

Comparison of Ultrasonographic Findings with Histopathological Findings of Thyroid Nodules - A Two Year Study

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A B S T R A C T

Introduction: Thyroid USG plays an important role in demonstrating thyroid anatomy and pathological conditions with remarkable clarity. The frequency of thyroid nodules by sonographic evaluation is 13% to 67% based on various literature reports globally. The present study was aimed to evaluate Ultrasonographic morphological features predictive of both benign and malignant thyroid nodules and correlation with FNAC.

Material and methods: A two year prospective study was conducted among patients with thyroid nodules. Ultrasonogram was performed with detailed clinical examination and history taking along with colour Doppler study and differentiated into benign and malignant. FNAC was performed on cases with suspicious malignancy and nodular goitre. Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV and Accuracy have been computed to find the correlation of Ultrasound and Histopathological diagnosis. P value: $0.05 < P < 0.10$ was considered significant.

Results: 50 cases with 82% females were included. Majority (54%) of cases were of solitary nodules and of 50 cases based on USG, 74% were Benign and 26% malignant but by FNAC, 78% were benign and 22% were malignant. Vascularity, margins, calcification, cystic degeneration and halo were found with significant association with malignancy. (P value < 0.01) Sensitivity and specificity of USG for differentiating benign and malignant thyroid nodules were 90.91% and 92.86%.

Discussion: Our study strongly recommends that features of USG of thyroid nodules are highly suggestive in determining the nodules as benign or malignant and clearly guides in performing FNAC. Our study suggests that Elastography and Colour Doppler USG are newer techniques which are introduced and may be good tools in determining the cases of malignant thyroid nodules. However the techniques are to be standardized.

Key words: Ultrasonogram, Thyroid nodules, Solitary nodule, Colour Doppler.

INTRODUCTION

Ultrasonography (USG) has become an important diagnostic modality in various disorders of human system. It is an important diagnostic modality in evaluating and differentiating thyroid nodules. Thyroid USG plays an important role in demonstrating thyroid anatomy and pathological conditions with remarkable clarity. Among various other imaging modalities like CT, MRI, USG is least expensive, and is non invasive, easy to perform and has does not involve ionizing radiation and with an additional advantages of real time image acquisition and portability. The frequency of thyroid nodules among general population by clinical examination is 4-7% whereas by sonographic evaluation is 13% to 67% based on various literature reports globally.¹ The incidence of malignant thyroid nodules is less than 7%. The clinical significance of thyroid nodules is related to exclude thyroid cancer, which is observed in 5-15% of cases and the causes are multifactorial depending on age, sex and other risk factors.² Various studies

conducted have described that Ultrasonographic features like microcalcifications, marked hypoechogenicity, irregular margins and central vascularity are significant characteristics in malignant nodules. These individually may be of limited value but when combined and assessed with combination of FNAC are accurate in predicting malignancy of thyroid nodules. Most of the studies report variability in diagnostic accuracy with overlapping features in USG to differentiate benign and malignant nodules of thyroid. The introduction of new Thyroid stimulating hormone (TSH) assays, widespread application of FNAC and the increasing availability and use of high – resolution USG have facilitated, modified, and improved the management of thyroid pathologies. USG should help in assessing the risk of nodule in determining benign or malignant and help in performance of USG-guided FNAC.³

The present study was aimed to evaluate Ultrasonographic morphological features predictive of both benign and malignant thyroid nodules. The study also compares the USG features in correlation with FNAC.

