Original Article

Role of ultrasonography (USG) and color Doppler in the evaluation of thyroid nodules and its association with USG-guided FNAC – A cross-sectional study

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Abstract

Introduction: Thyroid diseases affect approximately 42 million people in India. The majority (15%–40%) of these cases remain asymptomatic and benign and warrant special investigations such as ultrasonography (USG) and fine-needle aspiration cytology (FNAC) for diagnosis. Early diagnosis and management of thyroid disorders determine the disease course in many patients. **Objective:** To determine the role of USG and color Doppler in the evaluation of thyroid nodules and its association with USG-guided FNAC. **Methods:** We did a cross-sectional analytical study over 2 years, where we recruited 108 patients with thyroid swelling attending the OPD. We used a semi-structured data collection proforma that captured information on sociodemographic details, clinical symptoms, physical examination, and all ne cessary laboratory investigations. All patients underwent USG, color Doppler, and FNAC as a part of the investigation of thyroid nodules. The diagnostic value of ultrasound and Doppler parameters was assessed in terms of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for detection of malignancy in comparison to FNAC. **Results:** Approximately 155 nodules were identified from the selected 108 cases, and the prevalence of malignancy among the selected thyroid nodule patients was found to be 9.1%. We observed that malignant tumors were likely to be solitary with lobulated margins, >2 cm in size with <50% peripheral halo, with markedly hypoechoic, predominantly solid, with nodal involvement and extrathyroidal extension, microcalcifications, and central vascularity. We also observed that tumors that had USG characteristics of being taller than wide (91%), poorly defined margins (92%), marked hypoechoic (95%), and microcalcifications (96%) had the highest diagnostic accuracy in detecting malignancy when compared to FNAC. **Conclusion:** Thus, through our study findings, we conclude that USG and color Doppler can serve as vital tools for the evaluation of thyroid nodules with high sensitivity and specificity.

Keywords: Diagnostic accuracy, FNAC, thyroid nodules, ultrasonography (USG)

Introduction

Thyroid diseases are seen on the rise in many countries, especially among lower-middle-income countries and developing countries such as India, and have always remained an important public health problem. It is estimated that thyroid diseases affect approximately 42 million people in India alone, and the global trend is also on the rise.[1] Thyroid disorders diagnosis and presentation are unique in several aspects taking into consideration its ease of diagnosis (owing to the presence of neck swelling). The majority of thyroid disorders tend to remain dormant for long periods until they manifest in the latter part of life, especially during the middle ages with subtle signs and symptoms. Due to its longer duration of natural disease course, dormant nature, and subtle signs of presentation, diagnosis of thyroid disorders has been a challenge recently. Individuals tend

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to have poor health-seeking behavior until a visible swelling appears in the neck.[2]

Thyroid disorders encompass a large spectrum of diseases, including hypothyroidism, goiter or iodine deficiency disorders, autoimmune thyroid disorders, thyroid cancers, and hyperthyroidism. All these diseases have varying clinical features and differ largely with respect to the presentation and nature of investigations required. It is noted that around 3%–7% of the world's adult population suffer from nodular thyroid diseases.[3] The majority (15%–40%) of these cases remain asymptomatic and benign and warrant special investigations such as ultrasonography (USG) and fine-needle aspiration cytology (FNAC) for diagnosis. Solitary nodule thyroid is commonly encountered among these nodules that possess 10%–30% malignant potential.[4] Early diagnosis and management of thyroid disorders determine the disease course in many patients.[5]

Thyroid nodules are a common clinical finding, and primary care physicians are often the first healthcare professionals to encounter patients with neck masses or thyroid-related symptoms. Understanding the role of USG and color Doppler in evaluating thyroid nodules allows primary care physicians to make early and accurate assessments, potentially identifying nodules that require further investigation or monitoring.

