

*Original Research Article*

**The Use of Conventional and Color Ultrasound in The Differentiation of Thyroid Diseases**

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**Abstract**

Thyroid diseases has become widely distributed in the general population, examined and investigated by different methods. Due to its anatomically superficial location, with its informative, safe, non-invasive characters, Ultrasound has become an indispensable tool in evaluating different thyroid diseases, describing their natures, helping in their differentiation.

The objective of the study is to evaluate ultrasonically different thyroid diseases, characterizing their natures, describing their consistencies, internal vascularities, and the state of thyroid tissues surrounding the nodular form of them, helping to reach their diagnosis, compared with the fine needle aspiration (FNA) results.

This is a cross-sectional study conducted from May 2014–February 2015. A total of 100 patients with diffuse and nodular thyroid diseases, were collected between 18–58 years age, in Duhok city. Examined by Conventional and Color ultrasound, divided into diffuse, nodular, mixed (combination of diffuse and nodular) forms, the nodules were divided by their consistencies into (solid, cystic, mixed), echogenicities were described as (hyperechoic, mixed, hypoechoic) relative to strap muscles, their surrounding halo of reactive thyroid tissues were recorded, their internal vascular arrangement also was detected, compared with FNA results, to reach their exact diagnosis.

Thyroid diseases were more commonly seen in females, all of the diffuse form of thyroid diseases were of chronic inflammatory and benign natures, in the nodular form of thyroid diseases most of the solid nodules and all of the cystic lesions seen to have benign behavior, hypoechogenicity, microcalcification, internal central vascularity and absent halo sign (related to thyroid tissue reaction) were higher in malignant thyroid nodules.

Ultrasound provide useful informations about the behavior of different thyroid diseases, significant correlations were found between different ultrasonic thyroid findings with their final diagnosis, in comparison with FNA results.

**Key words:** Thyroid, Nodule, Ultrasonography, calcification, echogenicity.

**الخلاصة**

بسبب الموقع السطحي للغدة الدرقية، فإن بإمكان الدقة العالية لمقياس الموجات فوق الصوتية والدوبلر الملون تقييم انواع امراض الغدة الدرقية بشكل واضح و دقيق , تهدف هذه الدراسة الى تقييم المعلومات التشخيصية لامراض الغدة الدرقية من خلال استخدام جهاز السونار العادي و الملون وصولا الى التشخيص الصائب بالمقارنة مع نتائج الخزعة الدقيقة , تم إجراء دراسة مستعرضة من خلال فحص (100) مريض مصاب بأنواع مختلفة من أمراض الغدة الدرقية، يتراوح أعمارهم بين (18 - 58 سنة) وكان متوسط أعمارهم (47.9 سنة). كان هناك خمسة وثمانين مريضا من الإناث (87%) و خمسة عشر من الذكور (13%)، تم تقسيم امراض الغدة حسب رؤيتها بالسونار إلى ثلاث مجاميع،(المنتشرة و العقيدية والمختلطة) فكان سبعة وعشرين من المرضى لديهم مرض الغدة الدرقية العقيدية، ستة عشر كان لديهم مرض الغدة الدرقية المنتشرة و سبعة وخمسون كان يعانون من الإنتشار البؤري المختلط. من مجموع 27 اصابه عقيدية 22 منها كانت عقد صلبه و 5 منها كانت كيسيه , كل الانواع المنتشرة وكل العقد الكيسية كانت من النوع الالتهابي المزمن والحديد وكانت معظم العقد الخبيثة من النوع المختلط. فيما يخص العقد كان التشتت الموجي الاقل مقارنة بالعضلات المجاورة و والتكلس الصغير جدا وانعدام الهالة المحيطة وكذلك الترتيب الدموي الداخلي هم الاكثر شيوعا في العقد الخبيثة مقارنة بالنتائج الخزعية واثبتت دقتها إحصائيا .

**Introduction**

**T**hyroid diseases are common and can be observed, if not palpable, by Ultrasonography (US) in 50 % of the adult population [1]. Ultrasonography (US) is the most common and most useful way to image the thyroid gland and its pathology, as recognized in guidelines for managing thyroid disorders published by the American thyroid Association[2]. It has largely replaced other methods of investigation, due to their high resolution, non-invasive, superior dimensional examination, and superior natural descriptive characters, lack of radiation as well as isotope exposure[3,4].

Different forms of thyroid diseases used to be seen by US, mainly divided into diffuse (Hashimoto's thyroiditis), nodular, and mixed forms of diseases[5,6]. The diffuse form of thyroid diseases as seen in most of the chronic inflammatory and autoimmune diseases, tend to involve the whole gland, with variable degrees of echogenicities and echotexture (hyperechoic, hypoechoic), calcifications and internal vascularities[3].