MATERIAL AND METHODS

The present prospective study was conducted by Department of Radio diagnosis in association with Department of surgery and Department of pathology at a tertiary care Hospital of South India for a period of 2 years from January 2015 to December 2017 after approval from the ethical committee of the institute. The details of study were informed to all the patients participating in the study and written consent was obtained. Patients not willing to participate and not willing to give the consent were excluded from the study. Patients of all ages presenting to the OPD of general surgery with Thyroid nodules were referred for ultrasound examination of thyroid. The patient's demographic details, clinical history and signs and symptoms were noted by a senior resident of surgery department. Ultra sonogram of thyroid was performed by a single senior radiologist throughout the study with real time ultrasonographic scanner machine, PHILIPS EnVisor C HD using high frequency linear transducer (3 to 12 MHz). Curvilinear transducer of lower frequency (2 to 5 MHz) was used to measure the size of the thyroid whenever necessary (e.g. in case of marked thyroid enlargement). Colour Doppler Imaging of the thyroid gland was also performed. USG findings were recorded in a written format along with a thermal print of USG images. In case of thyroid nodules features noted were pattern, texture, vascularity, margins, halo, calcifications, colloid or cystic degeneration. Nodules were classified as benign or malignant based on the characteristic features. In cases of multi-nodular goitre, nodule with greatest diameter was considered.

Malignant: Solid nature, hypo-echogenicity, central vascularity, ill-defined margins, micro-calcifications, thick and incomplete halo were taken as features suggestive of malignancy.

Tissue diagnosis with FNAC or postoperative Histo pathological examination was done. FNAC was done under USG guidance and in case of multi-nodular goitre; the nodule with USG features suggestive of malignancy was selected for FNAC.

STATISTICAL ANALYSIS

Descriptive statistical analysis has been carried out in the present study. Descriptive statistical analysis has been carried out in the present study and categorical measurements in percentage. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. Diagnostic statistics viz. Sensitivity, Specificity, PPV, NPV and Accuracy have been computed to find the correlation of Ultrasound and Histopathological diagnosis. P value: $0.05 < P < 0.10$ was considered significant.

RESULTS

The present study was conducted for two years and 50 patients were enrolled in the study with 41 (82%) females and 9 (18%) males. Majority (26%) were in the age group of 31-40 and 41-50 years. 54% of cases presented with solitary nodule, 22% with two nodules and 24% with ≥ 3 nodules. Based on the USG, 37 (74%) were benign and 13 (26%) were malignant. By Histo pathological examination, 39 were

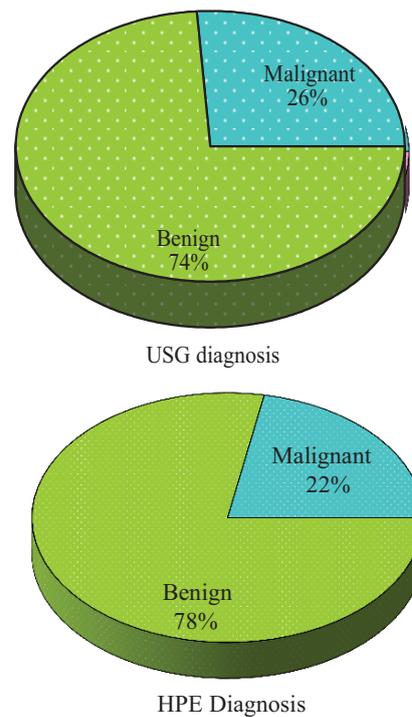


Figure-1: Ultrasound and HPE diagnosis in studied Group.

benign and 11 malignant. Three cases reported as malignant on USG were benign on HPE and one case reported as benign on USG was malignant on Tissue diagnosis. [Fig-1]

USG characteristics of thyroid nodules:

As described the various characteristics of nodules were studied and noted in a separate sheet. In the present study, 40% of nodules were solid, 16% cystic, 40% solid and cystic and 4% were cystic with septation. 76% were heterogenous and 24% were homogenous. 64% of the nodules were hypoechoic, 22% were isoechoic and 14% were hyperechoic in our study. Nodules with regular margins were observed in 78% of cases and ill-defined or irregular margins were observed in 22% of cases. 44% of the nodules in the study had calcifications with 20% micro-calcifications, 20% coarse calcifications and 4% with egg shell calcifications. 56% of cases had no calcifications. Halo was observed in 46% of nodules in the study with thin and complete halo in 38% and thick and incomplete halo in 8% of cases. Absence of halo in the nodules was observed in 54% of cases in the study. Colloid granulations were present in 18% and cystic degeneration in 50% of nodules in the present study.

