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Original Article

Radiology Section

Ultrasonographic Evaluation of Thyroid Nodules with Pathologic Correlation

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ABSTRACT

Introduction: Thyroid nodules are very common and can occur in upto 50% of the adult population. Ultrasonography is often the initial investigative modality used in the detection and characterisation of various thyroid nodules.

Aim: To evaluate the diagnostic accuracy of ultrasonography in characterising benign and malignant thyroid nodules by correlating the sonographic findings with pathological diagnosis as reference.

Materials and Methods: In this prospective study, a total of 138 thyroid nodules detected on ultrasonography were further evaluated with Fine Needle Aspiration Cytology (FNAC) and/or Histopathological Examination (HPE). The sonographic features such as internal composition, echotexture, shape, margins, presence or absence of peripheral halo, calcification and internal vascularity were correlated with the final diagnosis.

Results: The incidence of malignancy in this study was 10.1% (14/138). Malignant nodules tended to show solid or predominantly solid composition (sensitivity 100%, specificity 43.5%, accuracy 49.2%), hypoechoic pattern (sensitivity 85.7%, specificity 67.7%, accuracy 69.5%), taller-than-wider shape (sensitivity 64.2%, specificity 87%, accuracy 84.7%), irregular margins (sensitivity 78.5%, specificity 82.2%, accuracy 81.8%), calcifications (sensitivity 78.5%, specificity 77.4%, accuracy 77.5%), absence of peripheral halo (sensitivity 64.2%, specificity 53.2%, accuracy 54.3%) and internal vascularity (sensitivity 85.7%, specificity 64.5%, accuracy 66.6%).

Conclusion: Ultrasonography is a sensitive and specific modality in the assessment of thyroid nodules with good overall accuracy. The most useful sonographic feature that helped to predict malignancy were a solid composition, hypoechogenicity, taller-than-wider shape, irregular margins and presence of calcification.

Keywords: FNAC thyroid, Thyroid imaging, Thyroid malignancy

INTRODUCTION

Thyroid nodules are common [1]. With the widespread use of high resolution ultrasonography, many more subclinical nodules are being detected. They are found in 4% to 8% of adults by means of palpation, 10% to 41% by means of ultrasonography, and in upto 50% at autopsy [2].

However, while thyroid nodules are common, thyroid malignancy is relatively rare, constituting about 1% of all malignancies [2,3]. Thyroid cancer is reported to occur in about 5% to 7% of all thyroid nodules, irrespective of size [3-5] and 9.2% to 13.0% of all nodules undergoing cytologic evaluation are reported as malignant [2].

In view of this, the pre-operative evaluation of thyroid nodules is crucial to distinguish between benign and malignant nodules, so as to avoid unnecessary biopsies or surgeries in the vast majority of patients who have benign nodules.

Ultrasonography has emerged as the best method to evaluate the thyroid gland and thyroid nodules [4-6]. It is widely available, relatively inexpensive, non-invasive, has excellent resolution, detects non-palpable and clinically silent nodules, and guides for fine needle aspiration of suspicious nodules.

The purpose of this study was to study the sonographic features of various benign and malignant thyroid nodules, and to correlate the sonographic findings with Fine Needle Aspiration Cytology (FNAC) and/or Histopathological Examination (HPE), so as to evaluate the accuracy of ultrasonography in diagnosing malignant nodules.

MATERIALS AND METHODS

This prospective study was carried out at the AJ Institute of Medical Sciences, Mangalore, India, for two years between July 2013 and July 2015. The study was approved by our institutional ethics committee, and informed consent was obtained from all patients. Patients who were referred for ultrasonographic evaluation of the thyroid gland and detected to have thyroid nodules on USG, were subjected to further evaluation with fine needle aspiration cytology (FNAC). A total of 138 patients fulfilled these inclusion criteria, and were considered for the study. In patients with multiple nodules, the dominant nodule was evaluated with FNAC. Patients who were not evaluated with FNAC, or had inadequate or indeterminate FNAC reports were excluded from this study. Patients with diffusely enlarged glands with multiple nodules and no intervening normal parenchyma were classified as multinodular goitre were also excluded. All 138 patients had fine needle aspiration under USG guidance after ultrasonography. Twenty four patients with FNAC diagnosis of malignancy / follicular neoplasm underwent surgical excision with histologic evaluation of the thyroidectomy specimen, thus enabling us to differentiate follicular adenoma from carcinoma.