In the nodular form of thyroid diseases, certain criteria have been suggested for each thyroid nodule, including their sizes, consistencies (solid, cystic), their echogenicities compared to strap muscles, internal calcification, internal vascularity and surrounding halo[1, 10].

The echogenicity, is defined ultrasonically as the degree of grey shading that the nodule exhibits when ultrasonic waves passed through them, compared with the shading of the neighboring thyroid tissue, so hyper echogenicity means more bright while hypoechogenicity means more dark in comparison with the strap muscles.[1] One of the natures of the thyroid nodules is their internal calcifications or called (psammoma bodies), if present they highly excludes malignant nature, are 10 – 100 micron round laminar crystalline calcific deposits, seen on US as punctuate hyperechoic foci with posterior shadowing, they are divided according to their sizes into micro calcifications (less than 1mm), and macrocalcifications (more than 1mm) sizes [11,12,6]. Different patterns of

calcifications are seen with different thyroid diseases (diffuse, central, peripheral) [1,13,14]. The halo is a hypoechoic rim around thyroid nodule, produced by a pseudocapsule of fibrous connective tissue, a compressed thyroid parenchyma, and chronic inflammatory cells infiltrates, its presence gives an impression of a benign nature [15- 17].

Vascular flow within a thyroid nodule can be detected with color Doppler US. Divided into either one that is more predominantly distributed in the central part of the nodule, or that with more predominantly arranged peripheral to the nodule [15,11,18,19].

The mixed (nodular and diffuse) form of thyroid diseases, have mixed features of both of the nodular and diffuse forms [3].

### **Materials and Methods**

This is a cross-sectional study conducted from June 2014–February 2015. One hundred patients, between the ages of (18–58) years, with the age range of  $47.9 \pm 8.7$ , were selected from the Azadi Teaching Hospital in Duhok. The study protocol was approved by the Scientific and Ethics Committee of the Faculty of Medical Sciences of University of Duhok.

A pretested questionnaire was designed to obtain information about age, sex, past medical and surgical histories, thyroid hormonal blood investigations, also if any history of isotope treatment, or medical treatment. The patients were examined in supine position, with the neck mildly hyper extended, both thyroid lobes and isthmus were examined, by using Siemens (ACUSON X3000) machine with 13- 15 MHz linear array transducer, conventional ultrasound was performed first, taking the size, the texture of the gland, dividing the findings into diffuse, nodular, combined nodular and diffuse forms, regarding each nodule, we divided them into solid 22%, cystic 5%, recording the echogenicities of the solid ones as hyperechoic, hypoechoic, describing the patterns and sizes of calcification (microcalcification, macrocalcification), and the presence or absence of a halo sign, and dividing the internal

vascularity of the thyroid abnormal US changes as(hypovascular, hypervascular) . Fine needle aspiration biopsy, by using 10 cc plastic syringes and 22 – 25 gauge needles of (1–1.5) inch lengths, by a specialized histopathologist, under aseptic conditions, was done to the selected more affected abnormal tissue seen under ultrasonic guidance and all the results were correlated with the ultrasonic findings.

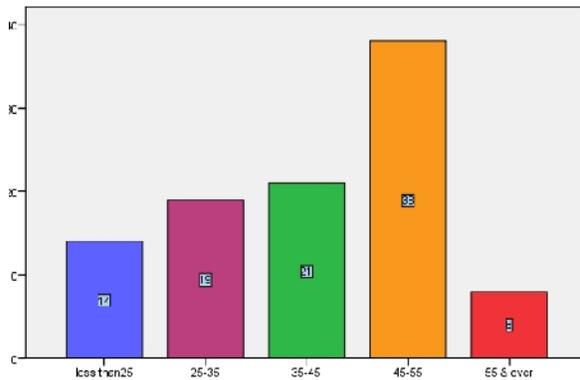
### **Statistical Analysis**

Collected data were entered into a Microsoft Excel 2010 sheet, and then converted into SPSS version 22 statistical package (IBM Corp., 2013). Frequency and frequency percentages were calculated to make relevant tables and graphs. The demographic, clinical and laboratory data have been tested for their relationship with US classification of thyroid diseases and with FNAB result. Fisher's exact test was used throughout with a significance level of

$P < 0.05$ . Validity of various US and Doppler indexes were compared with the final diagnosis of the pathologist examining the FNAB. Sensitivity was calculated as the percent of malignant nodules correctly diagnosed by US or Doppler out of all malignant nodules. Specificity was calculated as percent of benign nodules correctly diagnosed by US or Doppler out of all nonmalignant nodules. Positive predictive value (PPV) was calculated as percent of truly malignant nodules out of all nodules labeled as malignant by US or Doppler. Negative predictive value (NPV) was calculated as percent of truly benign nodules out of all nodules labeled as nonmalignant by US or Doppler (Petrie and Sabin, 2009[20]).