USG characteristics of nodules with FNAC/HPE correlation

On correlation of USG with HPE, significance (P value < 0.01) was found with Vascularity, margins, calcification, cystic degeneration and halo and moderate significance with P value < 0.05 was found with texture of the nodule. [Table -1]

Features of Benign Nodules: Well defined margins, avascularity and peripheral vascularity, egg shell calcifications, macro calcifications and absence of calcifications and thin and complete halo were observed in all the benign nodules.

Variables	HPE diagnosis		P value
	Benign (n=39)	Malignant (n=11)	
Number of nodules			
One	18(46.2%)	9(81.8%)	0.102
Two	9(23.1%)	2(18.2%)	
Three and above	12(30.8%)	0(0%)	
Pattern			
Solid	14(35.9%)	6(54.5%)	0.340
Cystic	8(20.5%)	0(0%)	
Solid with cystic component	15(38.5%)	5(45.5%)	
Cyst with septation	2(5.1%)	0(0%)	
Texture			
Heterogeneous	27(69.2%)	11(100%)	0.046*
Homogenous	12(30.8%)	0(0%)	
Echo			
Hypo echoic	24(61.5%)	8(72.7%)	0.586
Isoechoic	8(20.5%)	3(27.3%)	
Hyper echoic	7(17.9%)	0(0%)	
Vascularity			
Avascular	10(25.6%)	2(18.2%)	<0.001**
Peripheral vascularity	15(38.5%)	1(9.1%)	
Central vascularity	1(2.6%)	6(54.5%)	
Peripheral and central vascularity	13(33.3%)	2(18.2%)	
Margins			
Well defined	34(87.2%)	5(45.5%)	0.008**
Ill defined	5(12.8%)	6(54.5%)	
Calcification			
Absent calcifications	26(66.7%)	2(18.2%)	<0.001**
Micro calcifications	1(2.6%)	9(81.8%)	
Macro calcifications	10(25.6%)	0(0%)	
Egg shell calcifications	2(5.1%)	0(0%)	
Halo			
Absent	20(51.3%)	7(63.6%)	<0.001**
Thin and complete	19(48.7%)	0(0%)	
Thick and incomplete	0(0%)	4(36.4%)	
Colloid granulation			
Absent	31(79.5%)	10(90.9%)	0.662
Present	8(20.5%)	1(9.1%)	
Cystic degeneration			
Absent	15(38.5%)	10(90.9%)	0.005**
Present	24(61.5%)	1(9.1%)	

Table-1: Correlation of Morphological variables with HPE diagnosis.

Features of Malignant nodules: Irregular margins, central vascularity, Micro calcifications, thick and incomplete halo were observed in malignant nodules.

Presence of cystic degeneration was found to be highly suggestive of benignity, though its absence doesn't rule out benignity.

In our study, the sensitivity and specificity of USG for differentiating benign and malignant thyroid nodules were 90.91% and 92.86% respectively where as positive predictive value and negative predictive value were 76.92% and 97.50% respectively. An accuracy of 92.45% was obtained. Agreement between US diagnosis and Histopathology was Very good. (Kappa=0.78) (P value

<0.001) Ten patients were diagnosed malignant both by USG and Histopathology (TRUE POSITIVE). Three patients diagnosed as malignant by USG were shown to be benign by histopathology (FALSE POSITIVE). One patient diagnosed as benign sonographically was shown to be malignant histopathologically (FALSE NEGATIVE). Thirty nine patients were diagnosed to be benign both by USG and Histopathology (TRUE NEGATIVE)

