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Role of Gray Scale Ultrasound and Colour Doppler in Evaluation of Thyroid Nodules with Pathological Correlation

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Abstract
Background: *Nodular thyroid disease is detected in 3–7% of the adult population worldwide. Thyroid cancer is rare and accounts for <1% of all malignant neoplasms. The high prevalence of thyroid nodules in the general population calls for a clear strategy to identify patients in whom surgical excision is genuinely indicated as opposed to those who can be managed conservatively.*
Materials: *The study was carried out on 102 patients. Patients were examined in supine position with pillow underneath the shoulders to slightly extend the neck. GE LOGIQ P5 Ultrasound, SIEMENS ACUSON X300 were used for examination. On Gray Scale, each nodule was assessed for margins, Peripheral halo, echogenicity, composition, calcification, shape, and Lymph nodes were assessed for the loss of fatty hilum. All nodules were examined by Color Doppler to describe the vascular patterns. Each ultrasound diagnosis was matched with the histopathology/FNAC results and labelled as True Positive, True Negative, False Positive and False Negative. The pathology result was considered as the final diagnosis*
Results: *Of the 102 nodules examined, 9 were found to be malignant on pathology. Nodular thyroid disease was more common in female population as compared to male population. The malignant nodules demonstrated solid composition (sensitivity 100%, specificity 64.5%); presence of microcalcification (sensitivity 33.3%, specificity 95.7%); ill defined margins (sensitivity 33.3%, specificity 89.4%); loss of central hilum in lymph nodes(sensitivity 77.8%, specificity 71.4%) and markedly hypoechoic character (sensitivity 77.8%, specificity 95.6%). The sensitivity and specificity of Intranodular vascularity as a predictor for malignancy was 66.6% and 72.0 %.*
Conclusion: *Since Gray scale and Colour Doppler have their own strengths and weaknesses, they are complementary rather than competitive modalities in diagnosing benign from malignant thyroid nodules. Combinations of Gray Scale, Color Doppler improve the detection of malignancy in thyroid nodules.*
Keywords: *thyroid, FNAC, Ultrasound, Nodule.*

Introduction

Current management guidelines (American Thyroid Association) state that diagnostic USG should be performed in all patients with thyroid nodules and fine needle aspiration (FNA) in potentially malignant nodules.

In addition to the controversy regarding the use of Doppler US for the differentiation of benign and malignant nodules, there is no consensus which type of vascularity would be considered suspicious of malignancy.

Finally, even when vascularity is taken into consideration, other ultrasonographic characteristics of the nodule continue to be important, i.e., Doppler US does not replace gray-scale ultrasound (GSUS). It is therefore important to know whether (i) an apparently benign nodule on GSUS becomes suspicious when Doppler US reveals suspicious vascularity and the probability of the nodule being benign increases when Doppler US is also not suspicious; (ii) a suspicious nodule on GSUS is no longer suspicious when Doppler US is not suspicious and its risk of malignancy increases when Doppler US is also suspicious.

Hence the present study was done to assess the utility of gray-scale USG in evaluating thyroid nodules and accurately differentiate benign and malignant thyroid nodules by gray scale ultrasound and by evaluating vascular pattern of nodules on color Doppler.

Materials and Methods

Patients

A hospital based study was undertaken on 102 patients to assess the role of Gray Scale Ultrasound and Color Doppler in evaluation of thyroid nodules with pathological correlation. Both sexes and All age groups were included in the study.

Methodology

Patients were examined in supine position with pillow underneath the shoulders to slightly extend the neck. The diagnosis was based on Gray Scale features on Ultrasonography and findings on color and Power Doppler of thyroid lesions were evaluated and correlated with the cytological Features and histopathological features. Gray Scale sonographic characteristics for each nodule were described followed by the colour doppler. CT and MRI were used as an additional tool when required to know the extent of the lesion and to aid in differentiating benign and malignant nodules.

Equipments Used

- GE LOGIQ P5 Ultrasound, SIEMENS ACUSON X300 using High frequency 7.5 MHz probe and 2-5 MHz curvilinear probe when required
- SIEMENS 1.5 TESLA MRI, SIEMENS 16 slice CT scan

Gray Scale Evaluation

On Gray Scale, following parameters were assessed for each nodule.