### **Results**

Our results showed that thyroid diseases were more common in females more than in males (87% and 13% respectively).



**Figure 1:** Age group distribution of thyroid diseases, where the highest percentage was in the age of 45-55 years (38%).

Our results showed that ,from the total of 100 patients, 27 of them had nodular disease in which 22 of these nodules were of more solid consistency, 5 of them were of more cystic consistency, 16 of patients

show diffuse form , and 57 of them show mixed (both nodular and diffuse forms ) table 1 .

**Table 1:** Distribution of patients according to type of thyroid disease, as identified by US and the percentage of the cystic /solid components of the nodular form:

Thyroid disease	No.
<b>Nodular</b>	27
(Solid Nodular )	22
(Cystic nodular)	5
<b>Diffuse</b>	16
<b>Nodular +diffuse</b> (mixed)	57
Total	100

From the 22 of solid nodules, 19 (23.8 % ) of them were benign, 3 (15% )of them were malignant (table 2, figure 2). All the predominantly cystic nodules were benign (table2, figure 2).

All the diffuse form of thyroid disease were of benign nature, and because the inflammatory and the autoimmune diseases were considered benign we included them in the benign diseases.

From the 57 combined nodular and diffuse form of the thyroid disease, 40 (50 % ) of them were benign , and 17 (85 % ) of them were malignant (table 2, figure 2)

The percentage of the cystic/solid components of the nodular form was 1/5, which means from the total of 27 patients in the nodular form, 18.8 % of them had the cystic component, and 81.2 % had the solid component.

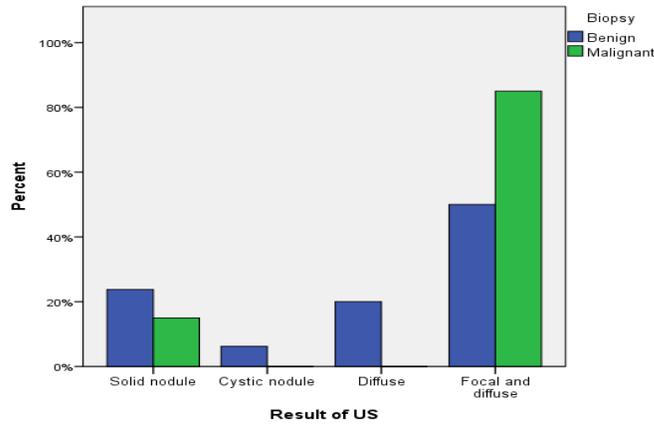
**Table 2:** Distribution of all cases of thyroid disease by biopsy result, the inflammatory and autoimmune thyroid diseases were included with the benign diseases

	Benign		Malignant		Total		P-value
	No.	(%)	No.	(%)	No.	(%)	
Solid nodule	19	(23.8)	3	(15.0)	22	(22.0)	<b>0.025</b>
Cystic nodule	5	(6.3)	0	(0.0)	5	(5.0)	
Diffuse	16	(20.0)	0	(0.0)	16	(16.0)	
Nodular and diffuse	40	(50.0)	17	(85.0)	57	(57.0)	
Total	80	(100)	20	(100)	100	(100)	

In the nodular form of thyroid diseases, 15 % of the solid nodules show malignant changes, no malignancy seen in the cystic component (table2).

Figure 2 shows that all the predominantly cystic nodular, and the diffuse forms of the

thyroid lesions were benign, the predominantly solid nodules were more commonly of benign nature, while the mixed nodular and diffuse form was more commonly of malignant behavior, all compared with FNA results.



**Figure 2:**Percent distribution of all types of thyroid disease by biopsy result.

Regarding the nodular thyroid diseases, Table 3 shows that halo sign was absent in 95 % of malignant, and in 17.2 % of the benign ones with a p value of less than 0.001.

With the sensitivity, specificity, PPV, NPV, of absent halo were 95 %, 82 %, 63%, 98 % respectively in the prediction of malignant changes, compared with FNA results.