USG has the advantages of being easy to perform, non-invasive, cost-effective, widely available for investigation, and highly sensitive for distinguishing cystic and solid thyroid nodules. It also has an added advantage where it can be used in conjunction with FNAC in diagnosing thyroid nodules.[6,7] The nodules are specifically evaluated for shape, calcifications, margins, echogenicity, and composition. In contrast, FNAC offers the advantage of being an accurate screening method for evaluating thyroid nodules. Studies have estimated that FNAC has reduced the rate of overzealous thyroid surgeries by 50% and overall medical costs by 25%. FNAC also plays a vital role in the prognostication of several malignant nodules. Recently, color flow Doppler USG has been gaining importance owing to its ability to assess the vascularity of thyroid nodules through color Doppler signals.[8,9] Thus, we undertook this study to determine the role of USG and color Doppler in the evaluation of thyroid nodules and its association with USG-guided FNAC

Methods

Study design and study settings

We did a cross-sectional analytical study over 2 years (2010–2012) in the departments of Radiodiagnosis, Pathology, and Surgery in a tertiary care institute in New Delhi, India.

Study participants

We conveniently recruited around 108 patients with thyroid swelling attending the OPD during the study period. We excluded patients who had history of ionizing radiation to the neck in the past and who had past history of malignancies or thyroid surgeries.

Study tool

We used a semi-structured data collection proforma that captured information on sociodemographic details, clinical symptoms, physical examination, and all necessary laboratory investigations.

Study procedure

The study was undertaken after obtaining ethics approval from the institute's ethics committee. We employed a high-resolution ultrasound using a 3–12 MHz linear transducer (HD11 XE, Philips Medical System) with color Doppler capability for evaluating the thyroid nodules. Thyroid sonography was performed with the patient in the supine position with the neck slightly hyperextended. The thyroid gland was scanned in the transverse and longitudinal planes. Every nodule was measured in three dimensions, and the echo characteristics were carefully evaluated using appropriate settings for gain, pre- and postprocessing, and other parameters. Imaging of the neck nodes was also done. USG evaluated the number, size, shape, margins, peripheral halo, echogenicity, nodular morphology, extrathyroidal extension, neck node contour, and micro or macro calcifications, if any. Color Doppler was done to assess the type of flow or vascularity, which was further classified as follows: type 1 - no vascularity, type 2 - peripheral vascularity, type 3 - intranodular vascularity, and type 4 - vascularity both in the periphery and within the nodule. Based on the grey scale, they were further reclassified as suspicious or probably benign. FNAC was performed under the guidance of USG by trained pathologists. The patient was made to lie in the supine position with a pillow under the neck so that the neck was extended. The patient was asked to refrain from swallowing or speaking during the procedure to prevent trauma to the surrounding structures. Aspiration was done with a standard disposable 22–23-F needle using a 20-mL syringe. The smears prepared from materials obtained from FNAC were air-dried and fixed in 95% ethanol. The air-dried smear was stained with May–Grunwald–Giemsa stain and fixed-smear-stained with hematoxylin and eosin and Papanicolaou stain. Diagnostic quality aspirations were classified as benign, indeterminate (suspicious), or positive for malignancy. Those with indeterminate (suspicious) results were followed up after histopathological examinations. Individual sonographic features as well as various combinations of features were then analyzed for their association with malignant pathologic findings. In patients with multiple thyroid nodules, FNAC was performed on the largest nodule with similar ultrasound features, but on each nodule when multiple nodules had several different ultrasound features.

Data analysis

Data were entered in Excel and analyzed using SPSS 20. The sonographic attributes of thyroid nodules were summarized in terms of frequency and proportions. The usefulness of these attributes to distinguish benign from malignant thyroid

nodules was compared to cytopathological (FNA) diagnosis. The diagnostic value of ultrasound and Doppler parameters was assessed in terms of sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy for detection of malignancy in comparison to FNA. The statistical significance of each parameter was assessed using the Chi-square test/Fisher's exact test. *P* values of < 0.05 was considered significant.

Results

We finally recruited around 108 patients who presented with a thyroid nodule for our study. Table 1 depicts the demographic, USG, cytopathological, and histological characteristics of the study participants. We found that the majority (71%) of the study participants belonged to the age group of >30 years, with a mean age distribution of 38 ± 7.6 years. Approximately 72% of the study participants were females, whereas 66% presented with a single solitary nodule. Thus, approximately 155 nodules were identified from the selected 108 cases, of which 116 nodules were seen in female patients and 39 nodules in males. Almost 90% of the cases observed were benign in nature (both by FNAC and cytopathology). Of the malignant tumors encountered, 64% were papillary in nature. Of the benign subtypes, colloid goiter was the most common finding (34%), followed by nodular forms (22%).