DISCUSSION

High Resolution USG of thyroid plays a very valuable role by identifying thyroid nodules at risk for malignancy depending on certain sonographic features including

hypoechoogenicity, increased vascularity, micro calcifications, irregular margins and the absence of a halo. Ultrasonography guides to determine which nodules require FNAC in cases of small or multiple nodules. In our present study as universally claimed female preponderance was observed with a male to female ratio of 1:4.5. In our present study 27% of females had malignant nodules in comparison with 18.2% of males with malignant nodules. In spite of small size of population in our study, the incidence was higher in females as compared with the studies of Sillery JC et al.⁴ Findings of our study were contrary to the findings of Polyzos et al who reported 8% of malignant thyroid nodules in males as compared to females with 4%.⁵ In the present study the age variation is very minimal and distributed at a rate of 12 patients under 30 yrs of age, 13 patients are within 31-40 yrs of age, 13 patients were between 41-50 and 12 patients are more than 50 yrs of age. In our study malignancy is associated with >40 years of age and is supported by society of Radiologists in USG consensus conference statement held in 2004, in Washington⁶ and also by Hegedus et al and Keston Jones et al.^{7,8} The incidence of malignant nodules in our study totally was 22% which is higher than compared to other studies who reported an incidence of 4-12%. Similar incidence of malignant nodules was observed in the study of Kamaljit Kaur et al who reported an incidence of 18% in her study.⁹ One of the reasons for such a higher incidence of malignancy in our series may be a referral bias as mainly those cases with clinical suspicion is referred for the ultrasonography and for further evaluation like FNAC.

USG plays a key role in assessment and distinguishing benign from malignant nodules based on appearance of sonographic features. Features suggestive of malignancy on USG were hypo echoic pattern, absent / incomplete peripheral halo, irregular margins, micro calcifications, intranodular vascularity. Features suggestive of benign disease on USG were – Halo sign (transonic uniform rim around the mass), variable echogenicity (hyperechoic / isoechoic/ anechoic), large cystic lesion and absent vascularity or peripheral vascularity. If a solid nodule showed 3 or more features of malignancy with absence of colloid granulations and cystic degeneration was taken as malignant. There were 20 (40.0%) solid nodules, 8(16.0%) cystic nodules, 20(40.0%) solid with cystic component and the rest 2 (4.0%) were cyst with septations. Out of the 20 solid nodules, 6 (54.5%) were found to be malignant and 5 out of 20 solid nodules with cystic component harboured malignancy. Out of 50 nodules, 32 were hypoechoic and 8 out of these were malignant and 24 benign nodules also showed hypoechoic pattern. A peripheral hypoechoic halo was absent in 7 out of 11 malignant nodules resulting in a sensitivity of 63.6%. Presence of a thick and incomplete halo has a sensitivity of 36.4% for malignancy. So, the absence of halo and presence of a thick incomplete halo were significant in predicting malignancy. According to Rago et al, the absence of halo has a specificity of 77% and sensitivity of 67% in predicting malignancy.¹⁰ According to USG consensus conference statement, absence of halo has a sensitivity of 17.4 – 77.5%, specificity of 38.9 – 85.0%, PPV of 9.3 – 60.0% and NPV of 38.9 – 97.8%.

In our study, micro calcifications were seen in 9 out of

10 malignant cases and in only 1 out of 39 benign cases. Micro calcifications have sensitivity of 81.8% in predicting malignancy which is in consensus with an article which says, presence of micro calcifications is known to be highly suggestive of malignancy.¹¹ Interruption and thickening of peripheral calcifications, and internal echogenicity showed statistical significance in differentiation of benign and malignant nodules in the present study which was similar to reports of Seiberling KA et al.¹²

CONCLUSION

Our study strongly recommends that features of USG of thyroid nodules are highly suggestive in determining the nodules as benign or malignant and clearly guides in performing FNAC. However based on the features of USG alone Benign or malignant cannot be ruled out. USG definitely would be helpful in selecting better patients for FNAC and in cases where surgery should be indicated with indeterminate cytology. Our study suggests that Elastography and Colour Doppler USG are newer techniques which are introduced and may be good tools in determining the cases of malignant thyroid nodules. However the techniques are to be standardized.

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