

Role of Grey Scale and Doppler Sonography in Thyroid Nodules and Correlation with Fine Needle Aspiration Cytology

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Abstract

Introduction: Discrete lesions that are radiologically distinct from surrounding thyroid parenchyma are defined as thyroid nodules. They may be clinically palpable or may be detected incidentally on high resolution ultrasonography. Though the prevalence of thyroid nodules in the general population is quite high but majority of them are benign. High resolution ultrasonography plays an important role in defining the characteristics & number of lesions but fine needle aspiration cytology is gold standard for final diagnosis allowing true distinction between benign and malignant nodules. **Material and Methods:** This hospital based, observational study was performed in the department of Radiodiagnosis of our institution on fifty patients presenting with thyroid swelling or palpable nodule with or without symptoms after obtaining a written consent. Each patient underwent high resolution ultrasonography by 7-12MHz linear transducer followed by FNAC using 23G needle. The results were statistically analyzed using appropriate tools and methods. **Results:** Majority of the patients in our study were female with maximum in the 30-60yrs age-group. FNAC failed to give the final diagnosis in 4/50 patients due to inadequacy of sample. The diagnosis of benign & malignant was quite accurate with USG. Majority of the adenoma were hyperechoic on USG, while majority of malignant nodules were hypoechoic on USG. Characteristic features of malignancy were hypoechogenicity, presence of microcalcification, invasion of strap muscles, presence of cervical adenopathy and intralesional vascularity. USG was most accurate in diagnosing thyroiditis & adenoma followed by colloid nodules and least accurate in diagnosing malignant nodules. **Conclusion:** Gray scale ultrasound coupled with color doppler imaging can reliably differentiate benign from malignant lesions; or diagnose lesions of toxic goitre adenoma or thyroiditis. It also helps in determining the solid and cystic nature of nodule. The number of lesions are well demonstrated by USG. In difficulty cases, FNAC can be used to provide the tissue diagnosis.

Keywords: Ultrasonography, fine needle aspiration cytology, thyroid nodules

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Introduction

Thyroid nodules are common, their prevalence being largely dependent on the identification method. The estimated prevalence by palpation alone ranges from 4% to 7%,^[1,2] whereas US detects nodules in 20% to 76% of the adult population,^[3,4] particularly with the current use of high-resolution US techniques.^[5] The reported frequencies detected by US correlate with the prevalence reported at surgery and autopsy with ranges between 50% and 65%.^[6]

The presence of thyroid nodules is approx 3%-8% among the general population. The profile of thyroid disorders encountered in all age groups in India is similar to that seen in most parts of the world except for the prevalence of iodine deficiency disorders in certain endemic regions like the

“Himalayan goiter belt”. Other pathological lesions such as thyroid neoplasms also present in the form of enlarged thyroid mass or thyroid nodule. Various immunological diseases of the thyroid including hypo and hyper thyroid states may present as thyroid enlargement.

HRUSG is commonly the first imaging modality after clinical examination. CT and MRI imaging can be applied more judiciously subsequently. Fine needle aspiration cytology (FNAC) is a well-established, first line, simple and quick screening test as well as the diagnostic tool for surgical and non-surgical goitres. Limitation of FNAC is mainly inadequate sampling and overlapping cytological features.

Sonographic features of potentially malignant thyroid nodules are Microcalcifications, marked hypoechogenicity, irregular or microlobulated margins and intranodular central vascular-

ity.^[1] In addition to facilitating the diagnosis of clinically apparent nodules, the wide spread use of ultrasonography has result in uncovering a multitude of clinically unapparent thyroid nodules, while differentiating majority of them which are benign from malignant nodules.

But only small number of thyroid nodules is cancerous. Most thyroid nodules which are cancerous are slow growing and might be small in size when they are initially discovered. Aggressive thyroid cancer are less with nodules and can be large, fixed and even Rapid growing.

Usually thyroid nodules are non-cancerous and do not cause any problems. But it is important to note if any unusual swelling occurs in the neck especially if problem relating to breathing or swallowing occurs. It is very necessary to know the possibility of Cancer as well.