The distribution of USG characteristics of the study participants stratified by the type of tumor is described in Table 2. We observed that malignant tumors were solitary with lobulated margins, >2 cm in size with <50% peripheral halo. The malignant tumors were also markedly hypoechoic, predominantly solid, with nodal involvement and extrathyroidal extension, microcalcifications, and central vascularity. In contrast, in the case of benign tumors, we found that they were characteristically smooth, without calcifications and nodal involvement.

Table 3 describes the distribution of the diagnostic accuracy of various USG characteristics in diagnosing malignancy when compared to FNAC. We observed that tumors that had USG characteristics of being taller than wide (91%),

Table 1: Demographic, USG, cytopathological, and histological characteristics of the study participants (*n*=108)

Characteristics	Frequency (%)
Age group	
<20 years	06 (5.5)
21–30 years	27 (25.0)
31–40 years	36 (33.3)
>41 years	40 (37.1)
Gender	
Female	77 (72.2)
Male	31 (28.8)
Number of nodules	
Solitary	71 (65.7)
Multiple	37 (44.3)
Cytopathological results (*n*=155)	
Benign	141 (90.9)
Malignant	14 (9.1)
FNAC findings	
Benign	140 (90.4)
Intermediate	5 (3.2)
Malignant	10 (6.4)
Histopathological types, Malignant (*n*=14)	
Papillary	9 (64.2)
Follicular	2 (14.2)
Medullary	1 (7.2)
Anaplastic	1 (7.2)
Non-Hodgkin's	1 (7.2)
Histopathological types, Benign	
Benign	141 (90.9)
Benign appearing follicular lesions	21 (14.8)
Colloid goiter	48 (34.0)
Nodular goiter	32 (22.5)
Hyperplastic nodules	31 (21.9)
Hashimoto's thyroiditis	9 (6.8)

Table 2: Distribution of USG characteristics among benign and malignant tumors, *n*=155

USG features	Characteristics	Benign (*n*=141) *n* (%)	Malignant (*n*=14) *n* (%)
Number of nodule(s)	Solitary	61 (85.9)	10 (14.1)
	Multiple	80 (95.3)	4 (4.7)
Size	<1 cm	13 (86.7)	2 (13.3)
	1–2 cm	57 (96.6)	2 (3.3)
	>2 cm	71 (87.7)	10 (12.3)
Shape	AP≥T	10 (45.5)	12 (54.5)
	AP<T	129 (96.9)	4 (3.1)
Margin	Smooth	110 (98.2)	2 (1.8)
	Lobulated	23 (88.4)	3 (11.6)
	Poorly defined	8 (47)	9 (53)
Peripheral Halo	≥50%	91 (98.9)	1 (1.1)
	<50%	50 (79.3)	13 (20.7)
Echogenicity	Hypoechoic	35 (77.7)	10 (22.3)
	Markedly hypoechoic	2 (18.1)	9 (81.9)
	Hyperechoic	70 (98.5)	1 (1.5)
	Isoechoic	21 (95.4)	1 (4.6)
	Mixed echogenicity	13 (86.6)	2 (13.4)
	Anechoic	2 (100)	0 (0.0)
	Solid	84 (88.4)	11 (11.6)
Internal Contents	Predominantly solid	46 (93.9)	3 (6.1)
	Predominantly cystic	9 (100)	0 (0%)
	Cystic	2 (100)	0 (0%)
Calcification	Absent	115 (98.2)	2 (1.8)
	Present	26 (68.4)	12 (31.6)
	Macrocalcification	23 (95.8)	1 (4.2)
	Microcalcification	2 (15.3)	11 (84.7)
Nodal involvement	Present	4 (36.7)	7 (63.3)
	Absent	145 (97.3)	4 (2.7)
Extrathyroidal extension	Present	0 (0.0)	2 (100)
	Absent	141	12
Vascularity	Absent	16 (100)	0 (0.0)
	Peripheral	75 (96.1)	3 (3.9)
	Central	15 (62.5)	9 (37.5)
	Mixed	35 (94.5)	2 (5.5)

