ACCURACY OF A NEW SONOGRAPHIC CLASSIFICATION SYSTEM IN DIFFERENTIATING BENIGN FROM MALIGNANT SOLID THYROID NODULES

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ABSTRACT

Objective: To determine diagnostic accuracy of sonographic criteria in differentiating benign from malignant solid thyroid nodule by using new sonographic classification system.

Study Design: Cross sectional validation study.

Place and Duration of Study: Department of Radiology, Combined Military Hospital Multan from Oct 2014 to Mar 2015.

Material and Methods: A total of 150 consecutive cases of either sex ranging in age from 19-60 years with palpable thyroid nodules referred for diagnostic workup were subjected to ultrasound (US) examination for assessment of solid thyroid nodules and it was followed by US-guided fine-needle aspiration (FNA) of all solid thyroid nodules. Each of the biopsied nodule was subsequently placed into one of five categories on the basis of sonographic features i.e. "malignant," "suspicious for malignancy," "borderline,""probably benign," and "benign". Evaluation of accuracy of sonographic diagnosis for solid thyroid nodule was done by comparing results of fine needle aspiration biopsy (FNAB).

Results: The mean age of the patients (n=150) was 42.34 ± 4.78 years; seventy three percent (n=109) were females and twenty seven percent (n=41) were males. Frequency of thyroid nodules (on FNAB as gold standard) was revealed as 20.7% (n=31) malignant and 79.3% (n=119) benign, accuracy of a new sonographic classification system in differentiating benign from malignant solid thyroid nodules, keeping FNAB as gold standard showed 18.7% (n=28) true positive, 4.7% (n=7) false positive, 2% (n=3) false negative and 74.6% (n=112) true negative. Ultrasound finding has sensitivity of 90.3%, specificity of 94.12% and diagnostic accuracy of 93.3%.

Conclusion: Accuracy of a new sonographic classification system in differentiating benign from malignant solid thyroid nodules, while keeping FNAB as gold standard was high and is recommended for diagnosis of malignant solid thyroid nodules.

Keywords: Accuracy, FNAB, Malignant, New sonographic classification system, Thyroid nodules.

INTRODUCTION

Thyroid nodules are a common clinical problem noted with frequency of 4-7% by palpation and 13% to 67% sonographically in the general population. Thyroid nodule is one of the major health problems of our country secondary to iodine deficient diet. About 70% of the Pakistani population is at risk of thyroid diseases secondary to deficiency of iodine, according to United Nations International Children's Emergency Fund (UNICEF). Thyroid malignancy is responsible for 1.2% cases of all malignant growth in Pakistan[1,2]. Sonography is the main diagnostic modality for the evaluation of thyroid nodules[3]. The incidence of detection of thyroid nodules has increased with use of ulrasound (US). With gray scale sonography a thyroid nodule is seen as a rounded or oval lesion within the thyroid gland that can be distinguished from the normal gland parenchyma. Characteristic ultrasound features of a benign nodule include an oval or flat shape, echogenicity similar to normal gland parenchyma, a smooth margin, hypoechoic halo around the nodule and peripheral vascularity on color doppler examination[1-5]. Whereas sonographic features suggestive of malignancy include micro calcifications, markedly reduced echogenicity, irregular margins, predominantly solid composition, taller-than-wide shape and intranodular vascularity on

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color doppler examination. Some of the investigators have suggested a combination of ultrasound features rather than only one of these features for better diagnostic accuracy[2,4-7]. Ultrasonography of the thyroid gland has been commonly used in differentiating benign from malignant thyroid nodules and to guide fine-needle aspiration (FNA) for the nodules[8]. On the basis of a new sonographic classification system, the features of solid thyroid nodules are placed into 1 of 5 categories i.e. benign, probably benign, borderline, possibly malignant, or malignant, it differs from old classification in a way that it only includes solid thyroid nodules and has 5 categories while old one included both solid and cystic nodules and had only 2 categories[4,9,10] Thyroid malignancy is seen in approximately 18.4% of patients with suspicious for malignancy, with sensitivity and specificity of 86% and 95% respectively for new ultrasound classification system where as the sensitivity and specificity for the old classification system is 93.8% and 66% respectively[4,10]. The new sonographic classification system can differentiate benign from malignant solid thyroid nodules, followed by fine needle aspiration biopsy (FNAB) and it is helpful to the clinicians for the accurate diagnosis.

