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Role of High Frequency Ultra-Sonogram & Color Duplex Findings with FNAC in Identifying Benign and Malignant Thyroid Nodule

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Abstract
Introduction: *High frequency ultra-sonogram is the best imaging investigation accessible, for the analysis of the thyroid tissue and because of frequent use of ultra-sonogram non palpable thyroid nodules were also identified before symptoms. In this present study I am correlating ultra sound B-Mode grayscale, color and spectral Doppler characteristics of benign versus malignant thyroid nodules with FNAC findings.*
Aim: *To study the specific B – mode grayscale characteristics, color Doppler and standard reference values of Doppler Resistive index of benign versus malignant thyroid nodules with that of FNAC findings. To assess the specificity and sensitivity of grayscale, color Doppler and FNAC elucidated criteria in differentiating benign from malignant nodules.*
Materials and Methodology: *We prospectively investigated 60 patients who were referred to our department for thyroid ultra sound investigation from various departments of our institute for thyroid swelling. Every nodule was assessed according to shape, margins, number, echo texture, halo, calcification on grey scale findings and vascularity, RI values on color Doppler findings. All nodules are designated as benign and malignant on the basis of grey scale USG and color Doppler usg findings. Cut off RI values for benign and malignant thyroid nodules by using Receiver operating characteristics curve.*
Results: *Based on the high frequency ultra-sonogram and color Doppler findings with cross verification with FNAC findings it was found out that out of 60 patients 40 benign, 4 malignant, 15hashimotos thyroiditis and 1 nonspecific thyroiditis. Significant correlation was noted with malignant nodule with following ultra – sonogram features of taller than wider shape, ii-defined margin, markedly hypoechoic, and micro calcification. significant intranodular vascularity and RI values >0.75 was feature of malignant nodules whereas benign nodule showed both intra and peri nodular vascularity and RI values <0.75.high sensitivity and specificity of diagnosing malignant nodule combining both high frequency ultra-sonogram and color Doppler than done either of them alone.*
Conclusion: *Both high frequency ultra-sonogram and color Doppler findings of thyroid nodule are complimentary in diagnosing malignant and benign nature rather than either of them alone.*
Keywords: *USG-Ultra-sonogram, FNAC-Fine needle aspiration cytology.*

Introduction

Thyroid nodules can present in up to 51% of the normal adult population and most of them could not detected by palpation [1]. However, it is only 7% of the thyroid nodules are detected are malignant and it is important that they are diagnosed early and treated [2]. Palpable nodules are seen in 5% to 9% of the population. Smaller nodules of size up to 2mm can be identified with high-frequency probe (USG) which is usually missed on routine palpation of thyroid examination [3]. Mostly these nodules are benign nodules and on further follow up, approximately 9% to 11 % of these nodules were found malignant [4]. The need of ultra-sonogram is to proficiently and accurately identify malignant cases that belong to minority population[5]. High frequency ultra-sonogram probe (USG) is the most susceptible imaging investigation available for the evaluation of the thyroid gland. CT and MRI investigations are used to detect extension and distant metastasis like nodal and organ metastasis. So, the investigation of choice for assessing thyroid nodules is high frequency ultra-sonogram.

All patients with thyroid swelling were assessed by using high frequency Ultra-sonogram as initial step [6]. Ultra-sonogram investigation can assess both palpable and non-palpable thyroid swellings, if present[7]. We can take the advantage of US for guiding FNAC biopsy for HPE correlation of both palpable and non-palpable thyroid nodules[8]. US can also be used to the pre-operative assessment and identify local extent and nodal involvement. However, conventional Ultra-sonogram alone is sufficient for differentiating benign and malignant nodules based on their grey scale findings and nodal assessment of thyroid gland lymphatic system .there are umpteen no of studies in literature stating that both high frequency ultra-sonogram and color Doppler were least sensitive for differentiating thyroid nodule as benign or malignant[9-18]. Few latest studies have supported the fact that color Doppler is useful in diagnosing malignant nodules[5,10,19]. However, some investigators substantiate that Resistive Index (RI) values or vascular patterns were not sufficient in differentiating between benign and malignant nodules[9,15-17,19]. In my study I would like to prove that grey scale ultra-sonogram and color Doppler findings in differentiating malignant from benign thyroid nodules and to compare it with FNAC histopathological findings.

