HIGH RESOLUTION SONOGRAPHIC EVALUATION OF PALPABLE THYROID LESIONS WITH HISTOPATHOLOGICAL CORRELATION- A PROSPECTIVE STUDY

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ABSTRACT: Thyroid lesions are found in 3-7% of population worldwide. The overwhelming majority of thyroid nodules are benign in nature. Thyroid cancers are rare; however thyroid carcinoma is the most common malignancy involving the endocrine glands and is responsible for approximately 1.5% of new cancer cases annually. The clinical challenge is to distinguish the few clinically significant malignant nodules from the many benign nodules because malignant thyroid lesions shows good long term prognosis after surgical excision. *Aims*: To Assess the sensitivity and specificity of sonographic findings in differentiation of benign and malignant thyroid lesion. *Method:* A hospital based prospective study was done on 100 patients with palpable thyroid nodules using high resolution ultrasonography and findings correlated with fine needle aspiration cytology. *Result:* Sensitivity and Specificity of sonography to differentiate benign and malignant thyroid lesions (FNAC correlation) was 70.59 % & 96.39 % respectively. Presence of non shadowing echogenic cholesterol crystals showed high sensitivity of 58.70 % and specificity of 83.33 % for benign thyroid nodules. Sensitivity and Specificity of absence of thin peripheral halo around malignant lesions were 70.4 % & 65.8% respectively. Sensitivity and Specificity of hypoechogenicity for malignant lesions were 64.71 % and 98.80 %.Presence of fine calcification was showing high Sensitivity & Specificity of 64.71 % and 93.98 % respectively in malignant lesions. Predominant intra-nodular colour flow pattern in solid nodules was predictive of malignancy with Sensitivity 82.35 and Specificity 84.34 %. Higher RI value (greater than 0.77) were significantly found in malignant lesions with sensitivity of 78.57 % and specificity of 92.31%. Solid and predominantly solid lesions show high Sensitivity, Specificity for being a malignant lesion 70.59 % & 55.42 respectively but less Positive Predictive Value of24.49 %. *Conclusion:* Sonographic characteristics of marked hypoechoic echotexture, solid and predominantly solid nature, absence of peripheral halo, presence of cholesterol crystals, fine calcification, and internal vascularity with high resistive index show high diagnostic accuracy to differentiate benign and malignant lesions.

INTRODUCTION: Thyroid lesions are common among general population. It may be due to nodular or diffuse involvement of thyroid gland. Nodular thyroid diseases are relatively common, found in 3-7% population worldwide[1]. Majority of these lesions are clinically occult, but rapidly detected by high resolution ultrasonography[2].Majority of nodular thyroid diseases are caused by hyperplasia of gland. The overwhelming majority of thyroid nodules are benign in nature. Thyroid cancers are rare. However, thyroid carcinoma is the most common malignancy involving the endocrine glands and is responsible for approximately 1.5% of new cancer cases detected annually[3].Diffuse thyroid diseases usually show generalized enlargement of gland and no palpable nodules. It occurs in hashimoto`s thyroiditis, adenomatous goiter and graves' disease. The prevalence of diffuse goiter declines with age, the greatest prevalence is in pre-menopausal women, and the ratio of women to men is at least 4:1[4].

The clinical challenge is to distinguish the few clinically significant malignant nodules from the many benign nodules because malignant thyroid lesions show good long term prognosis after surgical excision. During the past decade, the use of high resolution sonography has resulted in high rates of detection of thyroid nodules, but characterization of nodules as either benign or malignant remains problematic because of considerable overlap in sonographic features[5].

In the study, we want to explore the different characteristic echogenic patterns represented by the various types of thyroid nodules to provide information for diagnosis and to determine the sensitivity and specificity of each characteristic feature to differentiate between benign and malignant lesions with histopathological correlation.