The aim of this study is to explore the diagnostic accuracy of sonography in diagnosis of benign and malignant solid thyroid nodules by using a classification system comprised of five categories.

MATERIAL AND METHODS

This cross sectional validation study was carried out at Combined Military Hospital (CMH) Multan, from October 2014 to March 2015. Ultrasound examination and US guided FNA were done in the department of Radiology. A total of 150 patients were included in the study through non-probability consecutive sampling. Male and female patients with age ranging from 19-60 years were included in the study that were referred by clinician for diagnostic workup of palpable thyroid nodules, after taking informed consent. Patients with cystic thyroid nodule and those already operated upon for a thyroid lesion were excluded from the study. We performed US examination using a 7.5 MHz probe of Medison Sonoace X6 in dimly lit room with comfortable temperature (22-24C) in supine position. All cases who underwent US initially were also subjected to US guided FNA. Histopathology of FNA was carried out in Pathology Department of CMH Multan by consultant histopathologist. Thyroid nodules which demonstrated two or more sonographic features of malignancy were placed in malignant category regardless of the presence of borderline or benign US features. Thyroid nodules which demonstrated one sonographic feature suggestive of malignancy regardless of

Table-I: Age distribution of the patients (n=150).

Age (in years)	No. of Patients	Percentage (%)
20-30	18	12
31-40	23	15.3
41-50	55	36.7
51-60	33	22
61-70	21	14
Total	150	100
Mean and SD	42.34 ± 4.78	

Table-II: Gender distribution of the patients (n=150).

Gender	No. of Patients	Percentage (%)
Female	109	72.7
Male	41	27.3
Total	150	100

the existence of borderline or benign sonographic characteristics, these were placed in category of "suspicious for malignancy". If a thyroid nodule demonstrated one or more borderline sonographic characteristic without sonographic features that suggest malignancy regardless of the presence of benign US features, was placed in "borderline" category. Thyroid nodule which demonstrated one or two sonographic features that suggested a benign nodule with no malignant or borderline sonographic characteristic, were considered "probably benign"; the thyroid nodules which demonstrated three or more sonographic features of a benign nodule with no malignant or borderline sonographic characteristics, were considered "benign". Last three categories were considered being benign. All thyroid nodules were examined by same radiologist using same ultrasound machine. The ultrasound characteristics of thyroid nodules indeterminate for benignancy or malignancy, termed "borderline features" include hypoechogenicity; predominant central vascularity; and macro calcifications, like egg shell calcifications and intranodular macro calcifications[2]. US-guided FNA was performed without local anesthesia and each nodule was pricked only once. A smear was made on 4-6 slides for each sample and the slides were fixed in 95% ethanol and sent to Pathology department for histopathological examination[3]. Data were entered and analyzed in statistical package for the social sciences (SPSS) version 20.0. Categorical variables like gender, type of thyroid nodules and patients age group were presented by frequency and percentages and continuous variables like age was presented in mean ± SD. The ultrasound features were compared with the cytological diagnosis (FNAB as reference standard) to determine sensitivity, specificity, negative predictive value, and positive predictive value.

Table-III: Frequency of thyroid nodules (on FNAB as gold standard) (n=150).

Thyroid nodules	No. of Patients	Percentage (%)
Malignant	31	20.7
Benign	119	79.3
Total	150	100

Table-IV: Accuracy of a new sonographic classification system in differentiating benign from malignant solid thyroid nodules, keeping FNAB as gold standard (n=150).