Materials and Methods

Study Population

The prospective case control study was conducted over a period of 1 year starting from January 2017 to June 2018 after getting permission from institutional ethics committee. The study population included 60 persons with palpable thyroid who was referred to radiology department for from various departments in our institution for ultra-sonogram examination, in all patients who had undergone ultrasound examination were referred to pathology department for targeted FNAC of lesions was performed. 25 cases were excluded in the present study due to loss of follow-up/FNAC findings. Thyroid nodules were broadly categorized into benign and malignant of which 40thyroid nodules were benign, 4 nodules were malignant and 16 were assigned as has himotos thyroiditis. In the setting of MNG, single nodule was assessed by USG, color Doppler and FNAC findings for characterization in to benign versus malignant. All the patients who underwent USG, color Doppler and FNAC examination informed written consent was obtained. Self-prepared case sheet which contain the patients demographic details, complaints, present and past history, general examination and thyroid profile of patients who underwent high frequency ultra-sonogram, color Doppler and FNAC investigations. The ultra-sonogram examination of the thyroid nodules will be performed in gray scale and color Doppler modes using a high frequency,7.5 –10 MHz, linear array probe of ACCUSON ANTARES, These nodular lesions will be then characterized into benign, malignant and thyroiditis considering

the following gray scale and color Doppler findings :

B-Mode Ultrasonography

- Shape
  Wider than tall / taller than wide /irregular.
- No of nodules
  Single/Multiple.
- Echogenicity
  Anechoic/hypoechoic/hyperechoic/isoechoic/ markedly hypoechoic/heteroechoic
- Margin
  Well-defined smooth / Ill-defined.
- Halo
  Thin/ thick/ absent.
- Calcification
  Micro calcification /Macro calcification/Rim calcifications.

Color duplex sonogram

- Vascularity
  No significant vascularity /significant peripheral vascularity / mixed vascularity/ significant central vascularity.
- Resistive Indexes – (USG software)
  RI value of both intranodular and perinodular vessels.

Fine needle aspiration cytology of the thyroid nodules will be performed after taking informed consent.

The high frequency ultra-sonogram findings will be correlated with the FNAC (fine needle aspiration cytology) findings to consider malignant/benignity.

The specificity of high frequency ultrasonography and color Doppler findings in concluding benign and malignant lesions will be determined.

Statistical Analysis

SPSS software is utilized for statistical analysis from the results obtained by comparing the USG grey scale, color Doppler findings of thyroid nodule with that of FNAC findings chi – square test used to confirm the association of high frequency ultra-sonogram grey scale, color Doppler and FNAC findings .Statistical analysis is considered significant when p values are less than 0.05.

Results

Ultra-sonogram features.

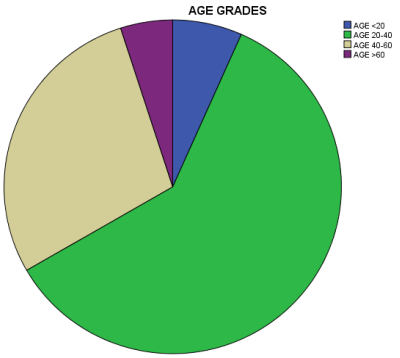
Age

In my study average age was 20-40 years and 40-60 years patients with benign as well as chronic thyroiditis and malignant nodules. Age wise there was no significant findings based on the p value.

