Role of Quantitative Doppler Assessment in the Differentiation between Graves` Disease and Hashimotos` Thyroiditis

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ROLE OF QUANTITATIVE DOPPLER ASSESMENT IN THE DIFFERENTIATION BETWEEN GRAVES DISEASE AND HASHIMOTOS THYRIODITIS

By

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هود:88

(صدق الله العظيم)

DEDICATION

I dedicate this thesis to my completely family members my mum

My husband and sons

My teatures

My friends

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I am acknowledge the great help of my supervisor

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Abbreviation:

AT	Autoimmune thyroiditis
T4	Tetraiodothyronine
T3	Tri iodothyronine
TSH	Thyroid Stimulating Hormone
TRH	Thyroid Releasing Hormone
CAMP	Cyclic adenosine monophosphate
IG4	Immunoglobulin 4
USA	United states association
PTC	Papillary Thyroid Carcinoma
TPO ABS	Thyroid peroxidase antibodies
TG ABS	Thyroglobulin antibodies
TSHR AB	Thyroid stimulating hormone receptor antibodies
US	Ultrasound
CFDS	Color Flow Doppler Sonography
FLT	Focal Lymphocytic Thyroiditis
PSV	Peak Systolic Velocity
EDV	End Diastolic Velocity
ITA	Inferior Thyroid Artery
STA	Superior Thyroid Artery
RI	Resistive index
GD	Graves 'Disease
HT	Hashimotos Thyroiditis
BMC	Benghazi Medical Center
BRC	Benghazi Radiology Center
AITD	Autoimmune Thyroid Disease
CLT	Chronic Lymphocytic Thyroiditis
PRF	Pulse Repetition Frequency
TBFA	Thyroid Blood Flow Area

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ABSTRACT

Key words: *Graves` Disease, Hashimotos Thyroiditis, Quantitative Doppler Assessment*

A Graves' disease GD, and Hashimoto`s thyroiditis HT are the most common forms of diffuse thyroid disease. Both GD and HT can present as an enlarged and hyperemic thyroid, however, needs differentiation, as management strategy differs. In our prospective case, series study of different stages of thyroiditis targeting to determine the usefulness of quantitative Doppler assessment in thyroid vessels in this particular group of patient and to differentiate between GD and HT. blood flow Doppler parameter was measure quantitatively by ultrasonography. A 69 patients with enlarged hyperemic thyroid (30 Graves' disease, 39 thyroiditis) were been carried out in (3males and 27 female) of Graves ' disease, however, (4males and 35 female) of thyroiditis cases, were examined. These groups of patients were diagnose clinically and biochemically, were referred form endocrinologist at Al-hawari General Hospital and Benghazi Medical Center (BMC) into Benghazi Radiology Center (BRC) blood flow Doppler parameter were measured quantitatively by ultrasonography. In the present study, we found no significant differences in a resistive index between GD and HT while there is a peak systolic velocity difference between GD. and HT. In conclusion, in this study confirmed that STA-PSV and/ or ITA-PSV are a potentially useful parameter to differentiation between graves` disease and hashimotos thyroiditis. In contrary to STA-RI and/or ITA –RI is useless in the differentiation between two types of thyroiditis. Further studies are required to confirm such differentiation.

CHAPTER 1

INTRODUCTION

1. INTRODUCTION:

The principal diseases of the human thyroid gland are goiter (diffuse or nodular), hyperthyroidism, hypothyroidism, autoimmune thyroiditis, and neoplasm (1). the human autoimmune thyroid disease AITDs broadly include Grave`s disease (GD) and Hashimoto's thyroiditis (HT) .The most common causes of thyroid gland dysfunctions and non-endemic goiter (2). These conditions arise due to complex interactions between environmental and genetic factors. Which characterized by reactivity to self-thyroid antigens, which expressed as distinctive inflammatory or antireceptor autoimmune diseases. Among the major AITD susceptibility genes that have been identified is the HLA-DR gene locus, the major environmental triggers of AITD include iodine, medications, infection, smoking, stress, and genetic predisposition to AITD, which lead to the genetic-environmental interactions may lead to the development of thyroid autoimmunity (1).The most common forms of thyroiditis are hashimotos thyroiditis, graves` disease (1). Graves' disease and hashimoto` thyroiditis are complex autoimmune thyroid diseases in which auto immunity against the thyroid auto antigen develops at certain genetic background, and aggravated by environmental factors (3) .

In addition, it characterized by reactivity to self-thyroid antigens, which expressed as distinctive inflammatory or anti-receptor autoimmune diseases (4) (5).

1.1. HASHIMOTO`S THYROIDITIS:

Also known as, chronic lymphocytic thyroiditis (CLT) or autoimmune thyroiditis (AT) is the most frequent cause of hypothyroidism and goiter in iodine sufficient areas (6) (7). In addition, called Hashimoto's disease is an autoimmune disease. The thyroid gland attacked by the immune system, causing symptoms of hypothyroidism (underactive thyroid gland).

In patients who are suffering from Hashimoto's thyroiditis, antibodies react against proteins in the thyroid gland, gradually killing thyroid cells. In the early stages of Hashimoto's thyroiditis, patients may experience few to no symptoms. However, as thyroid cells damaged during each autoimmune attack, those cells release their stored thyroid hormones. This causes the patient's thyroid hormone levels to be temporarily high, resulting in symptoms of hyperthyroidism such as panic attacks, anxiety, a fast heartbeat, sweating, shaking hands, diarrhea, and quick weight loss. Known as Hashitoxicosis (8).With each attack, more and more thyroid cells are killed, until the

thyroid becomes unable to produce enough thyroid hormones, and the patient begins to experience symptoms of hypothyroidism(8).

1.2. GRAVES` DISEASE:

Is an autoimmune disorder that causes the thyroid gland to become over-active. In Graves' disease, the body's immune system secretes immunoglobulin's (autoantibodies) against the thyroid gland. This immunoglobulin's irritate the thyroid gland and make it produce more thyroid hormone, which causes the symptoms related to Graves' disease. This overactive thyroid state is hyperthyroidism (9).

1.3. NORMAL STRUCTURE AND FUNCTION OF THYROID GLAND

1.3.1. NORMAL ANATOMY OF THE THYROID GLAND:

The thyroid gland is a firm, reddish brown, smooth gland, located in the anterior neck surrounded by a fibrous capsule and it is composed of two lobes connected by a median isthmus usually over the second and third cartilaginous rings of the trachea.

The thyroid lies in front of and on the sides of the trachea.

It is bounded postero-lateral by the carotid space; the strap muscles and the sternocleidomastoid muscles cover its anterior and lateral aspects. The posterior surfaces of the lobes are adjacent to the peri-vertebral space and on the left to the esophagus (10) (11).