Table 3: Distribution of diagnostic accuracy of various USG characteristics in diagnosing malignancy when compared to FNAC

Ultrasound characteristics	Sensitivity	Specificity	PPV	NPV	Diagnostic Accuracy	*P*
Solitary	71.4% (10/14)	56.7% (80/141)	14% (10/71)	95.2% (80/84)	58% (90/155)	0.08
Multiple	28.5% (4/14)	43.2% (61/141)	11.9% (10/84)	85.9% (61/71)	41.9% (65/155)	
Size <1 cm	14.2% (2/14)	9.2% (13/141)	13.3% (2/15)	90.7% (128/140)	9.6% (15/155)	0.1
1–2 cm	14.2% (2/14)	50.3% (71/141)	3.3% (2/59)	79.2% (84/106)	47% (73/155)	
>2 cm	71.4% (10/14)	42.5% (60/141)	12.3% (10/81)	94.5% (70/74)	45.1% (70/155)	
Shape taller than wide	85.7% (12/14)	91.4% (129/141)	54.5% (12/22)	96.8% (129/133)	90.9% (141/155)	<0.001
Lobulated/Poorly defined margins	85.7% (12/14)	78.5% (110/141)	38.7% (12/31)	98.2% (110/112)	78.7% (122/155)	0.0024
Poorly defined margins	64.2% (9/14)	94.3% (133/141)	52.9% (9/17)	96.3% (133/138)	91.6% (142/155)	
Incomplete/absent Halo	86.6% (13/14)	64.5% (91/141)	20.9% (13/63)	98.7% (91/92)	67% (104/155)	<0.001
Hypoechoic	78.5% (11/14)	75.1% (106/141)	24.4%(11/45)	97.2% (106/109)	75.4% (117/155)	0.007
Marked hypoechoic	64.2% (9/14)	97.8% (139/141)	81.8% (9/11)	95.8% (137/143)	95.4% (148/155)	<0.001
Solid	78.5% (11/14)	40.2% (57/141)	11.5% (11/95)	95% (57/60)	43.8% (68/155)	0.1
Predominantly solid	21.4% (3/14)	67.3% (95/141)	6.1% (3/49)	89.6% (95/106)	63.2% (98/155)	0.34
Solid/Predominantly solid composition	100% (14/14)	7.8% (11/141)	9.7% (14/144)	100% (11/11)	16.6% (25/155)	
Peripheral	21.4% (3/14)	46.8% (66/141)	3.8% (3/78)	43.1% (66/153)	44.5% (69/155)	
Central vascularity	64.2% (9/14)	89.3% (126/141)	37.5% (9/24)	89.3% (126/141)	87% (135/155)	<0.001
Mixed	14.2% (2/14)	75.1% (106/141)	5.4% (2/37)	98.3% (106/118)	69.6% (108/155)	
Presence of calcification	85.7% (12/14)	81.5% (115/141)	31.5% (12/38)	98.2% (115/117)	81.9% (127/155)	
Microcalcification	78.5% (11/14)	97.8% (138/141)	84.6% (11/13)	90.1% (138/153)	96.5% (149/155)	<0.001
Macrocalcification	7.1% (1/14)	98.2% (111/113)	4.2% (1/24)	88.9% (113/127)	73.5% (114/155)	

poorly defined margins (92%), marked hypoechoic (95%), and microcalcifications (96%) had the highest diagnostic accuracy in detecting malignancy when compared to FNAC. Characteristics such as solid internal contents (100%) and incomplete/absent halo (86%) had the maximum sensitivity in picking up malignant tumors, whereas microcalcifications/macrocalcifications (98%) and marked hypoechoic patterns had the maximum specificity in diagnosing malignant tumors.

Discussion

We performed a cross-sectional analytical study to determine the role of USG and color Doppler in the evaluation of thyroid nodules and its association with USG-guided FNAC among individuals presenting with thyroid swelling at a tertiary care institute in North India. We have also determined the diagnostic accuracy of individual greyscale and Doppler USG characteristics in detecting malignant tumors in comparison to FNAC (cytopathological diagnosis).