- The margins were assessed as well defined or ill defined.
- Peripheral halo for each nodule, was categorized as thin, regular halo; absent halo; or irregular halo.
- The echogenicity was assessed as hypoechoic, hyperechoic, isoechoic or anechoic in comparison to normal thyroid parenchyma. The hypoechoic nodules were further subclassified as markedly hypoechoic if less echogenic than strap muscles.
- The nodules were also categorized as solid(more than 75% solid), predominantly cystic(more than 75% cystic) or mixed based on their composition.
- The presence of calcification as well as type of calcification whether micro- or macro-calcification was noted. Calcification less than 2 mm was termed as microcalcification.
- The shape was determined as taller than wide or wider than taller by measuring the

antero-posterior diameter to transverse diameter ratio on transverse USG images. If AP:transverse ratio is more, then it was classified as a taller than wide nodule.

- Lymph nodes were assessed in each case for the loss of fatty hilum.

Colour Doppler Evaluation

All nodules were examined by Color Doppler to describe the vascular patterns. Nodules were identified as nonvascular, peripheral, central, or mixed (both peripheral and central vascularity). Nodules with vascularity were identified as peripheral, central, or mixed vascular.

Pathological Correlation and Statistical Analysis

Each ultrasound diagnosis was matched with the histopathology/FNAC results and labelled as following: true positive (TP) when positive USG result for malignancy is confirmed in the pathological study, false positive (FP) when positive USG result for malignancy was not confirmed in the pathological study; true negative (TN) when negative USG result for malignancy was obtained and no malignancy in the pathological result was found and false negative (FN) when negative USG result for malignancy was obtained but malignancy detected in pathological study.

Sensitivity, specificity were calculated using the formulas -

Sensitivity - SN = TP/ (TP + FN)

Specificity - SP= TN/ (TN + FP).

The pathology result was considered as the final diagnosis.

Results

Of the 102 nodules evaluated at USG, 7 were diagnosed to be malignant and 95 found to be benign After pathological evaluation, 9 of the 102 nodules were found to be malignant and 93 were benign. The most common benign lesion was colloid goiter (75.3%) followed by adenomatous nodule (17.2%), follicular adenoma (5.4%) and hashimoto's thyroiditis nodule (2.1%).The most common malignant lesions were follicular and papillary carcinoma (33.3%) followed by medullary carcinoma (22.3%) and anaplastic carcinoma (11.1%). 18.7% cases of males turned out to be malignant and 7% cases of females turned out to be malignant.

The gray scale features of benign and malignant nodules in this study are tabulated in table2.The colour doppler features of benign and malignant nodules in this study are tabulated in table 2.

Diagnostic accuracy of USG features of Thyroid nodules (Tabulated in Table 3)

The most specific sign for picking up malignancy on USG are microcalcifications, hypoechogenicity and ill-defined margins. Most sensitive signs include the loss of solid consistency, central echogenicity in lymph nodes, and hypoechogenicity.

The sensitivity of thin, peripheral halo being benign was 52.6% with a specificity of 88.9

Correlation of Ultrasound and Pathological Findings (Tabulated in Table 4)

Pathological findings showed that there were 9 cases of malignant nodules and 93 cases of benign nodules. Ultrasound accurately detected 6 cases as malignant and 92 cases as benign. There were 1 false positive and 3 false negative results. Ultrasound was found to have 66.7% sensitivity and 98.9% specificity in the detection of malignant and benign nodules.

Table 1 Gray Scale Ultrasound Features of malignant and benign thyroid nodules

Gray Scale Ultrasound Features	Malignant		Benign		Total
	N	%	N	%	
Microcalcification					
Present	3	33.3	4	4.3	7
Absent	6	66.7	89	95.7	95
Consistency					
Solid	9	100	33	35.4	42
Mixed	0	-	18	19.4	18
Cystic	0	-	42	45.2	42
Echogenicity					
Hyperechoic	0	-	38	40.8	38
Hypoechoic	7	77.8	4	4.3	11
Isoechoic	2	22.2	9	9.7	11
Anechoic	0	-	42	45.2	42
Peripheral Halo					
Thin regular Halo	1	11.1	49	52.6	50
Absent or irregular halo	8	88.9	44	47.4	52
Margin					
Well-Defined	6	66.7	85	91.4	91
Ill-Defined	3	33.3	8	8.6	11
Hilum					
Lost	7	77.8	4	28.6	11
Intact	2	22.2	10	71.4	12
Shape					
Taller than wider	4	44.4	26	28.0	30
Not taller than wider	5	55.6	67	72.0	72