MATERIALS AND METHODS-Present hospital based prospective study of 100 patients was conducted from December 2010 to December 2012 on patients referred for high resolution ultrasonographic evaluation from department of General Surgery , General medicine, ENT etc. To the Department of Radiodiagnosis and Imaging at Gandhi Medical College and Hamidia Hospital, Bhopal. A total of 100 nodules of thyroid were studied sonographically in these patients (one nodule from each patient is taken for sonographic evaluation, largest one was taken in patients with multiple nodules) and all the patients would then proceed for histopathological evaluation. The cyto-histopathology diagnosis was considered as the final diagnosis. All the subjects were enrolled after detailed oral and written consents. This study was approved by ethical and scientific committee of the institute.

Ultrasonographic evaluation was performed using GE Logic 3 Expert scanner with 7 MHz linear transducer. USG features of each thyroid nodule were assessed in consensus by one consultant radiologist and one radiology resident prior to FNAC examination, both were blinded to the pathologic results.

Sonographic findings were designed to assess echogenicity, shape, borders, size, composition, calcifications, peripheral halo, cholesterol crystals and vascularity. Echogenicity categories included markedly hypoechoic (the thyroid nodule was hypoechoic in relation to the adjacent strap muscles), hypoechoic, isoechoic, hyperechoic and anechoic in relation to the adjacent normal thyroid. Size was defined as the maximal dimensions of the nodule. Composition was defined as solid, cystic and mixed. Borders were defined as smooth and irregular. Calcifications were divided into those located centrally within the nodule, peripherally and none. Posterior acoustic shadowing of at least one of the suspected calcifications was required to consider the finding present. Vascularity as determined by colour Doppler imaging was defined as absent, peripheral, or central. If

both peripheral vascularity and central vascularity were identified, the lesions were characterized as having central vascularity. Resistive index was measured in the nodules showing internal vascularity.

RESULTS: In our study on 100 patients, eighty three patients were female and 17 were male. The patients were in the range of 13 to 85 years. Majority of the patients were in the age group of 21 to 50 years with mean age of 38.4 years. Pathological evaluation was performed on all the lesions. 9 of these nodules for which FNA sample was inadequate were excluded from the study.

Of 100 nodules evaluated by ultrasonography, 83 were benign and 17 were malignant. Majority of malignant lesions showed irregular shape (11/17) and margins (13/17) with predominantly heterogenous hypoechoic echotexture (10/17). Malignant nodules were predominantly solid. No predominantly cystic nodule showed malignant characteristics in our study. 14 out of 17 nodules (83%) showed calcification, out of which 11(64%) nodules had fine calcification. Lymphadenopathy was seen with 10 out of 17 nodules. Internal Vascularity was predominantly found in the 76% nodules (13/17), while rests 4 were showing peripheral vascularity. Intra-nodular vascularity was predominantly showing high resistive index (RI > 0.77). Thin peripheral halo around the nodules was seen only in 17% nodules (3/17), while83% nodules (14/17) showed thick and incomplete halo around the lesion. Only 1 out of 17 nodules showed cholesterol crystals in the regions of degeneration / necrosis.

Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of each sonographic characteristic were determined.

SONOGRAHIC FEATURES OF BENIGN AND MALIGNANT NODULES

SONOGRAPHIC FEATURES	BENIGN	MALIGNANT
Shape		
Round	20	5
Oval	30	1
Irregular	23	11
Margins		
Regular	43	4
Irregular	23	13
Echotexture		
Hyperechoic	14	2
Hypoechoic	8	10
Isoechoic	15	-
Mixed	41	5
Anechoic	5	-
Homogenicity		
Homogenous	26	2
Heterogenous	57	15
Calcification		
Fine	5	11
Coarse	23	3

Vascularity Peripheral Internal Avascular	 39 13 23	 4 13 -
Lymphadenopathy	8	10
Thin peripheral halo	56	3
Cholesterol crystals	27	1
Infiltration of adjacent muscles	-	1

In our study, overall Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of sonographic diagnosis in FNAC correlation were 70.59%, 96.39 %, 80.00 % and 94.12 % respectively.

SENSITIVITY &SPECIFICITY OF USG AND FNAC

	FNAC		TOTAL
USG	Malignant	Benign	
Malignant	12(12%)	3(3%)	15
Benign	5(5%)	80(80%)	85
Total	17	83	100

DISCUSSION: The thyroid diseases are eluding medical personnel since its evaluation. The diseases of thyroid have such a varying presentation that it is impossible to reach an accurate clinical diagnosis. Thyroid nodule was defined as a discrete lesion with in thyroid gland which was distinguished separately from adjacent normal parenchyma at sonography (Mortenson et al).

