have higher sensitivity in detecting malignant nodules. Specificity is high with metastatic lymph nodes, microcalcification, ill-defined margins and type III blood flow. Though none of these features can diagnose malignancy individually, presence of four or more features in a thyroid mass can diagnose malignancy accurately.

Limitation(s)

It was a single hospital-based study and participants were selected by convenient sampling method. Hence, the results could be different from what is seen in the community. Further large scale multicentric studies are the need of the hour to make strong clinical recommendations.

CONCLUSION(S)

The USG of thyroid nodules is a safe, non-invasive and effective method for evaluation of nodular thyroid masses and ruling out malignancy in thyroid nodules. Of the eight features taken into account, (namely echogenicity, homogeneity, margins, calcification, cyst, halo, lymph node and vascularity) during ultrasound and colour doppler of a thyroid nodule in the diagnosis of malignancy, it was observed that homogeneity and well-defined margins were significantly associated with benign lesion. It can be concluded that sensitivity was highest at 100% for detection of halo and presence of vascularity in identifying malignancy. Assessment of lymph node by ultrasound had higher sensitivity and specificity with high positive and negative predictive values in predicting a malignant nodule, although ultrasound-guided FNAC remains the gold standard for screening thyroid nodule and preoperative evaluation.

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