AGE GRADES * USG DIAGNOSIS Crosstabulation

Count

		USG DIAGNOSIS			
		BENIGN NODULE	MALIGNANT NODULE	CHRONIC THYROIDITIS	Total
AGE GRADES	AGE <20	2	0	2	4
	AGE 20-40	28	1	7	36
	AGE 40-60	13	4	0	17
	AGE >60	3	0	0	3
Total		46	5	9	60

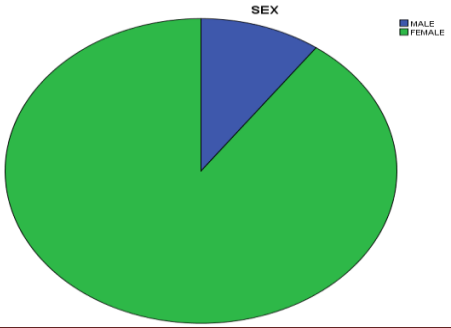


Sex wise my study shows that female predominance in benign, chronic thyroiditis and malignant nodules (40-benign, 5 malignant and 9 chronic thyroiditis). 5 males were diagnosed with benign nodule; none of them is diagnosed as malignant and chronic thyroiditis.

SEX * USG DIAGNOSIS Crosstabulation

Count

		USG DIAGNOSIS			
		BENIGN NODULE	MALIGNANT NODULE	CHRONIC THYROIDITIS	Total
SEX	MALE	6	0	0	6
	FEMALE	40	5	9	54
Total		46	5	9	60

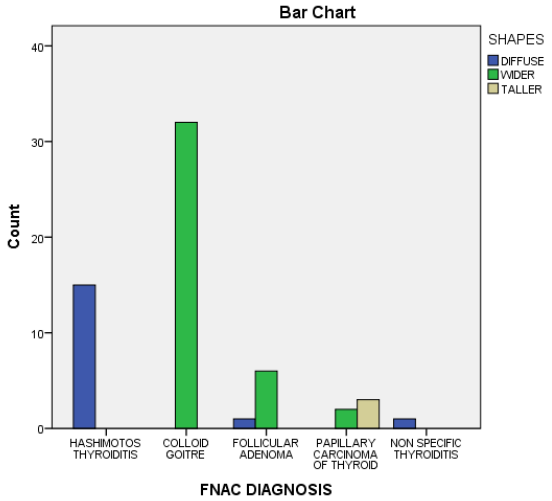


Shape

FNAC DIAGNOSIS * SHAPES Crosstabulation

Count

		Shapes			Total
		Diffuse	Wider	Taller	
Fnac Diagnosis	Hashimotos thyroiditis	15	0	0	15
	Colloid goiter	0	32	0	32
	Follicular adenoma	1	6	0	7
	Papillary carcinoma of thyroid	0	2	3	5
	Nonspecific thyroiditis	1	0	0	1
Total		17	40	3	60



Shape of the nodule showed that the malignant nodules were taller than wider and benign nodules were in favor of wider than taller, but thyroiditis did not fall in to either as it is a diffuse disease with multiple small nodules with increased vascularity.

Margins

MARGINS * USG DIAGNOSIS Crosstabulation

Count

		USG DIAGNOSIS			
		BENIGN NODULE	MALIGNANT NODULE	CHRONIC THYROIDITIS	Total
MARGINS	1.00	7	3	9	19
	2.00	39	2	0	41
Total		46	5	9	60

1-ILL DEFINED 2- WELL DEFINED

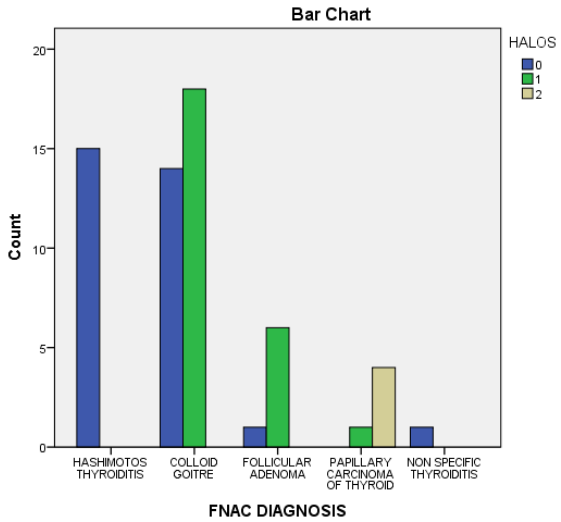
Based on the above table illdefined magin nodules go in favour of malignant and majority of the benign nodue shows well-defined margins.In this study based on the margins it is significant to tell benign or malignant.