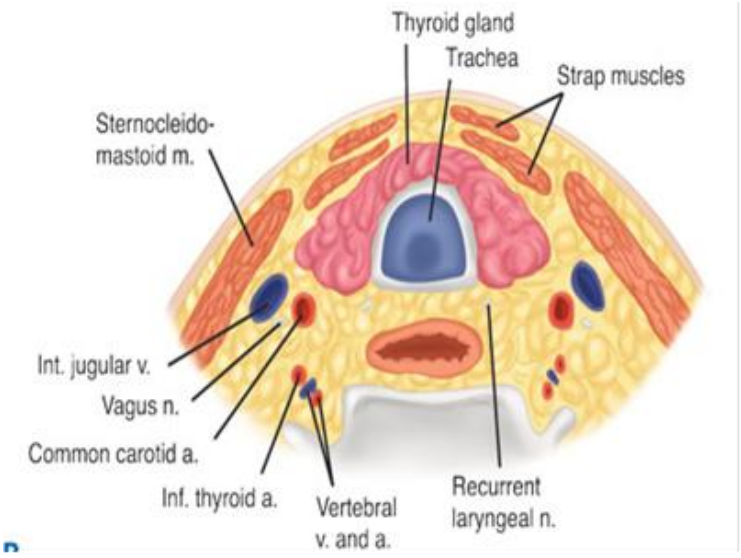

Figure 1: Thyroid Gland Cross Sectional Anatomy

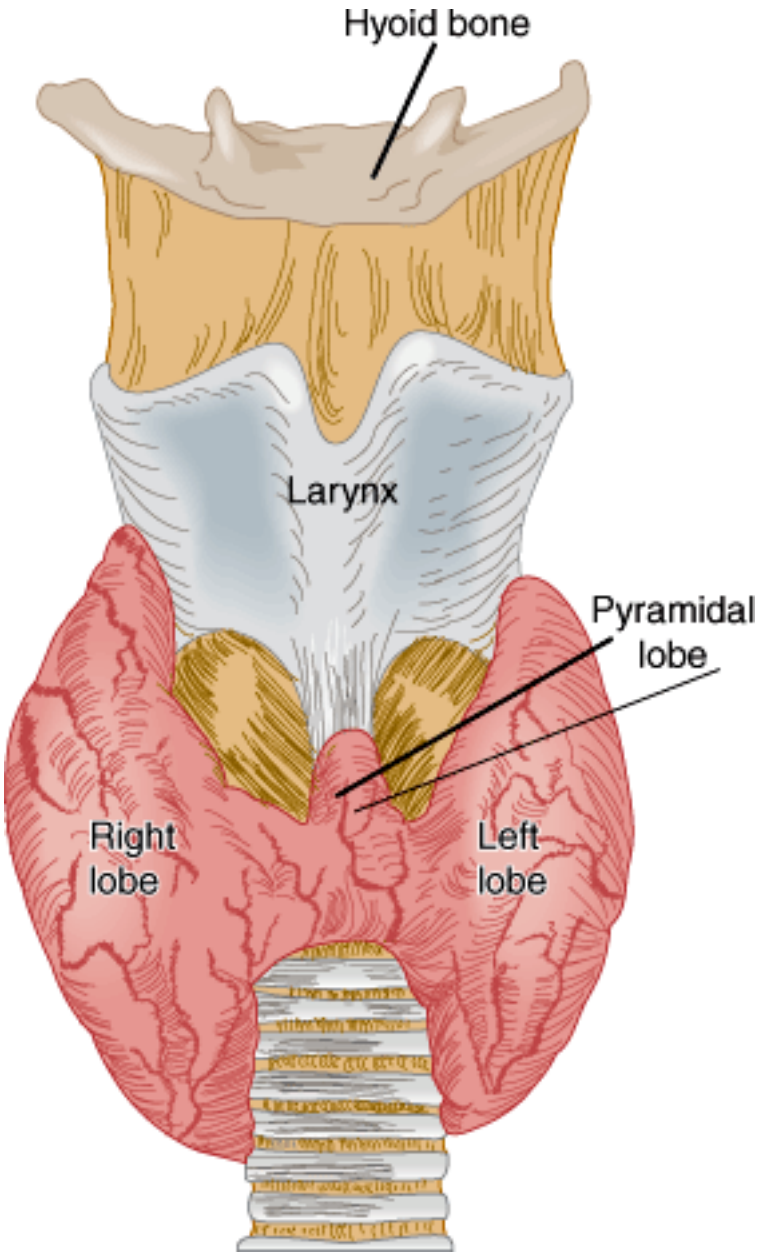

Figure 2: Thyroid Gland Gross Anatomy

1.3.2. THYROID VASCULAR ANATOMY:

Four arteries provide a rich blood supply to the thyroid gland. The upper poles of the gland receive blood from paired superior thyroid arteries that arise from the external carotids. Two inferior thyroid arteries originate at the thyrocervical trunk of the subclavian artery and supply the lower thyroid poles. Normal peak velocities from the major thyroid arteries are 20 to 40 cm/second and normal peak velocities from the intraparenchymal arteries are 15 to 30 cm/second (12) (13).

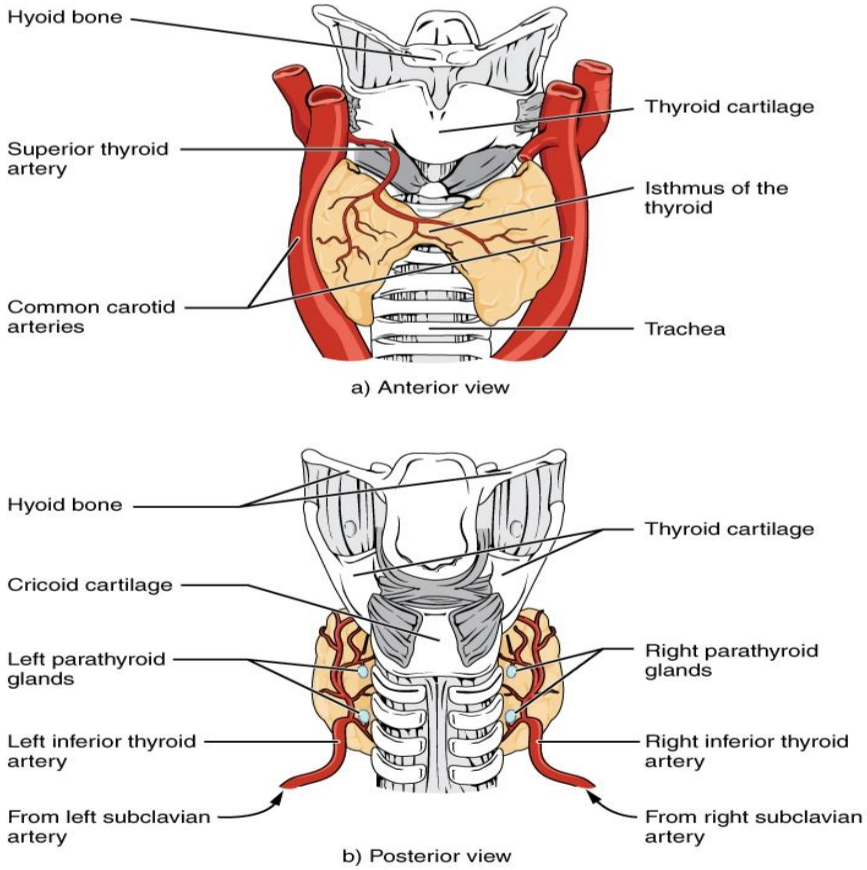

Figure 3: Thyroid Gland Vascularity

1.3.3. ANATOMIC LANDMARKES:

Many anatomic landmarks help to define the thyroid gland on a sonogram on transverse images, the common carotid artery and internal jugular vein form the posterior lateral border of the gland. The artery is located medial to the vein. These structures distinguished from the thyroid gland by echogenic walls and anechoic centers. Color Doppler or pulsed wave Doppler imaging may also assist in clarifying the anatomy. The longus colli muscle appears as a low-level, echogenic structure

Defining the posterior border of the gland. The air-filled trachea forms the medial border and appears hyperechoic, with posterior shadowing. The sternothyroid, sternohyoid, and omohyoid muscles, collectively called the strap muscles, form the anterolateral border of the gland. Directly superficial to the thyroid gland is the sternothyroid muscle, was bordered by the sternohyoid anteriorly and the omohyoid laterally. The sternocleidomastoid is located lateral and superficial to the omohyoid the very thin platysma muscle surrounds the neck, but its superficial location and indistinct density make it difficult to image with sonography. The thyroid gland appears as a rounded structure of low- to medium-level echoes, homogeneous in texture (13).