Ultrasound

Ultrasound implies the sound signal wave's pulse frequencies above the domain of real human hearing, and their publishing (propagation) in a medium. Diagnostic ultrasound in the medical field is a form that utilizing ultrasound power and acoustic features of the organs of human body or phantoms to produce an image from constant and moving tissue.^[7]

Grey Scale Sonography: According to medical dictionary Grey Scale Sonography Is the display of the ultrasound echo amplitude or signal intensity as different shades of gray, improving image quality compared to the obsolete black and white presentation.^[8]

Doppler ultrasound supply is an instrument, which it is using for measuring the blood speed and flow, also it is utilized in the research field and clinical field investigations to quantify the range and influence of arterial disease.^[9] In Doppler imaging of the blood, the constant object usually is the probe, and the shifting reflectors that produce the returning signal echoes are originally the red cells.^[10,11] The Doppler shift frequency or the Doppler-shift is known as the variation between the frequencies of transmitted and received of ultrasound waves echoes.^[12]

The use of ultrasound in clinical practice contributes to the detection of thyroid nodules in medical centers. However, ultrasound also has several drawbacks that lead to uncertainties in the diagnostic process.^[13,14] In ultrasound reporting systems, the inter observer agreement reported for echogenicity is quite low.

Karpagavalli, Dr. E. Manimekala*, Dr.R.Ravi, Dr. N. Kailasanathan. Strain USG Elastography With Gray Scale And Colour Doppler Imaging Of Thyroid Nodules – Efficacy Compared with Fnac A:^[15] the authors discussed about the sensitivity of grayscale USG in knowing about malignant thyroid nodules. It was found that the sensitivity of grayscale

USG in knowing about malignant thyroid nodules was 100%. Some lesions were overlooked compared with FNAC. Combining USG gray scale and Elastography showed sensitivity of 100%. The Overall accuracy was approx.99.5%.

Ayşegül CANSU*,Emin AYAN, Sibel KUL,İlker EYÜBOĞLU, Şükrü OĞUZ, and Sevdegül MUNGAN. Diagnostic value of 3D power Doppler ultrasound in the characterization of thyroid nodules.^[16] The study focused on evaluating the diagnostic value of vascular indices by using 3D power Doppler ultrasound (3D PDUS) in differentiating benign and malignant thyroid nodules. Vascular indices in malignant nodules were significantly higher than those in benign nodules ($P < 0.05$). In benign nodules, the mean VI was 11.61 ± 6.88 , mean FI was 39.75 ± 3.93 , and mean VFI was 4.82 ± 2.94 in comparison to 18.64 ± 12.81 , 41.82 ± 4.43 , and 8.17 ± 6.37 , respectively, in malignant nodules. At optimal cut off values of 10.2 for VI, 40.8 for FI, and 5.5 for VFI, the sensitivity and specificity were 72%/55.4%, 68%/57.1%, and 68%/67.9%, respectively. Thus, it can be concluded that 3D PDUS can prove to be of use in the characterization of thyroid nodules.

Manoj Kumar Palaniappan, Senthil Kumar Aiyappan, and Upasana Ranga Role of Gray Scale, Color Doppler and Spectral Doppler in Differentiation Between Malignant and Benign Thyroid Nodules.^[17] The authors used specific morphological pattern recognition features such as microcalcifications, hypoechoogenicity, taller than wide, irregular thick halo, lymphadenopathy and local extra thyroidal invasion which helped in differentiating malignant from benign features. Intranodular vascularity and high RI indices were the specific Doppler indicators for malignant thyroid nodules. Gray scale and Doppler both have their own good and bad points. They were found to be complementary to each other more than been competitive modalities in diagnosing benign from malignant thyroid nodules.

Papini et al,^[18] suggested the possibility of pericapsular inflammatory infiltrate as the underlying anatomic correlate of hypochoic halo on ultra sonography.

Solbiati L et al,^[19] suggested sonographic criteria that may help in the differentiation of benign and malignant lesions. They found a predominantly hyperechoic nodule to be most likely benign. They found that peripheral sonolucent halo was present in 60-80% of benign nodules and 15% of malignant lesions. Of these, malignant lesions often had irregular and incomplete peripheral halo while most of the benign lesions presented with thin complete peripheral halo. They have concluded that the location and pattern of calcification have more predictive value in distinguishing benign from malignant lesions.