Table 2: Colour Doppler findings of malignant and benign thyroid nodules

Colour Doppler findings	Malignant		Benign		Total
	N	%	N	%	
Absent blood flow	0	-	50	53.8	50
Perinodular blood flow	3	33.3	17	18.3	20
Intranodular with or without Perinodular blood flow	6	66.7	26	27.9	32
Total	9	100%	93	100%	102

Table 3 – Diagnostic accuracy of USG features for malignancy

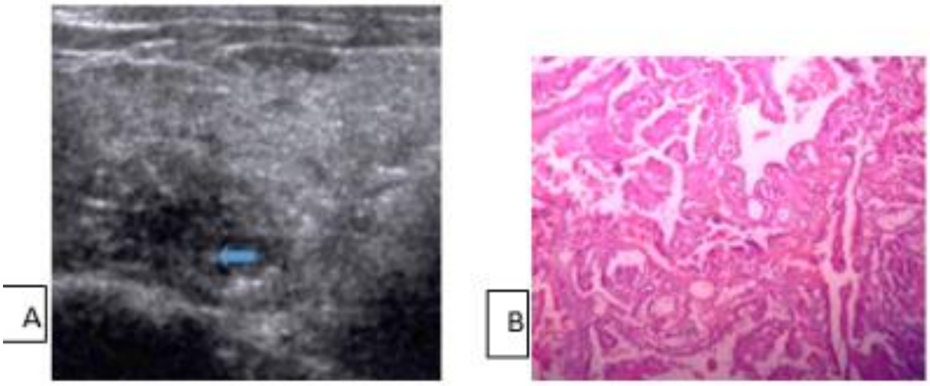
Ultrasound Features	Sensitivity%	Specificity%
Microcalcification	33.3	95.7
Solid Consistency	100	64.5
Ill defined margins	33.3	89.4
Hypoechogenicity	77.8	95.6
Taller than wide Shape	44.4	72.0
Loss of central echogenicity in lymph nodes	77.8	71.4
Intranodular Vascularity	66.6	72.0

Table 4: Correlation of Ultrasound and Pathological findings

			Pathological	
			Malignant	**Benign**
Ultrasound	**Malignant**	True Positive	6	
		False Positive		1
	Benign	False Negative	3	
		True Negative		92

	Sensitivity (%)	**Specificity (%)**	**PPV (%)**	**NPV (%)**
Ultrasound	66.7%	98.9%	85.7%	96.8%

Figure 1



A case of papillary Carcinoma-
40 y/ F came with neck swelling since 3 months.

A- USG revealed a Hypoechoic nodule with ill defined margins and microcalcifications (arrow)
B- Histopathological appearance of papillary carcinoma

Figure 2

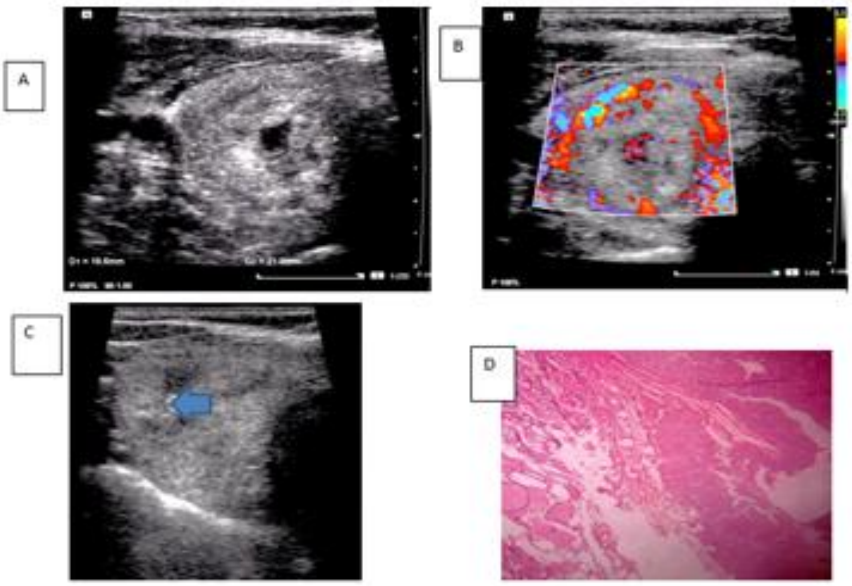


Figure 2 A case of Follicular Carcinoma

65 y/F came with painless, gradually progressive neck swelling since 5 months.