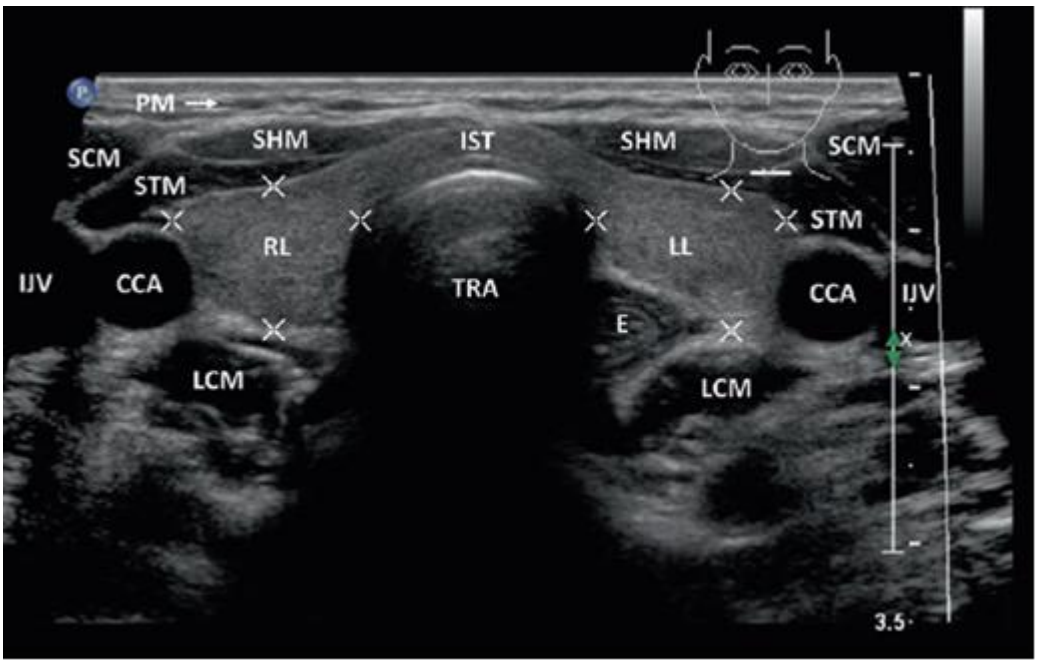

Figure 4: Normal Anatomical Land Marks Of Thyroid Gland

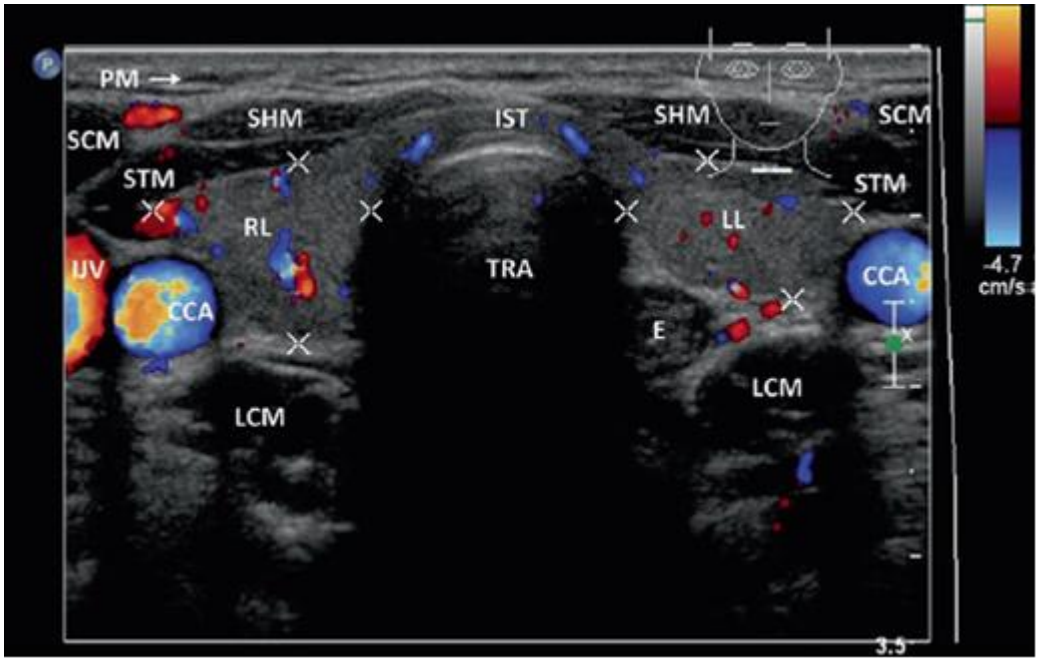

Figure 5: Demonstrating Normal Anatomical Landmarks with Color Flow.

1.4. HISTOLOGY:

Histologically, the thyroid gland consists of many closely packed acini, called follicles, each surrounded by capillaries and stroma. Each follicle is roughly spherical, lined by a single layer of cuboidal epithelial cells and filled with colloid; a proteinaceous material composed mainly of thyroglobulin and stored thyroid hormones. When the gland is inactive, the follicles are large, the lining cells are flat, and the colloid is abundant. When the gland is active, the follicles are small, the lining cells are cuboidal or columnar, the colloid is scanty, and its edges scalloped, forming reabsorption lacunae. Scattered between follicles are the parafollicular cells (C cells), which secrete calcitonin, a hormone that inhibits bone resorption and lowers the plasma Calcium level (14).