All scans were performed on a Philips iU22 Ultrasound equipment using a high frequency 5–12 MHz probe. The nodules were assessed on the basis of internal composition, echogenicity, margins, shape of the nodule, presence or absence of peripheral halo, calcifications and internal vascularity. The nodules were categorised as solid, predominantly solid (<50% cystic changes), cystic or predominantly cystic (>50% cystic changes). The echogenicity was assessed as hyperechoic, isoechoic, hypoechoic, or anechoic in comparison to normal thyroid parenchyma. The margins were assessed as smooth (or well defined), irregular (or ill defined), and whether surrounded by a circumferential peripheral halo. Based on the shape, nodules were characterised as taller-than-wider or otherwise. Calcifications, when present were characterised as microcalcifications (tiny calcifications <2mm without shadowing) or macrocalcifications (>2mm) which includes coarse as well as curvilinear, or "rim" calcifications. Presence of internal vascularity on Doppler was documented.

These ultrasonographic findings were tabulated and correlated with the final pathological diagnosis. The data thus obtained was entered into Microsoft Excel spreadsheet, and the sensitivity, specificity and accuracy for each of the findings were calculated.

RESULTS

There were 118 females (age range of 18 years to 67 years) and 20 males (26 years to 72 years) in this study. Of the 138 nodules that were encountered, 124 were benign and 14 were malignant [Table/Fig-1]. Ultrasonography was able to correctly identify 10 out of 14 malignancies, and 118 out of 124 benign nodules. Ten nodules were described as suspicious for malignancy on USG; final pathologic diagnosis was malignancy in 2 cases, benign follicular nodule in 7 cases and focal thyroiditis in 1 case.

Final Diagnosis (FNAC / HPE)	No. of Cases
Malignant (n = 14)	
Papillary Ca	9
Follicular Ca	3
Medullary Ca	1
Anaplastic Ca	1
Benign (n = 124)	
Colloid Nodule	90
Follicular Adenoma	10
Hashimoto's Thyroiditis	4
Subacute Thyroiditis	2
Cyst	18

[Table/Fig-1]: Final diagnosis and number of cases.

The USG findings in these 138 nodules are summarised in [Table/Fig-2]. All the nodules that were diagnosed as malignant in our series were solid or predominantly solid lesions on USG. None of the cystic/predominantly cystic nodules

USG Features	Malignant	Benign	Total
Internal composition			
Solid	10	46	56
Predominantly solid	2	24	26
Predominantly cystic	0	12	12
Cystic	0	18	18
Honeycomb	0	26	26
Echogenicity			
Hyperechoic	2	66	68
Hypoechoic	12	40	52
Anechoic	0	18	18
Shape			
Taller-than-wider	9	12	21
Not taller-than-wider	5	112	117
Margins			
Well defined	3	102	105
Ill defined	11	22	33
Peripheral Halo			
Present	7	15	22
Absent	5	111	116
Calcification			
Present	11	28	39
Absent	3	96	99
Internal vascularity			
Present	12	44	56
Absent	2	80	82

[Table/Fig-2]: USG features of various benign and malignant thyroid nodules.

were malignant. The majority of malignant nodules (12/14) showed hypoechoic internal echo texture, while most benign nodules (89/124) were either hyperechoic or anechoic (cystic). Similarly, majority of malignant nodules (9/14) demonstrated a taller-than-wider shape, while benign nodules tended to show a more oval shape. Most of the malignant nodules (10/14) had poorly defined margins, i.e., the margins were either indistinct or were irregular in outline, while the majority (102/124) benign nodules showed a smooth, well-defined outline. Calcifications were seen in 11/14 malignancies and in 28/124 benign nodules. These calcifications were either microcalcification or macrocalcification. Microcalcifications were seen exclusively in papillary carcinomas in our series, occurring in 8/9 cases. Macrocalcification was seen in 5/14 malignancies and in 28/124 benign nodules. Majority of malignant lesions (12/14) showed internal vascularity within the nodule, while benign nodules predominantly were either avascular or showed a perinodular vascular pattern.

The sensitivity, specificity and accuracy for each of the findings were calculated and is given in [Table/Fig-3]. A solid or predominantly solid nodule, hypoechogenicity, a taller-than-wider shape and an ill-defined or irregular margin were found to have the highest diagnostic accuracy for distinguishing malignant from benign nodules.

USG Feature	Sensitivity (%)	Specificity (%)	Accuracy (%)
Solid/predominantly solid	100.0	43.5	49.2
Hypoechogenicity	85.7	67.7	69.5
Taller-than-wider shape	64.2	87.0	84.7
Ill-defined margins	78.5	82.2	81.8
Absent halo sign	64.2	53.2	54.3
Calcification	78.5	77.4	77.5
Internal vascularity	85.7	64.5	66.6

[Table/Fig-3]: Diagnostic accuracy of USG features in malignant thyroid nodules.

DISCUSSION

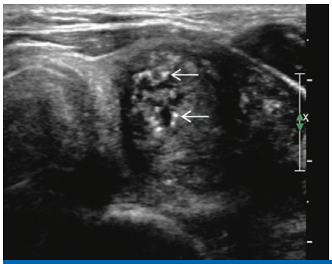
A thyroid nodule is defined as a discrete area of abnormality in the background of normal thyroid gland [2]. Thyroid nodules are common, and constitute the commonest referral for ultrasonography of the thyroid.