Takashima S et al,^[20] concluded that US-guided FNA is helpful in making the histologic diagnosis in thyroid nodules associated with Hashimoto's thyroiditis and that it can help

to select patients who need surgery, avoiding unnecessary surgery for patients with non-neoplastic disorders.

Aim and Objectives

The aims and objectives of the current study are as follows-

- The present study is aimed to evaluate the role of high resolution ultrasonography in the diagnosis of the thyroid nodules with FNAC correlation.
- To evaluate morphologic and vascularity pattern in High Frequency USG of clinically significant thyroid nodules.
- To evaluate the role and accuracy of Ultrasound in differentiating malignant nature of nodules from benign.

Subjects and Methods

This is a prospective hospital based observational study done over a period of 18 months in the department of Radiodiagnosis of our institution on fifty patients presenting with thyroid nodule after obtaining written consent according to following criteria.

Inclusion Criteria

- Patients with palpable Thyroid swelling with or without any symptoms
- Patients with non-palpable lesions in thyroid region as detected by High Resolution USG.

Real time grey scale USG and color Doppler study was done using high frequency linear probe of 7-12 MHz while FNAC was done using 23Gauge needle attached to a 10cc disposable syringe.

USG was done with patient in supine position and hyperextended neck and ultrasound neck examination is performed using high frequency linear probe. The material aspirated from the swelling was spread to form two smears - first air dried stained with MGG and second fixed wet in ether stained with H&E.

The sensitivity, specificity, positive predictive value, negative predictive value and clinical significance of different grey scale and doppler findings were evaluated. FNAC correlation taken as gold standard in all cases.

Results

In our study, female outnumbered male with 42 & 8 respectively. Majority of patients 32 (64%) belonged to 31-60 years age group followed by the 10 (20%) in 61+ years and 8 (16%) patients in 0-30 years.

Most of the patient included in the study had appreciable prominent swellings in the region of Thyroid. Other symptoms suggestive of thyroid were 6% with Tremors, 8% with

Difficulty in Swallowing, 8% with weight gain and 6% loss in weight, 2% with voice change [Figure 1].

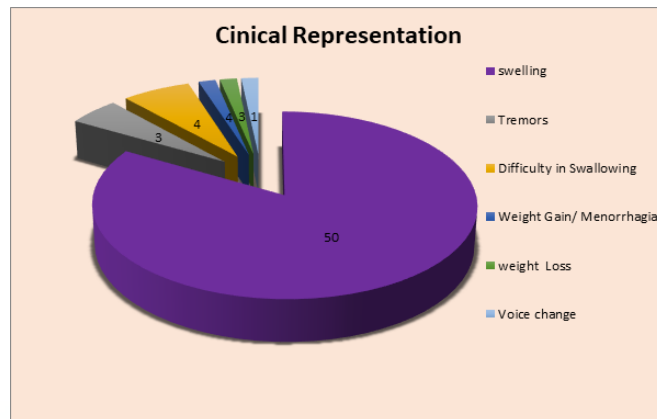


Figure 1: Clinical Representation

On USG, 9(18%) patients were detected with Adenoma, 11(22%) with Thyroiditis, 19(38%) with Colloid Goitre and rest 11(22%) were detected with Carcinoma [Table 1].

Table 1: Provisional Diagnosis Using Ultrasonography & Color Doppler

Classification	No of cases	Percentage
Colloid goiter	19	38%
Adenoma	9	18%
Thyroiditis	11	22%
Carcinoma	11	22%
Total	50	100

On Histopathology, were 17(34%) patients were detected with colloid Goitre, 9(18%) with Adenoma, 10(20%) with Carcinomas, 10(20%) with thyroiditis and rest 4(8%) with RBCs only [Table 2].

Table 2: Provisional Diagnosis Using Hispathology

Classification	No of cases	Percentage
Colloid Goiter	17	34%
Adenoma	9	18%
Thyroiditis	10	20%
Carcinoma	10	20%
RBCs only	4	8%
Total	50	100%

[Table 3] shows the comparison with USG findings with final diagnosis on FNAC.