**Table 3:**US findings in thyroid nodules (n= 84) by biopsy result, with their validity indexes compared with FNA

		Malignant		Benign		P-value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
		No.	(%)	No.	(%)					
Halo sign	Absent	19	(95.0)	11	(17.2)	<b>&lt; 0.001</b>	95.0	82.8	63.3	98.2
	Present	1	(5.0)	53	(82.8)					
Calcification	Microcalcification	18	(90.0)	4	(6.3)	<b>&lt; 0.001</b>	90.0	93.8	81.8	96.8
	macrocalcification	2	(10.0)	60	(93.)					
Echogenicity	Hypoechogetic	18	(90.0)	13	(20.3)	<b>&lt; 0.001</b>	90.0	79.7	58.1	96.2
	Hyperechogetic	2	(10.0)	51	(79.7)					
Color Doppler	Central vascular	17	(85.0)	11	(17.2)	<b>&lt; 0.001</b>	85	82.8	60.7	94.6
	peripheral vascular	3	(15.0)	43	(67.2)	<b>&lt; 0.001</b>				
	Total	20	(100)	64	(100)					

Table 3 also shows that microcalcification was seen in (90%) of malignant nodules and hence the solid malignant nodules were 15% of total number , so the percentage of microcalcification in the solid nodules was 6%, and microcalcification seen in 6.3 % of the benign ones , p value was less than 0.001.

Macrocalcification was seen in 93 % of the benign ones, with p value of less than 0.001 in predicting benign nature.

The sensitivity, specificity, PPV, NPV of microcalcification in predicting thyroid

malignancy were 90%, 93 %, 81% and 96 % respectively, compared with FNA results.

Table 3 also shows that hypoechogeticity was seen in 90 % of malignant nodules, and 20% of the benign ones, while hyperechoic nodules were seen in 10 % of the malignant nodules and 79.7 % of the benign ones.

The sensitivity, specificity, PPV, NPV of hypoechogeticity in the predilection of malignant changes were 90% , 79 % , 58% and 96 % respectively compared with FNA results.

In table 3 also, we see that 85 % of the malignant nodules were of predominantly central vascularization, while 17.2 % of the benign nodules exhibits a predominantly peripheral type of vascularity.

The sensitivity, specificity, PPV, NPV of centralvascularization in predicting malignancy were 85%, 82 %, 60.7% and 94 % respectively compared with FNA results.

### **Discussion**

The use of US in the detection of thyroid diseases has greatly increased the ability to detect small thyroid nodules, which were unrecognized by physical examinations. (6) There are many US criteria for differentiating benign from malignant thyroid nodules. Such differentiation is important for selecting patients for further FNAB in cases with suspicious of malignancy, or to avoid unnecessary biopsy for those with benign criteria.

It has been found in some literatures that no single criteria is sure of malignancy, and combination of the known criteria of malignancy gives higher sensitivity and specificity than depending on single individual one [8,11].

Variable validity values have been reported regarding the ultrasound criteria in the detection of thyroid diseases [5,6,7,8,9, 21, 22].

In the current study, the mean age of the involved patients was (45– 55) years , with a higher incidence seen in females than males (87 % in females and 13 % in males ) ,similar results was seen in [6,10 , 21 , 22]. In the current study we found that the diffuse and the solid nodular forms were more common in benign thyroid diseases, while the mixed form was more of malignant nature , similar results seen in [5,7], in the studies done by [23 ,7 , 9] the solid nodular form was more commonly seen in benign thyroid lesions.

Regarding cystic nodules, in this study we found that all cases with cystic nodules were benign, this result were higher than those found in a study done by [5, 6].

Hypoechoogenicity was more commonly seen in malignant thyroid diseases, similar findings were seen in. [6, 7, 8, 9, 25]

The sensitivity, specificity of hypoechoogenicity in predicting thyroid malignancy were 90%, 78 % respectively, lesser results were seen in [6, 7, 9, 10]

Regarding Halo sign it was absent in almost all cases of malignant nodules, and halo signs was highly predictive of benignity, similar findings seen in. [6, 5,8]

The sensitivity , specificity of absent halo sign as a predictor of malignancy were 95% and 83 % respectively , these results were higher than those seen in [9].

About sign of micro- calcification, in our study it was found in the majority of malignant nodules, similar to [5, 6], and higher than the result of [21, 25].

The sensitivity and specificity of micro-calcification detected by US as a predictor of malignancy is 90% and 93% respectively, supporting our results are those of [9, 6], both of them had similar sensitivities but lesser specificities, while in [7], the sensitivity was lesser (29.5) % and the specificity was higher (95%) and in [10], the sensitivity was 14 % and the specificity was (46 %).

regarding the internal vascularity of the nodules, central vascularity was more commonly seen in malignant thyroid nodules, while peripheral vascularity is a feature of benign nodules these results were in agreement with [6, 7, 9, 10, 22].

The sensitivity, specificity of central intranodular vascularization in predicting thyroid malignancy, were 85 % , and 83 % respectively, supporting similar results were seen in [6, 9, 22], while lesser results of sensitivity and specificity was seen in [10].

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