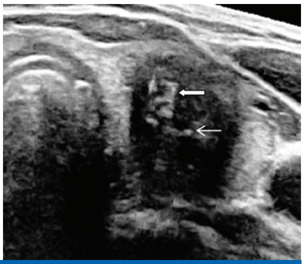
Ultrasonography is the modality of choice in the initial workup of thyroid nodules to differentiate between benign and malignant nodules [4,5]. USG features that are suspicious for malignancy include predominantly solid component, hypoechogenicity, microcalcifications, taller-than-wider shape, irregular margins, internal vascularity and absence of peripheral halo [2,4,6,7].

All the malignant nodules in our study were solid or predominantly solid, thus having a sensitivity of 100%. However, the specificity was low at 43.5%, indicating that while most malignant nodules are solid or predominantly solid, most solid or predominantly solid nodules are benign. Frates et al., reported that solid composition within a nodule had the highest sensitivity (of 69.0% to 75.4%) in predicting malignancy; however the predictive value is low, since a solid nodule has only a 15.6% - 27% chance of being malignant [2].

Malignant nodules typically appear hypoechoic [Table/Fig-4-6] when compared to the normal thyroid parenchyma. In our study, hypoechogenicity had a sensitivity of 85.7%, specificity of 67.7% and an accuracy of 69.5% in diagnosing malignancy. Moon et al., reported that a hypoechoic nodule had a sensitivity of 87.2%, specificity of 58.5% and an accuracy of 70.7% in predicting malignancy [7], which is somewhat similar to our study.

The shape of the nodule has also been studied as a potentially useful USG feature of malignancy. Malignant nodules often assume a taller-than-wider shape, i.e., antero-posterior diameter > transverse diameter on a transverse scan [Table/Fig-5]. Cappelli et al., opined that a taller-than-wider shape was a useful feature for the identification of malignant lesions in their series [8]. In our study, we found that nodules which

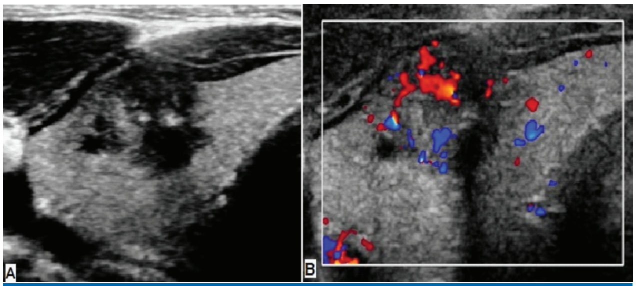




[Table/Fig-4]: A case of papillary carcinoma. USG shows a solid, hypoechoic nodule in the left lobe of thyroid gland with microcalcifications (arrows).

[Table/Fig-5]: A case of papillary carcinoma. USG shows a hypoechoic nodule in the left lobe of thyroid gland with macro (thick arrow) and micro (thin arrow) calcifications.

*Note the taller-than-wider shape and the ill-defined margins of the nodule.

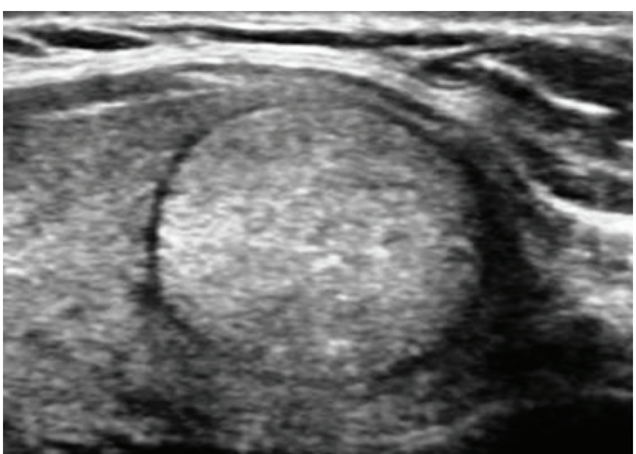


[Table/Fig-6]: Papillary carcinoma. (a) Grey scale USG showing a hypoechoic nodule in right lobe of thyroid gland with microcalcifications and ill-defined margins. (b) Doppler USG shows intranodular vascularity.

were taller-than-wider had a specificity of 87% and the highest diagnostic accuracy of 87.5% amongst all the characteristics for diagnosing a malignant nodule.

A thyroid nodule is considered to have ill-defined margins if more than 50% of its border is not clearly demarcated [6]. Malignant nodules tend to have ill-defined or irregular margins due to the infiltrative nature of their growth [Table/Fig-5,6]. The reported sensitivity of poorly defined margins in predicting malignancy varies widely (53% -89%) in the literature [6]. We found that poorly defined margins were useful in identifying malignant nodules with a sensitivity of 78.5%, specificity of 82.2% and a diagnostic accuracy of 81.8%.