Table 3: Comparative Provisional Diagnosis Using Ultrasonography and Histopathology

Pathology	USG	H/P
Colloid goiter	19	17
Adenoma	9	9
Carcinomas	11	10
Thyroiditis	11	10
RBCs only	0	4
Total	50	50

Table 4: Echo Texture Ultrasound

Echotexture	Adenoma	Colloid goitre	Thryoiditis	Malignant/ carcinoma
Hyper	6	0	1	0
ISO	3	0	0	0
Hypo	0	1	3	11
HETRO	0	0	7	0
Anechoic	0	18	0	0
Total	9	19	11	11

[Table 4] shows the distribution of cases based on echogenicity on USG and final diagnosis.

[Figure 2] shows the graphical distribution of cases based on Doppler findings.

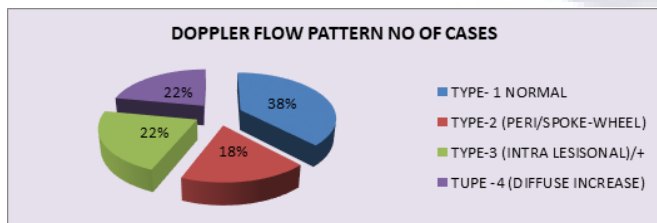


Figure 2: Doppler Flow Pattern

[Table 5] shows the characteristic of malignant nodules on USG

[Figure 3] shows the comparative features of malignant cases on USG & FNAC

[Table 6] shows the USG characteristics of adenoma

[Table 7] shows the statistical evaluation of USG characteristic based diagnosis of thyroid nodules.

The most sensitive signs of malignancy (sensitivity 100%) is MICROCALCIFICATION, ABSENT HALO, LYMPH NODE and INTRALESIONAL VASCULARITY, while INVASION being 27.27% sensitive. LYMPHADENOPATHY proves to be the most specific (85.18%), though the Sensitivity is 100 % for the INVASION but the no of cases

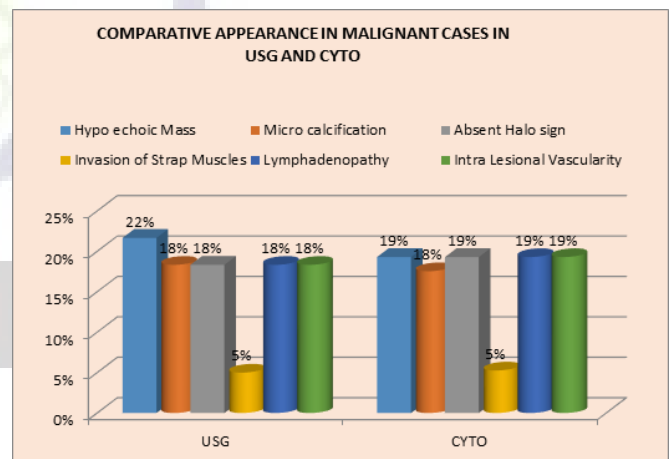


Figure 3: Comparative Appearances in Malignant Cases in USG & H/P

showing in INVASION are only 3 it may be prove to be 100% but its true value cannot be predicted.

While gray scale ultrasound showed heteroechogenicity and coarse calcification to be common finding in thyroiditis, they were not very sensitive for the disorder (63.63% and 72.72%) and showed a specificity ranging from 75 to 85% only but in comparison to it color flow imaging showed sensitivity of 90.90% with positive predication of thyroiditis in 85.57%.

Table 5: Appearances in Malignant Cases USG

Appearances In Malignant Cases USG		
	USG Appearances	% IN Malignant cases
HYPO Echoic Mass	11	100%
MICRO Calcification	11	100%
Absent Halo Sign	11	100%
Invasion of strap muscles	3	100 %
Lymphadenopathy	11	100%
Intra lesional vascularity	11	100%

Table 6: Evaluation of Ultrasonographic Criteria for Diganosis of Adenoma

Criteria	Cases	Others	Sens	SPEC	PPV	NPV
Hyperchoic	6/9	1/41	66.67%	97.56%	59.23%	94.93%
Isoechoic	3/9	1/41	33.33%	97.56%	42.66%	90.23%
HALO+	9/9	30/41	100%	26.82%	22.75%	100%
Perinodular Vascularity	9/9	1/41	100%	92.85%	72.75%	100%

Table 7: Ultrasonographic Evaluation of Malignancy in Thyroid Nodule.