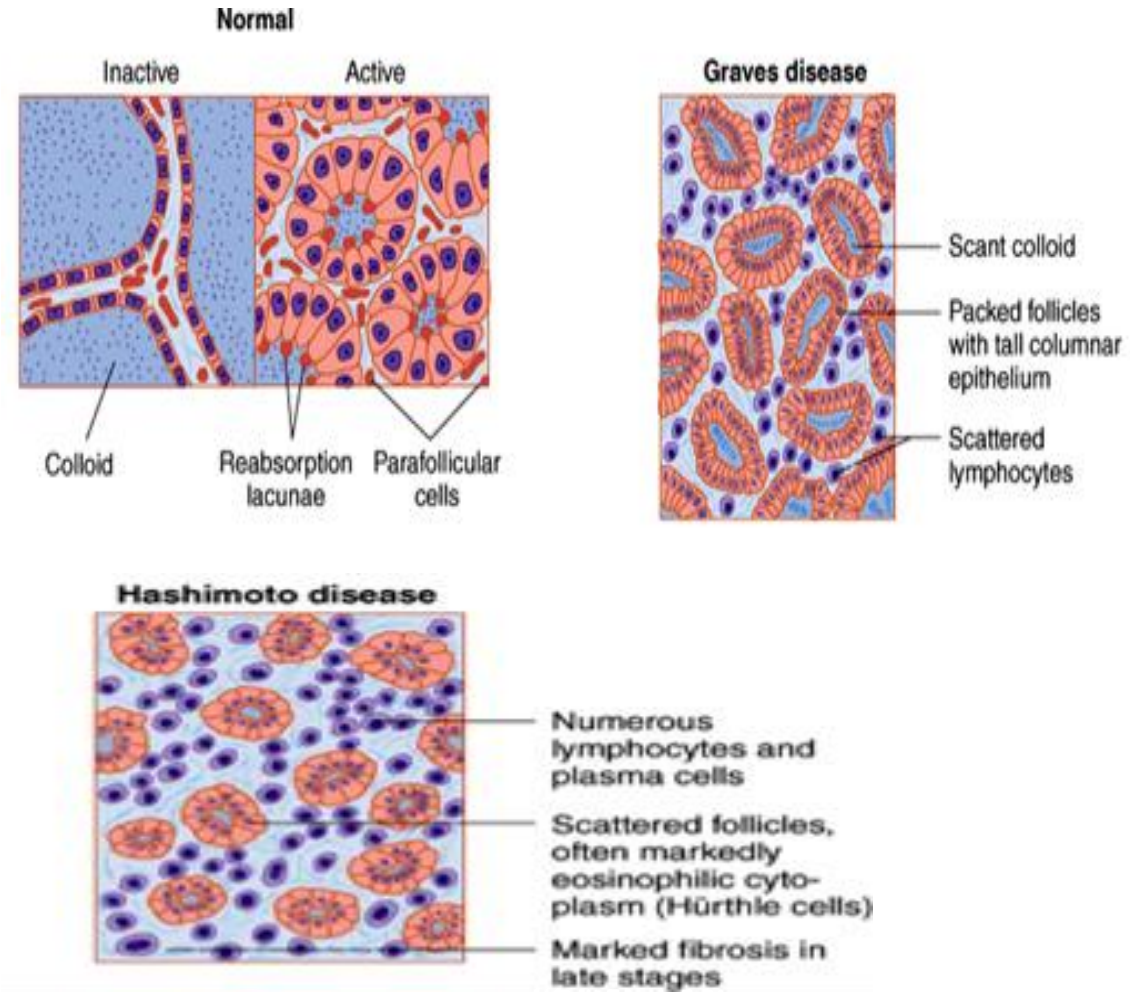

Figure 6: Histology of Autoimmune Thyroid Disease

1.4.1. Histology of Graves ' disease:

In graves` disease, the follicles lined by tall, columnar epithelium. The crowded enlarged epithelial cells project into the lumens of the follicles .these cells actively resorb the colloid in the centers of the follicles, resulting in the scalloped appearance of the edges of the colloid.

Key histological findings:

Hypercellular gland, papillary like folds common and colloid with scalloping and vacuoles adjacent to follicles

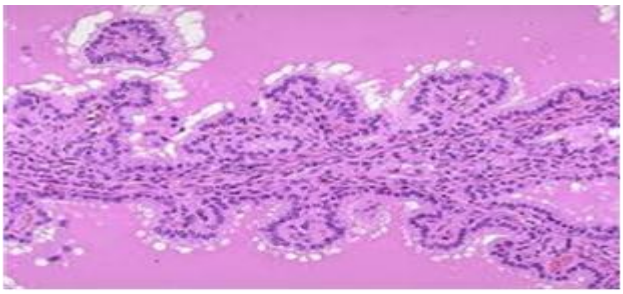

Figure 7: Histology of Graves` Thyroiditis

1.4.2. Histology of Hashimotos Thyroiditis: In Hashimotos thyroiditis significant lymphoid infiltration, the follicles are small and atrophic, most lined by variably sized hurthle cells. Extensive fibrosis, atrophy of follicular epithelium, and squamous metaplasia.

Key histological findings: Lymphocytic aggregation with germinal center formation, minimal tissue destruction and focal oxyphylic cytoplasmic changes.

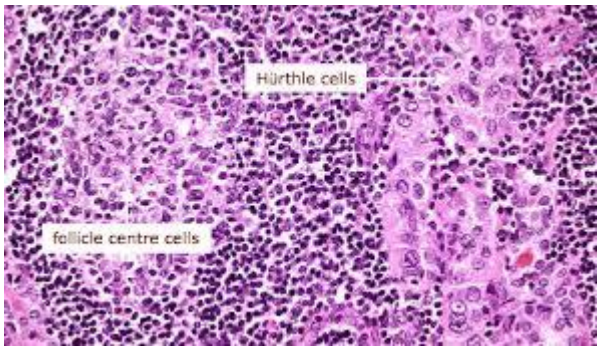

Figure 8: Histology of Hashimotos Thyroiditis

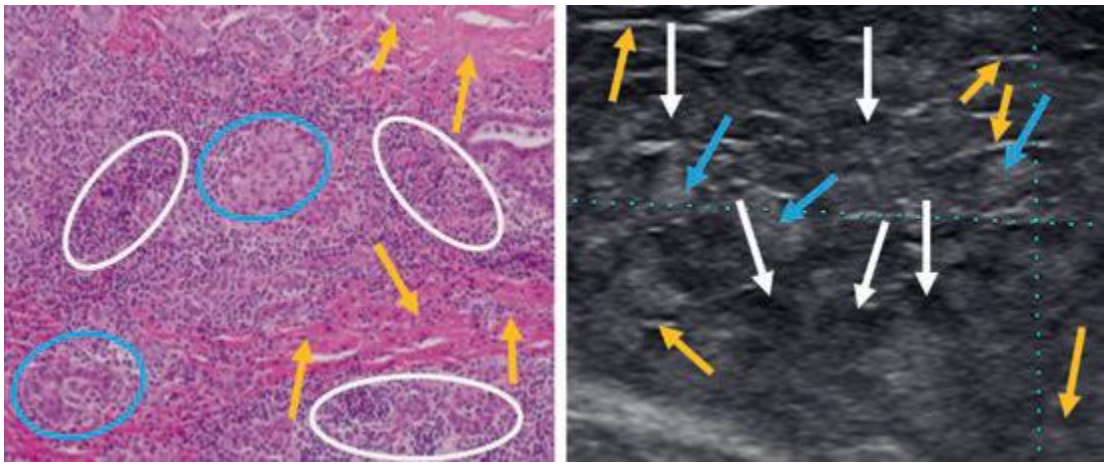

Figure 9: Hashimoto's Thyroiditis Pathology, and Ultrasound Correlation. White circle and white arrows: hypoechoic lymphocytic infiltration. Blue circle and blue arrows: isoechoic thyroid follicular cells. Yellow arrows: hyperechoic fibrotic lines *(16).*

The gland has either focal or diffuse lymphocytic infiltration with occasional germinal centers, small thyroid follicles with sparse colloid, and variable amounts of fibrosis (15) (16) (17).

1.5. Pathophysiology of Thyroid Diseases:

The thyroid produces and releases into the circulation at least two potent hormones, thyroxin (T_4) and tri-iodothyronine (T_3) (18). which influence basal metabolic processes and have effects on almost all body tissues (19).Thyroid hormones also influence linear growth, brain function including intelligence and memory, neural development, dentition, and bone development (Larsen, 2003) (18).Thyroid hormone affects virtually every organ system in the body, including the heart, CNS, autonomic nervous system, Bone, GI, and metabolism (20). The thyroid gland produces T_4 and T_3 utilizing iodide obtained either from dietary sources or from the metabolism of thyroid hormones and other iodinated compound (18).