In our study, we diagnosed 85 nodules as benign, out of which 80 nodules were found to be benign on FNAC. 5 cases were found to be false negative. Sonographically, 15 nodules were diagnosed as malignant, out of which 12 nodules were confirmed as malignant by FNAC. 3 nodules were diagnosed false negatively as malignant and were diagnosed as benign lesions by FNAC.

In our study Sensitivity , Specificity , Positive Predictive Value and Negative Predictive Value of sonographic diagnosis with FNAC correlation were 70.59 % , 96.39 % , 80.00 % & 94.12 % respectively .So accuracy of our sonographic examination yields up to 92% , which corresponds to the accuracy of studies of Rausen (1979) , Ahuja(1992) , Park(2000) ,Beland (2010) and others .

USG Characteristics Of Malignancy	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Predominantly solid nature	70.59 %	55.42 %	24.49 %	90.20 %
Hypoechoic echotexture	64.71 %	98.80 %	91.67 %	93.18 %
Incomplete thick peripheral halo	70.4 %	65.8%	31.6 %	90.8 %
Microcalcification	64.71 %	93.98 %	68.75 %	92.86 %
Intra-nodular vascularity	82.35 %	84.34 %	51.85 %	95.89 %.
R.I. > .77 in intra-nodular vascularity	78.57 %	92.31 %	91.67 %	80.00 %

Internal composition of the lesion is divided into solid, mixed and cystic types. According to Moon et al, mixed lesions and those containing less than 50% cystic areas are considered as predominantly solid and those containing more than 50% cystic areas are considered predominantly cystic. Using the same criteria our study showed solid and predominantly solid lesions were more in number than cystic and predominantly cystic lesions. We found high Sensitivity, Specificity and Negative Predictive Value of solid and predominantly solid lesion being a malignant lesion and these were 70.59%, 55.42 % & 90.20 % respectively[7]. But Positive Predictive Value was less -24.49 %, consistent with the findings of popli and Rastogi et al, which indicates most malignant lesions were solid and predominantly solid[6].

Marked hypoechoic pattern of thyroid nodule was favoring the diagnosis of malignant nodules as 11 out of 17 malignant nodules showed hypoechoic echotexture in our study while only 1 out of 83 benign nodules was showing hypoechoic echotexture. None of the malignant nodule was showing purely hyperechoic or anechoic echotexture. Kim et al defined marked hypoechoic nodule as one that is hypoechoic to strap muscles anterior to thyroid gland[8]. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of hypoechogenicity for malignant nodules in recent study were 64.71 %, 98.80 %, 91.67 % and 93.18%.Moon and Jung et al, found sensitivity of 41.4% and specificity of 92.3% for hypoechogenicity in their study[7].

A peripheral halo of decreased echogenicity is seen around hypoechoic and isoechoic nodules and is caused by either the capsule of the nodule and surrounding vessels in benign nodules. This halo is usually complete and thin. Thick, irregular and incomplete halo seen around malignant nodules is thought to be due to compression of the normal thyroid tissue by rapid growth of the tumors. 51 out of 83 benign nodules were showing thin peripheral halo around them, while only 3 out of 17 malignant nodules were showing peripheral halo. Our study demonstrates Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of presence of incomplete thick irregular halo around malignant nodules as70.4 %, 65.8%, 31.6 %and 90.8 % respectively. Our findings were consistent with the study of Popli and Rastogi et al.

Calcification found in the thyroid lesions were predominantly fine and coarse pattern. Fine or micro calcification shows significant relation with the malignant lesions however benign lesions also show fine pattern of calcification. Micro calcifications are seen sonographically as multiple punctate bright echoes of size less than 2 mm, with or without acoustic shadow. In our study 11 out of 17

malignant nodules were showing fine calcification while 5 cases out of 83 benign nodules showed fine calcification. The Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of presence of fine calcification in malignant nodules were 64.71 % , 93.98 % , 68.75 % and 92.86 % respectively in our study , which were correlated with the findings of Moon and Jung et al , they find out sensitivity 44.2%and specificity 90.8% for fine calcification in their study[7]. Kakkos, Scopa and Chalmoukis et al, stated micro calcifications are highly specific for malignancy with a sonographic specificity of 93% to 95%.The sensitivity is lower at 29% to 59%.The positive predictive value of these calcifications for malignancy has been reported to be 70% to 71%[9].