USG revealed

A- Well defined, isoechoic to hypoechoic solid nodule in right lobe of thyroid.
B- Nodule shows intranodular as well as perinodular vascularity. (predominanatlyperinodular)
C- Areas of microcalcifications(arrow) noted within the nodule
D- Histopathological appearance of Follicular Carcinoma

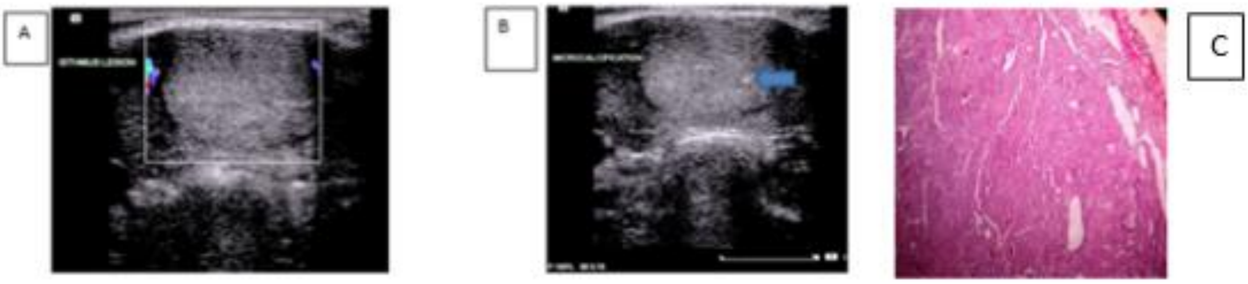


Figure 3 A case of Follicular Adenoma

50 year/M

A- Colour Doppler shows perinodular vascularity.
B- GrayScale USG -Round to oval, well defined, hyperechoic, solid nodule, located in the isthmus with thin, regular peripheral halo, and microcalcifications(arrow)
C- Histopathological appearance of Follicular adenoma

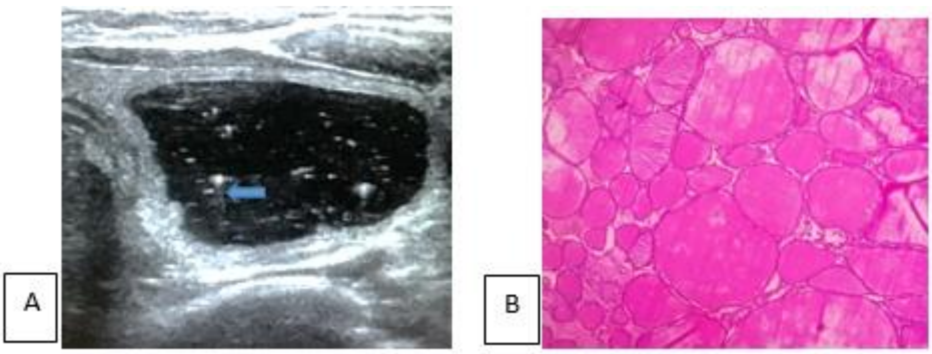


Figure 4- A case of Colloid Goitre in a 56 y/F

A- A well defined cystic nodule located in left lobe of thyroid with multiple hyperechoic foci giving a comet tail artefact.(arrow)
B- Histopathological appearance of Colloid goitre

Discussion

A thyroid nodule is defined as a discrete lesion within the thyroid gland that is distinguishable from the adjacent parenchyma at USG. Ultrasonography is the modality of choice in the initial workup of thyroid nodules to differentiate between benign and malignant nodules.

USG features that are suspicious for malignancy include predominantly solid component, hypoechogenicity, microcalcifications, ill defined margins, intranodular vascularity and loss of fatty hilum in lymph nodes.