The specialized thyroid epithelial cells of the thyroid gland are equipped with a Na /I symporter that helps concentrate iodide in the follicular cell to ensure adequate amounts for the synthesis of thyroid hormone (18). The iodide trapped by the thyroid gland then oxidized to iodine by the enzyme thyroid peroxidase. The iodine then undergoes a series of organic reactions within the thyroid gland to produce tetraiodothyronine or thyroxine (T_4) and triiodothyronine (T_3) (18).

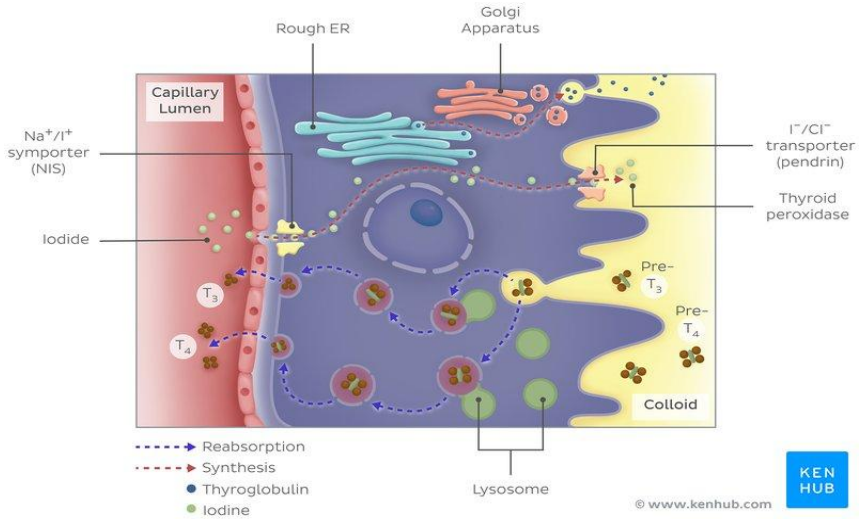

Figure 10: Synthesis of the Thyroid Hormones.

T_3 produced in other tissues such as the pituitary, liver, and kidney by the removal of an iodine molecule from T4 (18). T_4 considered more of a pro-hormone, while T_3 is the most potent thyroid hormone produced (21). T_4 and T_3 are both stored in the colloid of the follicular cells and controlled by thyroid stimulating hormone (TSH) from the anterior pituitary gland (22).

The synthesis and release of thyroid hormones are regulates by TSH which secreted by thyrotroph cells located in the anterior pituitary gland. The pituitary secretion of TSH in turn is regulates by the releasing factor, thyrotropin-releasing hormone (TRH) from the hypothalamus (21). The secretion of both TSH and TRH regulated by negative feedback from thyroid hormone, predominantly T_3, from the circulation and/or T_3 that produced locally from intracellular conversion of T_4 to T_3. When circulating thyroid hormone levels are elevated, both the synthesis and secretion of serum TSH blunted. In contrast, when circulating levels of T_4 and T_3 are low, serum TSH levels increased in a compensatory fashion. The geometric mean level of serum TSH in normal individuals is approximately 1.5 µU/ml as recently reported in the NHANES III study (Hollowell et al., 2002)(21).

When hypothalamic pituitary function is intact, serum TSH levels are markedly suppressed (to <0.05 µU/ml) in patients with hyperthyroidism and elevated circulatory levels of serum thyroxine, while a marked increase in TSH (>five µU/ml) occurs in patients with hypothyroidism and low blood levels of serum T_4. The mechanism through which TSH binds to and activates the thyroid gland understood. TSH binds to a specific membrane receptor located on the surface of the thyroid epithelial cell and activates the cell signaling mechanisms through the enzyme adenylate cyclase located in the plasma membrane. Activation of adenylate cyclase increases intracellular cyclic adenosine monophosphate (cAMP) levels, which in turn stimulate additional intracellular signaling events that lead to thyroid hormone formation and secretion (23).

In GD the T-lymphocytes become sensitive to antigen presented in thyroid gland ,and stimulate B lymphocytes to synthesize antibodies against antigens.one of These antibodies ,the TSH-R Ab is aimed against the TSH membrane receptor of thyroid cells and it is able to stimulate cells function. Circulating antibody is associated with disease positivity and recurrence (24). In HT. the thyroid cells destroys by cell and antibody-mediated immune processes ,is thought to be autoimmune with lymphocytic infiltration and fibrosis as typical features .There is little evidence of demonstrating a role for antithyroid peroxidase antibody (anti- TPO) in the pathogenesis of autoimmune thyroid disease (AITD) (25).

The pathogenesis of HT is the result of cell-mediated autoimmune, whereas GD results from humoral autoimmunity (26).