A thin, well-defined peripheral halo represents displaced blood vessels coursing around the lesion [Table/Fig-7] and is considered highly suggestive of a benign nodule [6]. An incomplete or complete absence of peripheral halo is often associated with a malignant nodule, probably due to rapid growth of the tumour. Rago et al., found that the absent halo sign was the USG pattern which was most predictive of malignancy in their series, with a sensitivity of 66.6% and specificity of 77% [9]. Our study demonstrated that the absent halo sign had a sensitivity of 64.2% and an accuracy of 54.3%, indicating that it is only a modest marker for malignancy.

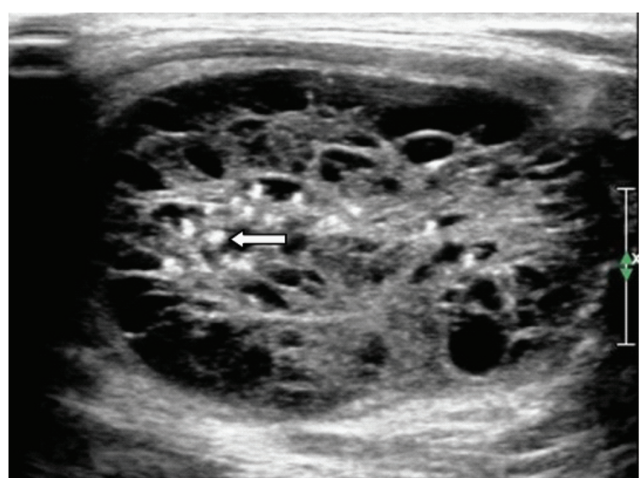


[Table/Fig-7]: FNAC proven benign follicular nodule (Bethesda thyroid grade II). Grey scale USG shows a well-defined, isoechoic nodule in right lobe of thyroid gland.
*Note the thin, well-defined hypoechoic peripheral halo, characteristic of a benign nodule.

We found that macrocalcifications were seen in 5/14 (35.7%) malignant nodules, and in 28/124 (22.5%) benign nodules, suggesting that it is not a significant discriminator for malignancy. Microcalcifications were seen in 8/14 (57%) malignant nodules and in none of the benign nodules. Moreover, all the microcalcifications in our study occurred in papillary cancers, suggesting 100% specificity. Several reports have suggested a high specificity of 85.8% to 95% for the presence of microcalcifications in papillary cancers [6]. More recently, Pallaniappan et al., reported that microcalcifications had 100% specificity for papillary carcinoma [10], which is similar to our study.

Intrinsic vascularity is defined as flow that is higher in the central part of the nodule than in the thyroid parenchyma, and is a feature of malignant thyroid nodule [Table/Fig-6b]. The published opinion about this finding is rather contradictory with some reports suggesting that Doppler USG is useful [11] and some others suggesting that Doppler USG did not satisfactorily improve diagnostic accuracy [12]. We found central vascularity in a sizeable number of malignant nodules with a sensitivity of 85.7% and an accuracy of 66.6%. However, central vascularity was also found in a large number of benign nodules and was therefore not a very useful feature in discriminating malignant nodules.

Eighteen nodules in our study showed a honeycomb internal echotexture, described as multiple tiny cystic spaces within the nodule which are separated by thin septae [Table/Fig-8]. All these nodules were reported as benign colloid nodule on cytology. Bonavita et al., reported that a honeycomb or "spongiform" appearance was highly specific for a benign colloid nodule, especially if it was also avascular [13]. Similarly, Reading et al., opined that a spongiform appearance was sufficiently characteristic of a benign aetiology so as to obviate the need for FNAC [14].



[Table/Fig-8]: A 27-year-old male patient with solitary nodule in right lobe of thyroid. USG shows a well-defined nodule with multiple tiny cystic spaces separated by thin septae, characteristic of "honeycomb" pattern. FNAC was reported as colloid nodule. Punctate hyperechoic spots within cystic spaces (arrow) represents inspissated colloid.

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. In patients with multiple nodules, only the dominant nodule was evaluated and other nodules were not evaluated.

CONCLUSION

USG is a sensitive and specific modality for assessing thyroid nodules with good overall accuracy in differentiating benign from malignant thyroid nodules. While FNAC/HPE remains the gold standard for establishing the final diagnosis, awareness of the specific sonographic features might be useful to target suspicious nodules, and to avoid unnecessary intervention in the vast majority of nodules that are benign. The most useful indicators of malignancy in this study were a solid composition, hypoechogenicity, poorly defined margins and a taller-than-wider shape of the nodule. Presence of microcalcifications was highly specific for papillary cancer.

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