Criteria	Malignant nodule	Other nodule diseases	SENS%	SPEC%	PPV	NPV	X2	P VALUE
HYPERCH	11/11	8/39	100%	81.48%	36.5	94.5	4.99	<0.001
MICRA CALC	11/11	10/39	100%	75.18%	29	95.4	3.18	<0.001
ABSENT HALO	11/11	17/39	100%	55.55%	24	100	4.23	<0.001
LYMPH NODE	11/11	6/39	100%	85.18%	23	100	11.9	<0.001
INVASION	3/11	0/39	27.27%	92.15%	50	92.29	5.61	<0.001
INTRALESIONAL VASCULARITY	11/11	10/39	100%	74.07%	36.46	100	8.4	<0.001

Table 8: Ultrasonographic and Color Flow Imaging in Evaluation of Thyroid Disorders

Criteria	SENS%	SPEC%	PPV	NPV	X2	P-Value
Malignant nodule	100%	94.75%	44.44%	100%	2.02	p>0.05
Thyrodits	100%	100%	100%	100%	8.07	P<0.001
Adenoma	93.75%	100%	100%	98.82%	4.1	P<0.001
Colloid	100%	96.72%	95.12%	100%	8.04	P<0.001

[Table 8] shows the statistical values of color doppler based diagnosis of thyroid nodules.

From the table, it is evident that ULTRASOUND & CYPTO together proves to be significant prediction for diagnosing the THYROIDITIS, ADENOMA & colloid disorders with maximum significance in Thyroiditis.

Discussion

Age Sex Distribution

Majority of patients in our study who presented with thyroid swellings were females in the age group of 30 to 60 years.

Ezzat et al,^[3] in a prospective study of 100 subjects in North America found higher prevalence in women (72%) than in men (41%) ($P < 0.02$), with mean age range being 43 to 50 years.

Colloid Goitre

Out of 50 cases we reported 19 cases as colloid on USG out of which 17 proved to be colloid goitre on FNAC, most of the cases showed detectable anechoic cystic changes.

The most common echo patterns seen on ultrasound were anechoic with Comet tail artifacts and normal vascularity on color flow imaging. The ultrasound appearance varies considerably with stage of the process but the typical pattern is that of poorly echogenic nodules, lobular contour foci of increased echogenicity representing fibrosis and anechoic degenerative areas.^[21]

In 1996 Ahuja et al reported the significance of comet tail artefact in a thyroid nodule. They studied 100 patients and in 85% of patients with this artifact, abundant colloid was seen on F.N.A.C. suggesting that artifact may be related to presence of colloid. The comet tail artifact was appreciated by us in a number of cases which were provisionally thought of as colloid nodules on ultrasound and subsequently prove on F.N.A.C. in all cases.^[22] Our study confirms that the most common echo pattern seen on ultrasound is Anechoic with normal vascularity on color flow imaging and Comet tail artefacts.

Thyroiditis

Out of 50 cases, 11 came out to be thyroiditis on USG and the number was 10 on FNAC. The most common echo pattern seen on ultrasound was heterogeneous with diffuse vasculature and septas formations. Among the 11 thyroiditis cases, 10 had diffuse vasculature, 7 had hetero echogenicity, 3 had hypochoic eco texture, 1 had hyper echoic ecotexture and 8 had coarse calcification.

Langer et al,^[23] reported the Sonographic appearance of focal thyroid nodule that proved to be lymphocytic thyroiditis on FNAC, appears as solid hyperechoic nodules with ill defined margins. However the echogenicity was variable and calcification and cystic appearing lesions were noted. The

vascularity of these nodules on Doppler also varied widely. Biopsy of these lesions is still necessary because there are no Sonographic features that can reliably diagnose these lesions as thyroiditis and differentiate from other lesions.