Halos

FNAC DIAGNOSIS* HALOS Cross tabulation

Count

		Halos			Total
		0	1	2	
Fnac diagnosis	Hashimotos thyroiditis	15	0	0	15
	Colloid goiter	14	18	0	32
	Follicular adenoma	1	6	0	7
	Papillary carcinoma of thyroid	0	1	4	5
	Nonspecific thyroiditis	1	0	0	1
Total		31	25	4	60



0-No Halo, 1-Complete and 2-Incomplete

The above table shows that incomplete halo is a feature of malignant nodule where as complete and no halo is feature of benign nodule .In this study it is significant to tell whether a nodule is either malignant or benign.

No of nodules

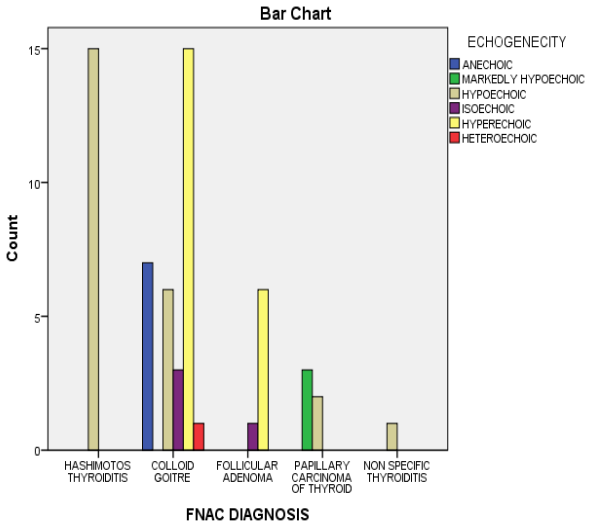
NO. OF NODULES * USG DIAGNOSIS Crosstabulation

Count

		USG DIAGNOSIS			
		BENIGN NODULE	MALIGNANT NODULE	CHRONIC THYROIDITIS	Total
NO. OF NODULES	SINGLE	18	2	0	20
	MULTIPLE	28	3	9	40
Total		46	5	9	60

Based on the above table no of nodules does not show significant sensitiveness in identifying the nature of the thyroid disease (benign vs malignant vs thyroiditis).

Echotexture



FNAC DIAGNOSIS * ECHOGENECITY Crosstabulation

Count

		Echogenicity						Total
		Anechoic	Markedly hypoechoic	Hypoechoic	Isoechoic	Hyperechoic	Heteroechoic	
Fnac diagnosis	Hashimotos thyroiditis	0	0	15	0	0	0	15
	Colloid goiter	7	0	6	3	15	1	32
	Follicular adenoma	0	0	0	1	6	0	7
	Papillary carcinoma of thyroid	0	3	2	0	0	0	5
	Nonspecific thyroiditis	0	0	1	0	0	0	1
Total		7	3	24	4	21	1	60

Based on the above table malignant lesions shows markedly hypoechoicechotexture and benign lesions show wide variety of echotexture from anechoic, isoechoic, hyperechoic, hypoechoic to heteroechoic nature. By this we come to conclusion that most of the malignant lesions are hypoechoic in nature. Benign nodules show wide variety of echotexture.