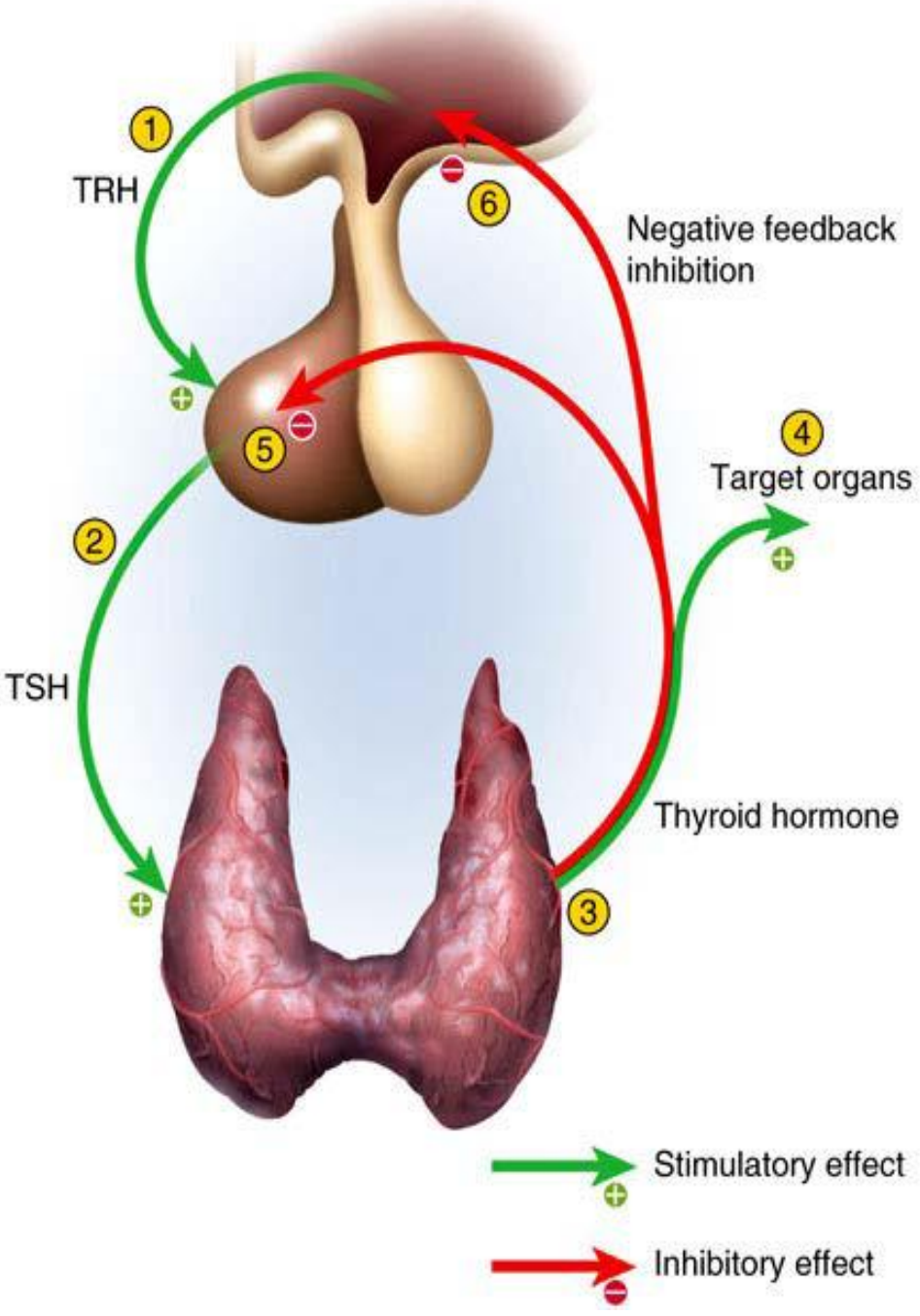

Figure1 1: Normal Thyroid Physiology

1.6. Epidemiology of Hashimoto's Thyroiditis:

It is most common among middle-aged women the disorder is most prevalent between 45 and 65 years of age, has a female predominance of 10:1 to 20:1 (27) (28). It affects 1.3% of children (29) (32).In addition to classic form, several other clinico-pathological entities are now included under the term of HT: fibrous variant, IgG4-related variant, juvenile form, Hashitoxicosis, and painless thyroiditis (sporadic or post-partum) (30) (32).HT is more common in iodine sufficient (e.g., USA) or excess (e.g., Japan) countries. Atrophy often noted in the gland with diffusely infiltrated lymphocytes (31) (32).Patients with Hashimoto thyroiditis may also present with other autoimmune disorders such as Jorgen syndrome, lupus, rheumatoid arthritis, fibrosing mediastinitis, sclerosing cholangitis, and pernicious anemia and are at an increased risk for the development of B-cell lymphoma (non-Hodgkin) (33) (34)(28).

1.6.1. Clinical, Biochemical Parameters of Hashimoto's Thyroiditis:

Clinical findings: the presence of a firm, painless, diffusely enlarged gland; a large number of patients with lymphocytic thyroiditis have nodular enlargement (35) (32). long- standing HT causes shrinking and atrophy of the thyroid, but may also lead to diffuse enlargement of the gland and/or formation of nodules .These nodules should be differentiated from PTC(papillary thyroid carcinoma) and primary thyroidal non -Hodgkin lymphoma , which are possible complications of HT. Pathologically proven HT. It usually defined as the presence of diffuse lymphocytic infiltration with occasional germinal centers, small thyroid follicles with sparse colloid, and fibrosis (36) (32).

Laboratory findings: high TSH (thyroid stimulating hormone), Low T 3 (triiodothyronine), low T4 (thyroxin).Diagnosis of HT was defined as elevated thyroid peroxidase (TPO Abs) and thyroglobulin antibodies (Tg-Abs),High serum TPO-Abs concentrations are present in more than 90–95%of patients (37)(32). Major specific antibodies in HT are TPO-AB and TG –AB; however, these antibodies also occur in ≈70 percentage of GD patients. The major antibody in GD thyroid hormone receptor antibody (stimulating TSHR-ABS) may also occur in a few patients with HT (31) (32). Elevated TSH with TPO antibodies is the gold standard for diagnosis of chronic Hashimoto's thyroiditis (31) (32).

The clinical manifestations of hypothyroidism vary, depending on its cause, duration, and severity. The spectrum extends from subclinical hypothyroidism to overt hypothyroidism to myxedema coma (38) (28).Common signs and symptoms include

weakness and fatigue, dry skin, cold intolerance, hoarseness, weight gain, constipation, menstrual irregularities, and decreased sweating (8).

1.7. Epidemiology of Graves ' disease (GD):

GD has the highest incidence in between 20 and 49 years of age, with a secondary peak at the age of 60-69 years (39) (32).It affects 0.02% of children (29) (32).

Which more common among Women than among men, with a w/m ratio ranging from 5:1 to 10:1(40) (28).Graves' disease characterized as a multisystem syndrome consisting of one or more of the following: (1) hyperthyroidism, (2) diffuse thyroid enlargement (goiter), (3) ophthalmopathy and, (4) Graves dermopathy (38) (28).

1.7.1. Clinical, Biochemical Findings of Graves` Disease:

Clinical finding: The early symptoms include Weight loss, anxiety, irritability, difficulty sleeping, and heat intolerance, sweating, shortness of breath, difficulty breathing, and increased stool frequency irregular menstrual periods in women. If graves not treated, diffuse goiter, ophthalmopathy and pretibial myxedema, and Acropachia (41) (32). ***Laboratory finding***: Low level of TSH, high level of triiodothyronine (T3), high level of thyroxine (T4). High thyrotropin receptor antibodies (TSHR -AB).

1.8. Ultrasound Characteristic of the Normal Thyroid Gland:

Ultrasound of the gland with a high-frequency transducer provides excellent detail. The normal thyroid gland has a homogeneous echo texture of medium echogenicity. The carotid vessels seen as anechoic structures on either side of the gland. The strap muscles are structures of low echogenicity. Linear echogenic lines may be separating the muscles. The prevertebral muscles may identified posteriorly. Numerous vascular structures maybe seen surrounding the gland and its extreme vascularity appreciated with color flow imaging (42).

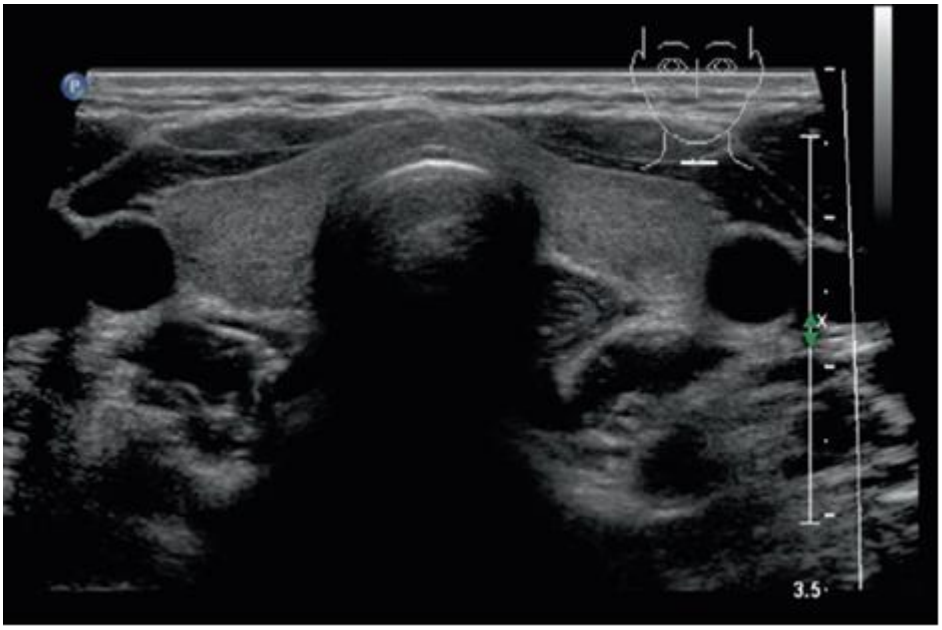

Figure 12: Normal Ultrasound Appearance of the Thyroid Gland

1.9. Arterial Resistivity Index **:** The arterial flow resistive index RI. is reflecting the intraparenchymal flow resistance in the thyroid tissue. Resistive index a sonographic indicator of an organ to perfusion. Calculated from the peak systolic velocity and the end diastolic velocity of blood flow.