De Nicola et al, classified the patterns of flow as types 0 to 4, defined as follows: type 0, no visible flow; type 1, peripheral flow only; type 2, peripheral flow with a small amount of central flow; type 3, peripheral flow with extensive internal flow; and type 4, central flow only[10]. The overall sensitivity of color Doppler ultrasound was 85%, specificity of 86% and positive and negative predictive values were 51% and 97%, respectively. Marked intra-nodular vascularity is seen predominantly in the malignant nodules. In recent study predominant central colour flow pattern in solid nodules was predictive of malignancy with Sensitivity, Specificity , Positive Predictive Value and Negative Predictive Value found to be 82.35 % 84.34 %, 51.85 % and 95.89 % respectively. Our findings were consistent with the study of Yunus and Ahmed et al. Their findings were 84% sensitivity and 90% specificity of intra-nodular vascularity in malignant nodules[11].

Spectral analysis demonstrated that nodules with an RI greater than 0.77 are at high risk of malignancy. The multivariate analysis showed that to select malignant nodules, the vascular patterns and RI are enough and significant. The nodules with intra-nodular vascularity demonstrated high risk when the RI was greater than 0.77. The sensitivity of this model is 78.57 % and specificity is 92.31 %. Positive Predictive Value and Negative Predictive Values were 91.67 % and 80.00 % respectively.

CONCLUSIONS: Sonographic evaluation of thyroid lesion is highly effective, accurate and helps to differentiate a malignant lesions from benign lesions with high sensitivity and specificity. In our study ultrasound features of hypoechoic echotexture, solid and predominantly solid nature, absence of peripheral halo, fine calcification, internal vascularity, high resistive index show high diagnostic accuracy to differentiate malignant lesions from benign lesions. So it should be used as a valuable adjunct to clinical examination and should be offered to all patients presenting with palpable thyroid.

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FIGURE1: An oval shaped large anechoic lesion showing bright echogenic foci (Cholesterol crystals) and horizontal fluid-fluid level of debris - colloid nodule with cystic degenerative changes.

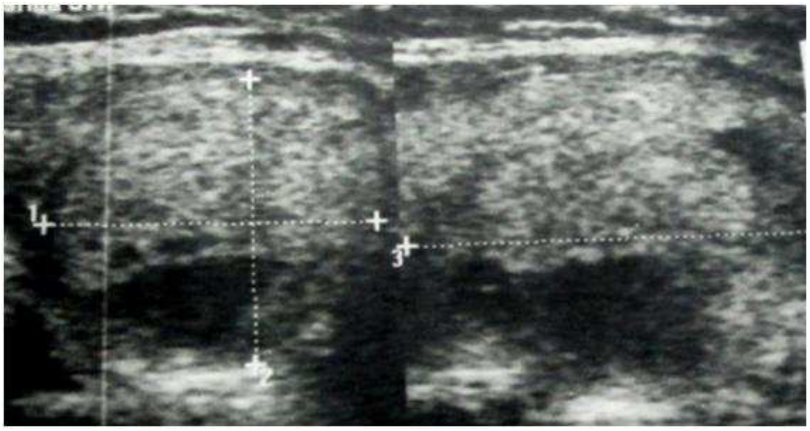
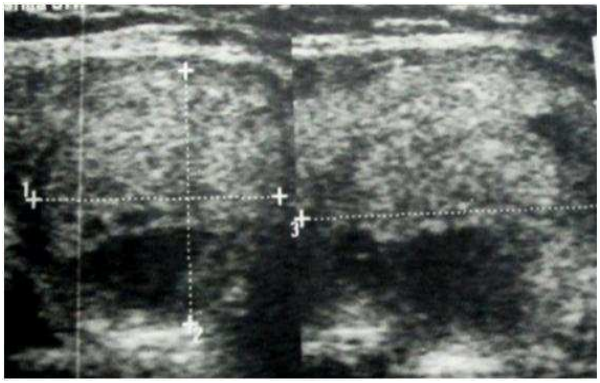


FIGURE 2: A well defined solid hyperechoic nodule with anechoic areas of degeneration, showing peripheral halo -colloid adenoma with cystic degenerative changes.