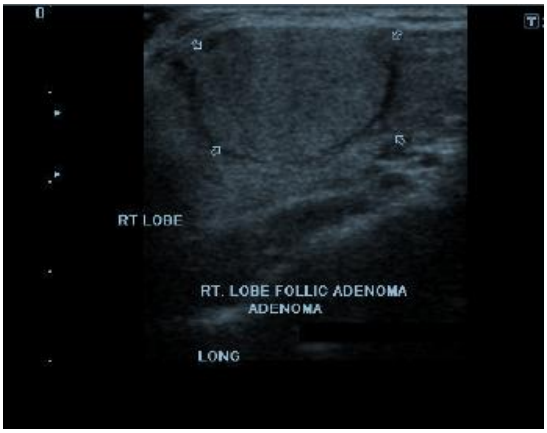


Fig. Transverse ultrasound scans showing a well-defined solitary echogenic nodule in (R) lobe of thyroid suggestive of follicular neoplasm

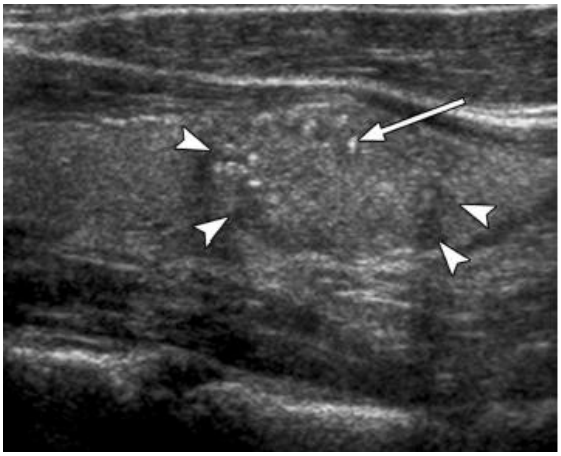
Calcification

CALCIFICATION STATUS * USG DIAGNOSIS Crosstabulation

Count

		USG DIAGNOSIS			
		BENIGN NODULE	MALIGNANT NODULE	CHRONIC THYROIDITIS	Total
CALCIFICATION STATUS	NO CALCIFICATION	39	3	9	51
	EGG SHELL CALCIFICATION	1	1	0	2
	MICRO CALCIFICATION	0	1	0	1
	MACRO CALCIFICATION	6	0	0	6
Total		46	5	9	60

The above table shows that most of the thyroid lesions show no calcification but in case of benign lesion macro calcifications are common, with malignant lesions it shows micro calcifications are common. Egg shell calcification shown equally in both benign and malignant lesion in the present study. There is a significant in the presence of calcification in diagnosing malignant from benign lesion.



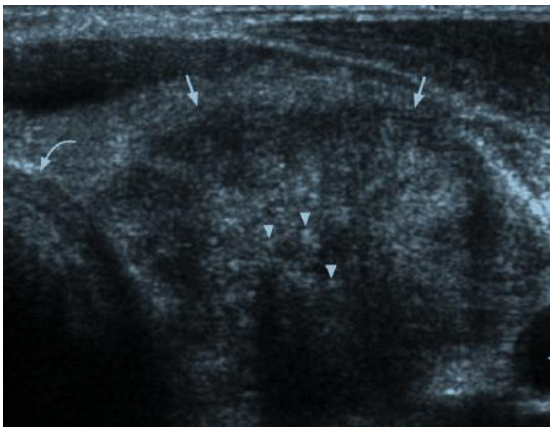


Fig. Transverse scan showing well defined markedly hypoechoic nodule in left lobe of thyroid with micro calcifications and thick irregular halo around it suggestive of malignancy

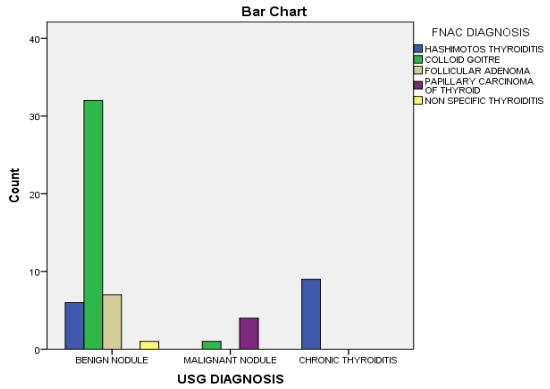
Lymph node status: In this all the malignant nodule showed lymph node involvement while benign and inflammatory nodules did not show lymph node involvement in this study we did Detailed study was not done due to small sample size.