Leander Pourcelo formula used to calculate resistance index is:

Resistive Index = $\frac{(\boldsymbol{systolic\ velocity - diastolic\ velocity})}{\boldsymbol{systolic\ velocity}}$

DESCREPTION:

RI	
0	Continuous flow
1	Systolic flow, but no diastolic flow
>1	Triphasic flow

The RI it is alter by combination of vascular resistance and vascular compliance.

Normal mean artery RI for an adult is 0.6 with 0.7 the upper limit of normal (43) (44) (45) (46) (47) (48). Analysis of the Doppler spectrum allows, determining velocity and resistance of the flow. By analyzing the waveform, the peak systolic and diastolic velocities were calculated. Resistive index (RI) calculated directly in some ultrasound machines and can calculated manually by using the above mention formulas.

The values more often use in studies of peripheral vascular disease. The peak flow velocity and resistive index also used to provide a reproducible quantification in reporting the degree of vascularity of thyroid tissue (17).

1.10. Ultrasound (US) Features Of Hashimotos` Thyroiditis: (US Imaging of Classical HT. Pattern):

An enlarged thyroid gland, diffusely coarse, heterogeneous echo texture, Micro lobulated margin. Multiple discrete hypo echoic micro nodules ranging from (one – six mm) in diameter separated by coarse septations from fibrous bands. (figure12)

A presence of peri-thyroidal satellite lymph nodes, especially the "Delphian" node just cephalic to the isthmus. (Figure 13)

Color flow Doppler sonography (CFDS): may demonstrate slight-to-markedly increased vascularity, Often, color Doppler demonstrates hypervascularity in the early stages of Hashimoto thyroiditis ,and in Graves' disease (6)(49)(32).

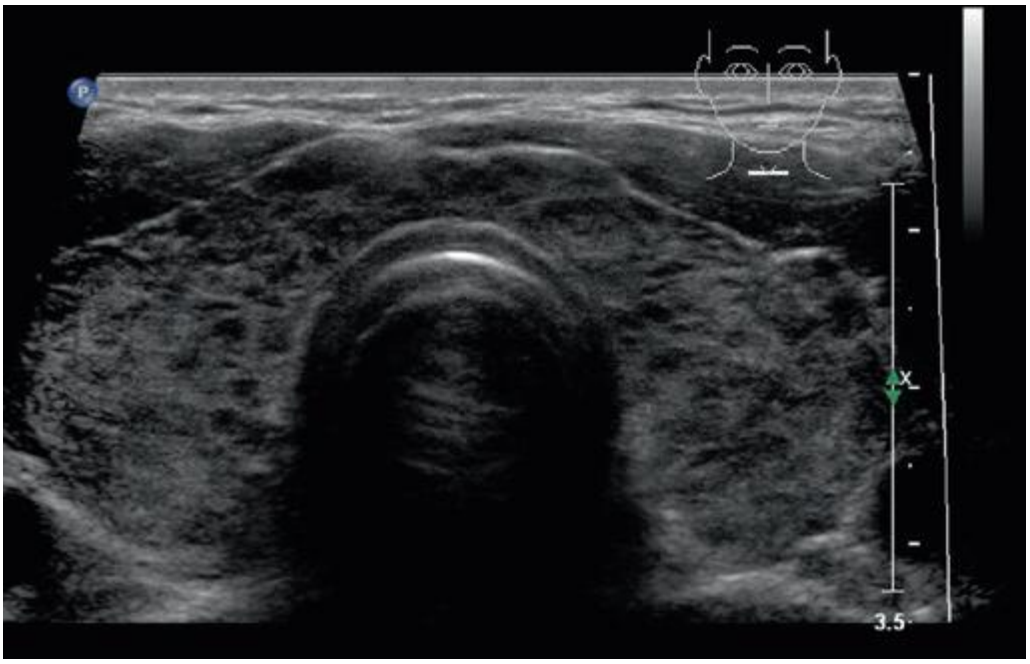

Figure 13: Classical Ultrasound Appearance: Heterogeneous, Micro Nodulation, Hypoechoechogenic Texture With Thin Fibrous Septations.

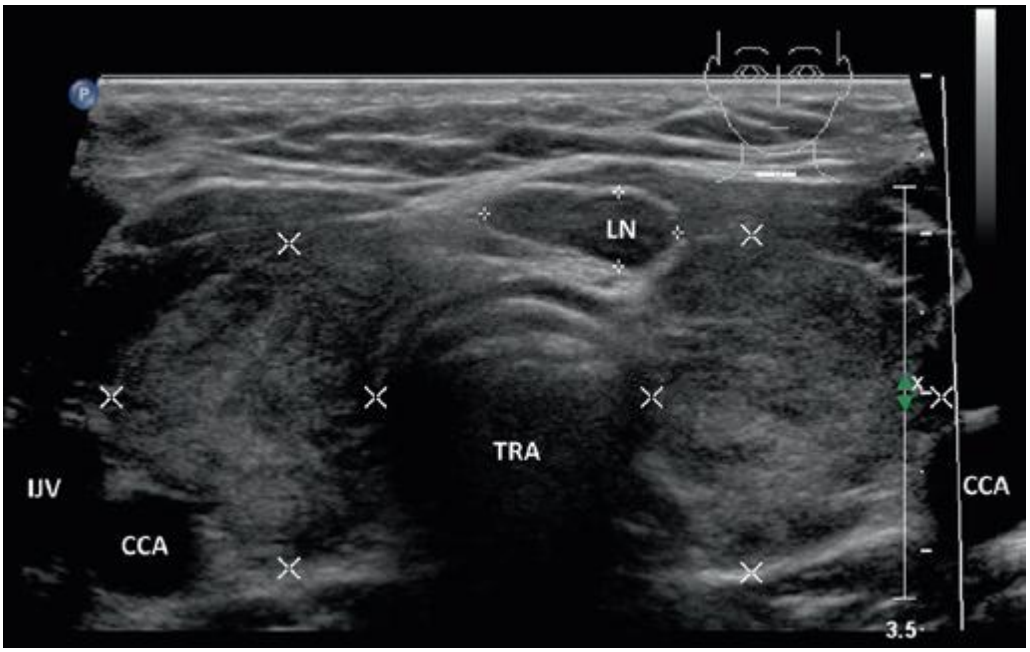

Figure 14: Ultrasound Appearance of Paratracheal Lymph Node (Level-VI), Delphian Lymph Node.