Hirromastu et al,^[24] studied the utility of color Doppler sonography in patients with subacute thyroiditis. During the acute state of subacute thyroidities CDS showed low echogenicity without increased tissue vascularity in affected swollen thyroid. In the recovery stage, CDS shows isoechogenicity with slight increased vascularity. Vascularisation became normal at one year follow up time, in contrast, marked increased vascularisation was observed in untreated patients. CDS may be useful, noninvasive and rapid method for differentiating SAT from other diseases.

Our study concludes that most common echopattern seen on USG was heterogenous echotexture with diffuse vascularity and coarse calcifications.

Adenoma

Out of 50 thyroids nodules studied 11 were detected as adenoma on USG while 10 were confirmed adenomatous on FNAC. The most sensitive and specific USG feature for diagnosis of adenoma proved to be hyperechoic nodule with perinodular vascularity and halo present. The most common echo pattern is hyperechoic with 75% sensitivity and 89.89% specificity.

Becker et al,^[25] prospectively studies 53 thyroid nodules to assess possibility of recognizing autonomous adenomas of thyroid with color Doppler, using internal hyper vascularisation for identification. Out of 29 patients having autonomous adenomas, 28 present internal hyper vascularisation resulting in a sensitivity of 96% and specificity of 75%. Interestingly, color Doppler detected 6 adenomas in patients showing normal lab data. Color Doppler can be used to exclude focal adenomas with negative predictive value of 94%.

Our study concludes that the most sensitive and specific USG feature for diagnosis of adenoma proved to be hyper echoic nodule with perinodular vascularity and halo present.

Malignancy

Out of 50 cases 11 cases were reported malignant of USG, and 10 cases were confirmed as malignant on FNAC. The most reliable signs were absent halo, Lymphadenopathy, vascularity, and microcalcification. The most common echo pattern seen on USG was hypoechogenicity.

Solbiati et al,^[26] concluded that USG not only detected lesion, but also characterized disease and distinguished benign from malignant lesions with high sensitivity and specificity which could be further improved by employing ultrasound contrast agents and harmonic imaging. Although no single criterion is specific for benign or malignant nature of the lesions, a combination of different signs can be markedly helpful to

speed up the diagnostic process. FNAB (cytology) remains the most accurate modality for definitive assessment of thyroid gland nodules.

Erdem et al prospectively studied 26 patients with cold thyroid nodules (5 malignant and 21 benign) to investigate value of Tc 99m scintigraphy and color Doppler sonography in differentiating malignant from benign thyroid nodules. The sensitivity, specificity, negative predictive value and positive predictive value of scintigraphy and color doppler were determined to be 100% and 80%, 85% and 80%, 62% and 50% and 100% and 94% respectively. They concluded that color Doppler sonography seemed to have limited value in detection of malignant thyroid nodules.^[27]

Rago et al studied usefulness of conventional thyroid USG and CD sonography in assessment of 'cold' thyroid nodules. On US, the echographic pattern most predictive for malignancy was absent halo sign, which was found in 20/30 CA and in 17/72 BN (specifically 77.0%; sensitivity 66.6%, p value 0.0001). The most specific combination on US, absent halo sign/microcalcifications, was found in 8/30 CA and in 5/74 BN. The type III pattern on CFD was found in 20/30 CA and 38/74 BN. US and CFD became highly predictive for malignancy only when multiple signs are simultaneously present in a thyroid nodule.^[28]

To our best knowledge it's sometimes difficult to distinguish between benign & malignant nodules as in case of previous studies showed by Katz Et Al & Clark Et Al.

Our study concludes that the most reliable signs were absent halo, Lymphadenopathy, vascularity, microcalcification and hypoechoogenicity.

Conclusions

In conclusion gray scale ultrasound is superior to clinical palpation and inspection in evaluating the thyroid morphology by differentiating single from multiple nodules and predicting their nature whether solid or cystic. It can reliably differentiate benign from malignant lesions; or diagnose lesions of toxic goitre adenoma or thyroiditis. The addition of color flow imaging has added value to the prediction of thyroid pathology especially toxic goitre and thyroiditis, but definitive diagnosis can be reached only with FNAC/Biopsy.

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