USG	FNAB		Total
	Positive	Negative	
Positive	True positive(a) 28 (18.7%)	False positive (b) 7 (4.7%)	a + b 35 (23.3%)
Negative	False negative(c) 3 (2%)	True negative (d) 112 (74.6%)	c + d 115(76.7%)
Total	a + c 31 (20.7%)	b + d 119(79.3%)	150 (100%)

Sensitivity = a/(a+c) x 100 = 90.3%, Specificity = d/(d+b) x 100 = 94.12%, Positive predictive value = a/(a+b) x 100 = 80%, Negative predictive value = d/(d+c) x 100 = 97.3%, Accuracy = a+d/(a+d+b+c) x 100 = 93.3

RESULTS

A total of those 150 cases that fulfilled the inclusion/exclusion criteria were selected for the study to determine the diagnostic accuracy of a new sonographic classification system in differentiating benign from malignant solid thyroid nodules, keeping FNAB as gold standard.

Majority of patients (37%) age ranges between 41-50 years and mean age was 42.34 ± 4.78, as shown in table-I. The sample was predominantly female (table-II).

The thyroid nodules on ultra-sonography was classified as benign and other categories as

malignant (fig-1) by radiologist. Most of the patient's (79%) thyroid nodules (on FNAB as gold standard) were found benign (table-III). Diagnostic accuracy of a new US classification system in differentiating benign from malignant solid thyroid nodules, keeping FNAB as gold standard was calculated. Almost nineteen percent of the sample was true positive, whereas seventy seven percent found to be true negative. The sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy of thyroid US for differentiating a malignant lesion from a benign were measured as 90.3%, 94.7%, 80%, 97.3% and 93.3% respectively as shown in table-IV. The US cut-off criteria applied for thyroid lesions were significant for over receiver operating characteristic (ROC) curve (fig-2). The diagnostic accuracy of thyroid ultrasonography via new US classification was very good on ROC curve.

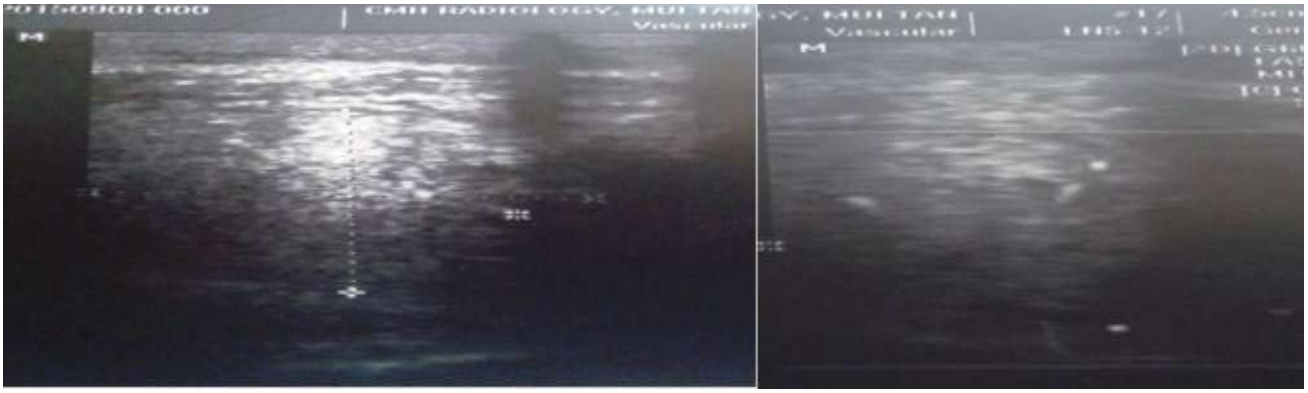

Figure-1: Gray scale and colour doppler ultrasound image showing well defined rounded solid nodulewith central vascularity without peripheral halo suggestive of malignancy; FNAB also supported the ultrasound diagnosis.

DISCUSSION

The purpose of this study was to determine the accuracy of sonographic diagnosis for benign and malignant solid thyroid nodules on real-time US examination, using classification system with 5 categories. All recent guidelines for the diagnosis of benign and malignant solid thyroid nodule endorse the use of US as very important way to determine, which of the thyroid nodules need to be studied by FNAB because of suspicion for malignancy[11,12]. FNAB of the thyroid gland is now a well-recognized, first line test for the evaluation and diagnosis of diffuse thyroid lesions or thyroid nodules. As far as cost-effectivenessis concerned, not all the thyroid lesions should be submitted for FNAB. Sonographic characteristics suggestive of malignancy should help to determine which of the thyroid lesions need to be evaluated by FNAB, this can help in reducing the number of FNAB and the cost of health care system.