Ultra-sonogram versus FNAC

USG DIAGNOSIS * FNAC DIAGNOSIS Crosstabulation

Count

		FNAC DIAGNOSIS					
		HASHIMOTOS THYROIDITIS	COLLOID GOITRE	FOLLICULAR ADENOMA	PAPILLARY CARCINOMA OF THYROID	NON SPECIFIC THYROIDITIS	Total
USG DIAGNOSIS	BENIGN NODULE	6	32	7	0	1	46
	MALIGNANT NODULE	0	1	0	4	0	5
	CHRONIC THYROIDITIS	9	0	0	0	0	9
Total		15	33	7	4	1	60



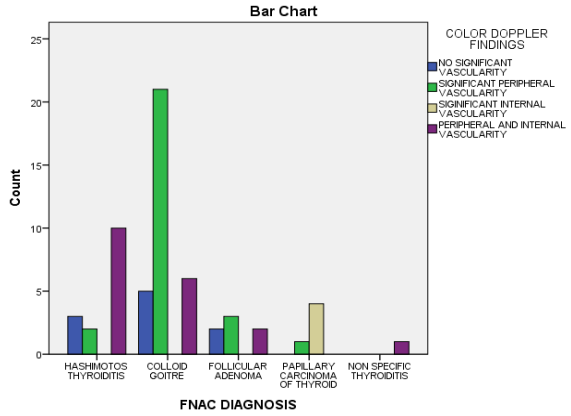
Above table shows high frequency ultra-sonogram shows significant p value (0.0001) suggesting that based on the grey scale features (Shape, margin, echotexture, halo and calcification) is 100 % sensitive in diagnosing benign lesions like colloid goiter, follicular adenoma),malignant (papillary carcinoma) and chronic inflammatory conditions like hashimotos thyroiditis.

Color Doppler

COLOR DOPPLER FINDINGS * FNAC DIAGNOSIS Crosstabulation

Count

		FNAC DIAGNOSIS					
		HASHIMOTOS THYROIDITIS	COLLOID GOITRE	FOLLICULAR ADENOMA	PAPILLARY CARCINOMA OF THYROID	NON SPECIFIC THYROIDITIS	Total
COLOR DOPPLER FINDINGS	NO SIGNIFICANT VASCULARITY	3	5	2	0	0	10
	SIGNIFICANT PERIPHERAL VASCULARITY	2	22	3	0	0	27
	SIGINIFICANT INTERNAL VASCULARITY	0	0	0	4	0	4
	PERIPHERAL AND INTERNAL VASCULARITY	10	6	2	0	1	19
Total		15	33	7	4	1	60



The above table shows that malignant lesions show significant internal vascularity when compared to benign (colloid, follicular adenoma) showed significant peripheral vascularity. Whereas thyroiditis showed both peripheral and internal vascularity.as per p value 0.0003 thyroid nodule vascularity is significant in diagnosing benign and malignant thyroid lesions as well as thyroiditis.