Microcalcification had high specificity of 95.7% as a predictor for malignancy. Other patterns of calcifications found in our study included- Intranodular macrocalcifications, egg shell calcifications. Macrocalcifications were found in 1/7(14.3%) malignant nodule and 10/95(10.5%)

benign nodules. So macrocalcifications were unhelpful for diagnosis of malignancy in our study.

3 nodules were found to have egg-shell type of calcifications and were proven to be benign lesions in our study.

The specificity of hypoechogenicity as an ultrasound risk factor for malignancy was found to be high (95.6%). Popli et al in their study found that most of the malignant nodules (33/44) were hypoechoic in appearance, though the majority of the hypoechoic nodules were benign (165/198). In contrast, none of the malignant nodules were found to be purely hyperechoic or anechoic. So, they found a low sensitivity (65.9%) but an appreciable specificity (87.2%) of marked hypoechogenecity for malignant thyroid nodules. This finding was comparable with the study conducted by Popli et al

The sensitivity and specificity of solid consistency of a nodule as a predictor of malignancy is 100% and 64.5 %. Popli et alfound that most thyroid nodules were solid or predominantly solid rather than cystic or predominantly cystic. The sensitivity of solid/predominantly solid composition was found to be the high (88.6%) but the positive predictive value was only 30%, indicating that most malignant nodules are solid or predominantly solid; however, most solid or predominantly solid nodules are benign.

The sensitivity and specificity of ill-defined margins as a risk factor for malignancy was found to be 33.3% and 89.4% indicating high specificity.

The sensitivity and specificity of association of lymph node with loss of central echogenicity with thyroid malignancy was 77.8 % and 71.4 % respectively.

Colour Doppler findings in the present study showed that absent blood flow was noted in 50/93 (53.8%) benign cases. Perinodular blood flow was noted in 17/93 (18.3%) benign cases. Intranodular with or without perinodular blood flow was noted in 6/9(66.7%) of malignant cases and 26/93 (27.9%) of benign nodules. The sensitivity and specificity of Intranodular vascularity as a predictor for malignancy was 66.6% and 72.0 %.

In the malignant nodules, the findings that favored papillary carcinoma included a solid, hypoechoic nodule with irregular margins and punctate calcifications. (Figure 1) These punctate calcifications are thought to represent the psammoma bodies.

In follicular Neoplasm, the findings included hypoechoic/isoechoic, solid nodules with a peripheral halo. Hypoechoic halo represents the pseudocapsule of fibrous connective tissue or compressed thyroid parenchyma. It was difficult to differentiate follicular adenomas (figure 3) from follicular carcinomas. Findings which favoured carcinoma (Figure 2) included vascular invasion, metastases and hypoechoic component in other-wise iso/hyperechoic nodule. Nodal metastases were less common in follicular carcinoma as compared to medullary and papillary carcinoma.

There is significant overlap in USG characteristics of medullary and papillary carcinomas. In medullary carcinomas, macrocalcification may be seen and calcifications may also be seen in lymph nodes.

Colloid nodules were isoechoic to hypoechoic to anechoic. Many had echogenic foci with comet tail artifact (Figure 4). Some were completely anechoic caused by serous or colloid fluid. A spongiform/honeycomb pattern was also noted characterized by clustered similar sized, microcystic spaces separated by thin echogenic septa. Some of the nodules had echogenic debris within them likely due to hemorrhage.

In nodules due to Hashimoto's thyroiditis, the rest of the thyroid will be enlarged with heterogeneously hypoechogenicity and increased vascularity with multiple micronodules.

Within a background of diffuse Hashimoto thyroiditis, nodular Hashimoto thyroiditis is more likely to be solid, to be hyperechoic, to have a thin regular hypoechoic halo, to have no calcifications, and occur as a solitary nodule. CT scan was also done in few nodules to study the extent of local and vascular invasion and lymph nodal metastases. Thyroid nodal metastases occur in central compartment (level VI) and lateral nodal groups (level II-IV). Ct is more helpful in staging the cancer.

Limitations

The small sample size of malignancies that we encountered in our study is an important limitation.

Another potential limitation was that most of the diagnosis was made on cytology rather than histology.

Conclusion

Since Gray scale and Colour Doppler have their own strengths and weaknesses, they were complementary rather than competitive modalities in diagnosing benign from malignant thyroid nodules. Combinations of Gray Scale, Color Doppler improve the detection of malignancy in thyroid nodules and can guide us to recommend for FNAC.

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