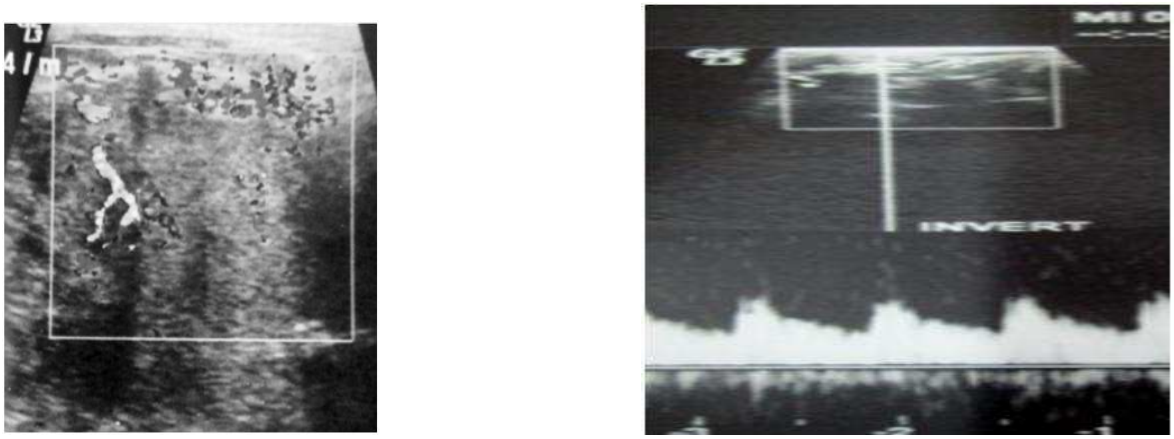


FIGURE 3: A large heterogeneous hypoechoic lesion of irregular shape and irregular margins showing internal vascularity of high resistance and low peak systolic velocity(Papillary carcinoma).Cervical lymphadenopathy was seen.

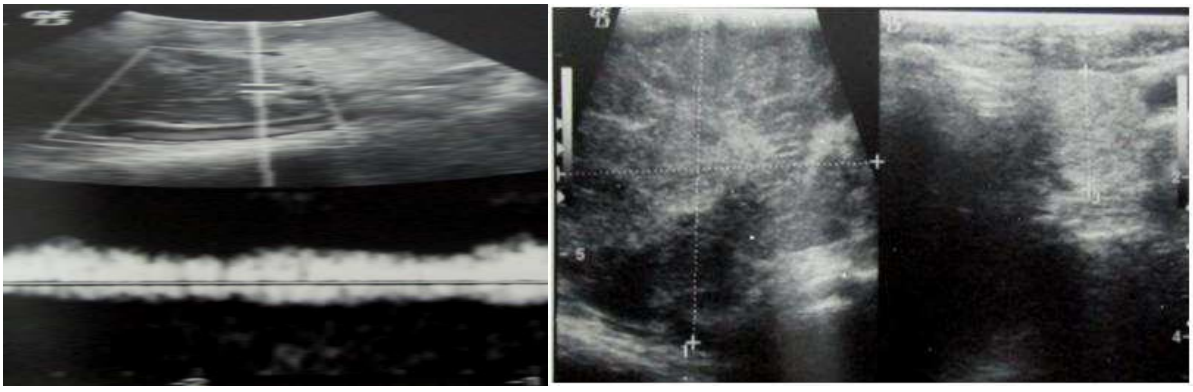


FIGURE 4: Large heterogeneous lesion in the right lobe of thyroid. Left lobe and isthmus appear normal (Follicular carcinoma).Lesion showing internal vascularity with high resistive index and low peak systolic velocity.