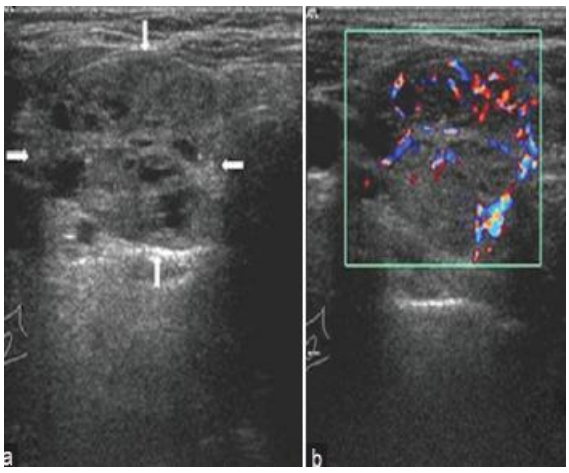


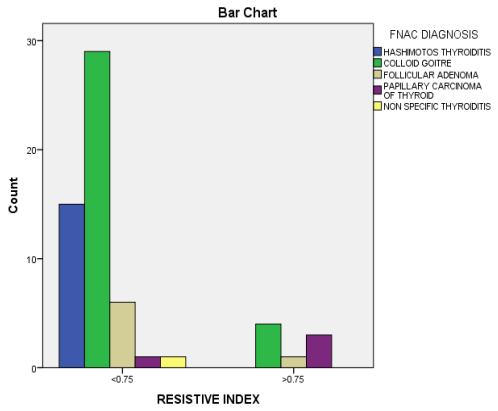
Fig. Trans verse scans showing increased intra nodular vascularity in left lobe of thyroid biopsy proven papillary carcinoma of thyroid.

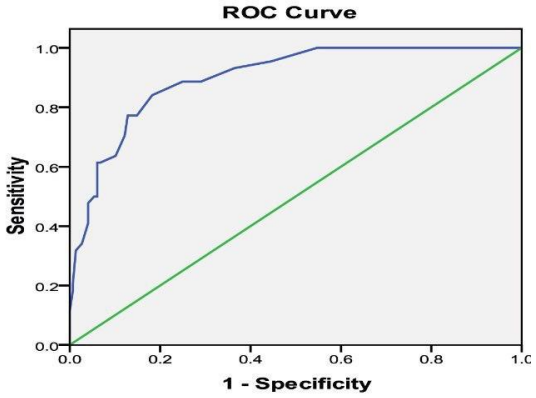
Resistive index

RESISTIVE INDEX * FNAC DIAGNOSIS Crosstabulation

Count

		FNAC DIAGNOSIS					
		HASHIMOTOS THYROIDITIS	COLLOID GOITRE	FOLLICULAR ADENOMA	PAPILLARY CARCINOMA OF THYROID	NON SPECIFIC THYROIDITIS	Total
RESISTIVE INDEX	<0.75	15	29	6	1	1	52
	>0.75	0	4	1	3	0	8
Total		15	33	7	4	1	60





Receiver operating characteristics curve shows relationship between sensitivity and specificity of RI for each cut off value.

The above table shows resistive index is significant parameter to diagnose benign and malignant .RI value >0.75 is in favor of malignant and RI value < 0.75 goes in favor of benign (follicular, colloid goiter) and thyroiditis (hashimotos and non-specific).

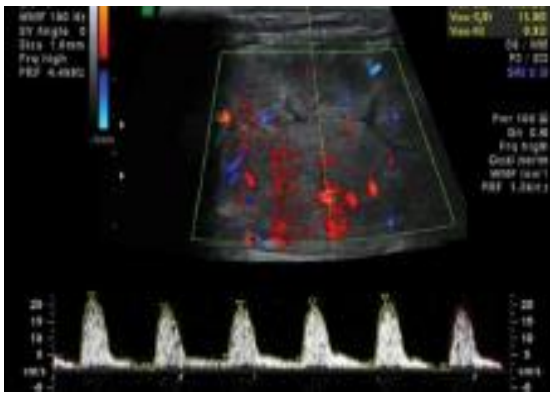


Fig Transverse scan shows (RI>0.75) in a biopsy proven papillary carcinoma.