In our study, we observed that the prevalence of malignancy among the selected thyroid nodule patients was 9.1%. This was found to be in line with findings from other studies[3,4,10] We observed that females had more prevalence of nodules when compared to males, which is again a known finding[11,12] Interestingly, we observed that the male gender had a higher incidence of malignancy when compared to females, which was consistent with findings from Frates *et al.* and Sipos *et al.*[3,13]

We also observed that malignancy was found to be more prevalent among individuals with solitary nodules (71%) compared to multinodular cases (28.5%) but was statistically insignificant. This was found to be consistent with findings from Papini *et al.*[4] However, recent studies have also documented that the risk of malignancy is comparable in both[14] We observed that the size of the nodule might not be a vital predictor for malignancy, which is again proved by studies from other settings.[15] It was noted that the shape of the nodule can be used as a supportive feature for detecting malignancy, as we saw that shapes taller than width had an accuracy of 91% in detecting cancers. This was found to be better than in a study done by Kim *et al.*[16]

Malignant lesions tend to have poorly defined or irregular margins, suggestive of infiltration of surrounding parenchyma. In contrast, benign thyroid nodules tend to have sharp, well-defined margins, as documented by our study.[15] We found that poorly defined or lobulated margins had a sensitivity of 85.7% for the detection of malignancy. This has been previously reported to range widely from 8.3% to 77.5%.[12,17] In our study, we observed that a >50% peripheral halo was seen among benign cases. Studies have also shown that a complete halo around the lesion is 12 times more common in a benign lesion, and even an incomplete halo denotes a benign lesion[18] A few studies have even documented that sensitivity and specificity of absent or thick, irregular halo was found to be 86.6% and 64.5%, respectively, in detecting malignancy, which is similar to our study findings.[19]

With respect to echogenicity, it is documented that hypoechoic lesions have 63% of turning out to be malignant, which is similar to our study findings of 71%[16] Our study reported that solid or predominantly solid suggested malignant nodule (100%), which is, in turn, backed up by studies done by Frates *et al.*[3] (a sensitivity of 75%). Our study showed that microcalcifications and macrocalcifications had the highest specificity for diagnosing

malignant cancers, which has been proven by other study settings (64%). Extrathyroidal extension is observed as one of the vital characteristics of malignant change, as documented by several studies, similar to our study findings. Most thyroid cancers metastasize to organs such as cervical nodes, lungs, brain, and liver.[20] USG-guided FNAC is a very useful tool for diagnosing nodal spread in thyroid cancers. Benign lymph nodes appear oval and hypoechoic and have a smooth border; in contrast, malignant nodes appear rounded and heterogeneous. Color Doppler has an added advantage for investigating the vascularity of tumors. In our study, the vascularity of a thyroid malignant nodule was assessed as absent, peripheral, central, or mixed peripheral and central, similar to studies such as Algin *et al.*[21] Thus, our study findings highlight the importance of utilizing USG and color Doppler in the evaluation of thyroid nodules.

Our study had the strength of evaluating the role of importance of utilizing USG and color Doppler in the evaluation of thyroid nodules from the northern part of India as there is a paucity of literature available among this specific ethnicity of India. We also attempted to estimate the diagnostic accuracy of individual USG characteristics in predicting malignant tumors. Our study had a few limitations. First, our sample size was small to capture all the factors associated with a malignant nature. Second, our findings were from a single tertiary care hospital in Northern India; thus, it is generalizable only to similar settings.

Conclusion

Thus, through our study results, we conclude that USG and color Doppler can serve as vital tools for the evaluation of thyroid nodules. We also conclude that several USG characteristics were highly sensitive and specific for predicting malignant tumors. Our study showed that characteristics of being taller than wide, poorly defined margins, marked hypoechoic, and microcalcifications had the highest diagnostic accuracy in detecting malignancy when compared to FNAC. Furthermore, we encourage future research to comprehensively study the other uses of color Doppler in the prognostication of thyroid nodules.

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Conflicts of interest

There are no conflicts of interest.

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