Our findings revealed that the frequency of thyroid nodules (on FNAB as gold standard) as 20.7% (n=31) malignant and 79.3% (n=119) benign, accuracy of a new sonographic classification system in differentiating benign from malignant solid thyroid nodules, keeping FNAB as gold standard was calculated as 18.7% (n=28) true positive, 4.7% (n=7) false positive, 2% (n=3) false negative, 74.6% (n=112) true negative, while sensitivity, specificity, positive predictive

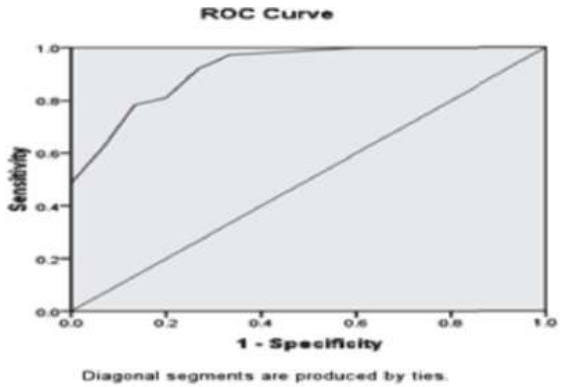

Figure-2: Receiver-operating characteristic (ROC) curve analysis.

value, negative predictive value and validity/ diagnostic accuracy was recorded as 90.3%, 94.1%, 80%, 97.3% and 93.3% respectively. The results of the study are similar to a studies by Kawak et al and Ozel et al who reported thyroid malignancy in 25.5% of patients with suspicion for malignancy, with sensitivity of 83.3% and specificity of 94.9%[7,9]. The new sonographic classification system can differentiate between benign and malignant thyroid nodule more efficiently, followed by FNAB and is thus helpful for the physicians in timely and accurate diagnosis of the thyroid malignancy. Our findings are not consistent with studies by Kim et al (sensitivity of 100% and specificity of 95.1%)[6], the difference may be due to the difference in sample size, age of participants and sampling procedure (studied solid and non-solid thyroid nodules together). The clinical significance of thyroid nodules rests with the need to exclude thyroid malignancy which occurs in about 15% of the nodules depending on age, gender, radiation exposure history, family history, and other factors[13,14].

Ultrasound is superior to other diagnostic modalities as it is cost-effective imaging procedure and has high sensitivity in assessing nodule size and number and in the evaluation of cervical lymphadenopathy. In previous experience it is noted that diagnostic yield of cytological material is better by US-guided aspiration compared to blind FNA, so US-guided FNA can lower the rate of non diagnostic smears[2,15].

There several US characteristic of thyroid nodules suggesting increased risk of malignancy ie calcification, hypoechogenicity, consistency margins, vascularity and taller than wide shape. Some of these characteristics are sensitive while others are relatively specific for malignant lesions[16]. Taller than wide shape has highest sensitivity and specificity followed by irregular margins and intranodular vascularity. Use of a combination of US features is recommended by the American Thyroid Association for the selection of thyroid nodule to be biopsied[13-15].

However, the diagnostic accuracy of sonography in differentiating benign and malignant solid thyroid nodules using a real-time ultrasound examination and classification system comprising 5 categories is better and results of this study are better and show higher diagnostic accuracy, so it is strongly recommended for diagnosis of malignant solid thyroid nodules in future[16].

There were some limitations of our study which include, the unavoidable selection bias (non-random sampling) and single centered study (diversity of population was lacking) due to limited resources. These limitations could be overcome by conducting a large-scale prospective study.

CONCLUSION

Diagnostic accuracy of a new sonographic classification system in the differentiation of benign from malignant solid thyroid nodules, while keeping FNAB as gold standard was very high and is recommended for diagnosis of malignant solid thyroid nodules.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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