Discussion

As thyroid nodule is one of the presentations in the spectrum of thyroid lesions it becomes essential to identify malignant condition by using reliable investigations [20]. The exact pathology of the thyroid nodule is characterized by Tru-cut biopsy. Old studies indicate that it is not necessary to do FNAC for all incidentally diagnosed thyroid nodules because cost and unpractical. Nodules which show features suggestive of malignancyin ultra-sonogram are subjected to needle aspiration. In my study age and sex did not show any significant p values though there was female sex predominance in both benign and malignant nodules but it did not show any importance in differentiating benign from malignant but there are some studies which showed that age and sex significant[2,5,21]. In my study number of nodules did not show any prediction of malignancy size criteria was not included in this study as such in some of the studies done earlier also stated that number and size of the nodules did not matter[2,5,21]. Whereas the echotexture of the nodule shows that more the hypoechoic in nature it signifies malignancy and this was substantiated one of the studies[5]. While anechoic nature goes in favor of the benign nodule which could not be justified in some of the older studies[9]. In this study there were significant p values (<0.05) for the following USG features margins, micro calcification, halo showed that based on the earlier said features it was able predict and diagnose thyroid nodule as benign or malignant which was later confirmed with the biopsy.[5, 20, 22]

The importance of color Doppler investigations as shown by many older studies it is affected by PRF, filter, position of the nodule, swallowing, respiratory movements and noncooperation of the patient however recent studies showed it did not matter that color Doppler are able to predict benign and malignant nodules as well as chronic thyroiditis.[5,10,19]In this study malignant nodules showed significant intra nodular vascularity which is supported by the study done by Mohammad et al.[28] however there are studies which showed contradictory to the above said vascularity pattern such as Tamsel et al, Argalia et al.[25,26,27]

RI assessment of thyroid nodule showed no interference either arterial course, angle of the probe and size of the nodule but however velocity of the blood flow is affected to an extent by the above said parameters. The present study shows higher RI values for malignant conditions. There are studies which showed similar results of higher RI values for malignancy, this was similar to the present study. As the study population is too small for the study it actually requires larger population to analysis comprehensively.

With the above findings the present study shows both ultra-sonogram and color Doppler investigations are significant in diagnosing benign and malignant nodules with accuracy rate of 100 % then either of them alone high frequency ultra-sonogram (98%), color and RI spectral (94%).

Modality	SEN in %	SPE in %	PPV in%	Accuracy in %
USG	100	98.25	80	98.3
Color + RI	100	100	59.7	94.3

Study limitations

Elastography is not used because of non-availability in the USG equipment used for study. Recent studies show that Elastography features of thyroid are utilized for identifying malignant nodules based on the density parameter. Since our institution is located in economically backward place the study population is very limited and follow up of patients is difficult due to constant referral to other centers for further evaluation so post-operative Histo-pathological findings was not available for the comparison.

Conclusion

Color Doppler sonography is a safe, fast, inexpensive, popular, and cost-effective.

Repeatable noninvasive procedure for investigating thyroid gland. Because of the superficial location and good vascularization of the Thyroid gland, high resolution grayscale and color Doppler sonography can demonstrate normal thyroid anatomy and pathological conditions with remarkable clarity. Our experience demonstrates significantly improved sensitivity for highreso-lution ultrasound over other investigations for the anatomic characterization of thyroid lesions. Ultrasound is valuable for identifying many malignant or potentially malignant thyroid nodules. Although there is some overlap between the ultrasound appearance of benign nodules and that of malignant nodules, certain features are helpful in differentiating between the two. The newly developed high resolution ultrasonography with color doppler flow mapping function canreveal fine details of the thyroid gland and the hemodynamic features of thyroidneoplasms.

Color flow doppler sonography is gaining importance for the functional evaluation of the thyroid disorders. Color flow Doppler sonography could differentiate the untreated Graves disease from the Hashimotos thyroiditis, which has similar gray scale findings. Thyroid ultrasound differentiates solid from cystic lesions, solitarynodules from multinodular and diffuse enlargement, and extra thyroidal lesions. The other advantages of thyroid ultrasound are very accurate method of calculation of thyroid volume. Finely in selected cases, direction of fine needle aspiration biopsy can be best accomplished with sonography.

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