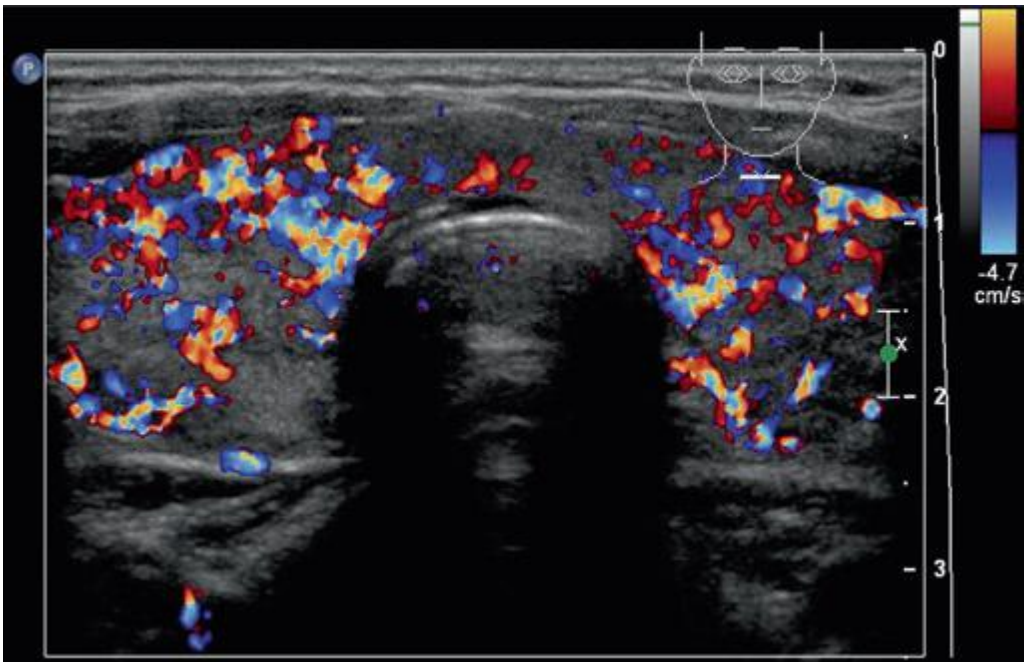

Figure 15: Qualitative Doppler Assessment (Diffusely Increased Vascularity, Pattern II).

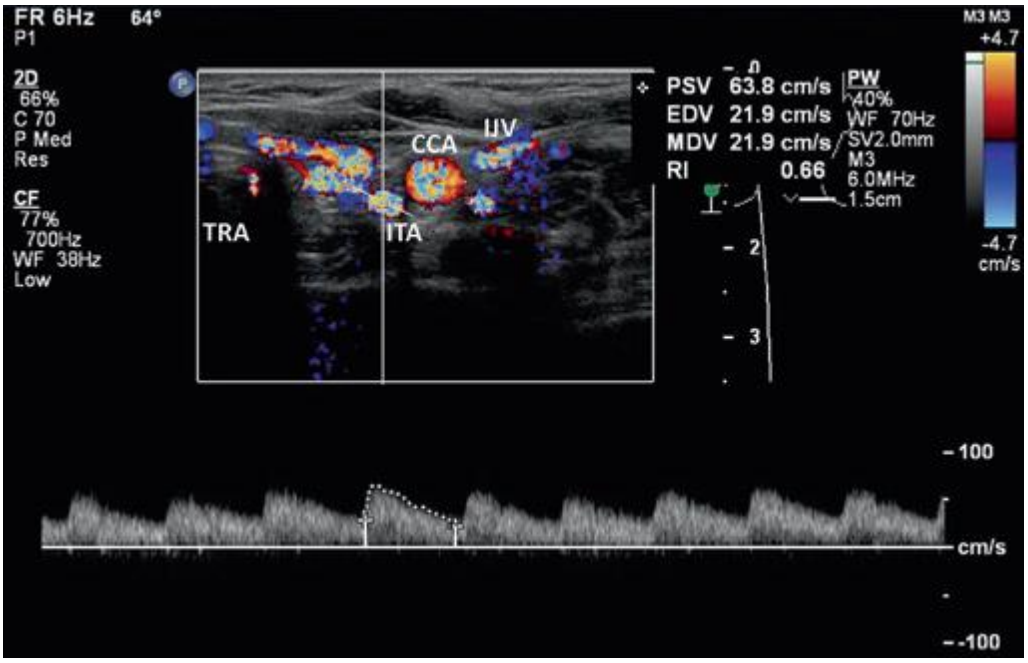

Figure 16: CFDS: Rt. Inferior Thyroid Artery Located between the Lower Pole of Rt. Lobe and Rt. CCA. Flow Parameter Measured the Peak Systolic Velocity (PSV) and (RI).

A diffusely heterogeneous, hypoechoic gland is not specific for HT and that maybe seen in Graves' disease, and sub-acute thyroiditis (35) (32).

Thyroid volume changes throughout the course of hashimoto disease for the evaluation of goiter (51) (32). Micro nodules of HT can increase in size as focal lymphocytic thyroiditis (FLT). In addition, be present as hypo echoic or hyperechoic nodules with ill-defined margins on US. These nodules known as "pseudo-tumors" constituted 36% of the nodules of focal thyroiditis detected by US and are simulating nodular disease indistinguishable from thyroid cancer or lymphoma (35) (32).

Color flow Doppler sonography is a useful, inexpensive, non-invasive and widely available method for measuring tissue vascularization and blood flow. CFDS can evaluate both qualitative parameters – (visual assessment of thyroid vascularity) and quantitative parameters (Doppler spectral analysis measurement)—inferior /superior thyroid arteries peak systolic (PSV), end diastolic (EDV), and mean blood flow velocities (52).

Both autoimmune thyroid diseases GD and HT have similar US pattern characterized by an enlarged thyroid gland, diffusely heterogeneous echo texture, and predominant hypo

echogenicity. A diffusely increased thyroid blood flow, so-called “thyroid inferno" is pathognomonic of untreated GD and this CFDS pattern identifies the majority of Graves’ patients. However, HT during the initial hyperthyroid phase can also Present CFDS qualitative pattern of marked and diffusely increased vascularity Could be easily confused with graves 'disease(53)(32) . However, the hashimoto` thyroiditis may also be associated with any degree of vascular flow (17).

Quantitative parameters are useful in distinguishing (the hyperemic gland and goiter)
In patients with GD and HT. (PSV, EDV, and mean velocities) of inferior thyroid artery (ITA). In patients with GD were significantly higher than in patients with HT (54).

1.11. Qualitative Assessment of Color Flow Doppler Sonography (CFDS):

- Pattern 0: absent intraparenchymal (or nodular) vascularity or minimal spots.
- Pattern I: presence of parenchymal (or nodular) blood flow with patchy uneven distribution.
- Pattern II: mild increase of color flow Doppler signal with patchy distribution (for nodules: mainly peripheral).
- Pattern III: markedly increased color flow Doppler signal with diffuse homogeneous distribution, including the so-called “thyroid inferno"(32).

1.12. US Features of Graves’ disease: *(US Imaging of Classical GD Pattern)*

Can either present with a normal sized or an enlarged gland with round-shaped lobes -sometimes-giant goiter diffusely hypoechoic, heterogeneous or coarse echotexture, typically hypoechoic micronodular structure with-short fibrous septa. CFDS demonstrate markedly increased vascularity pattern III—“thyroid inferno".

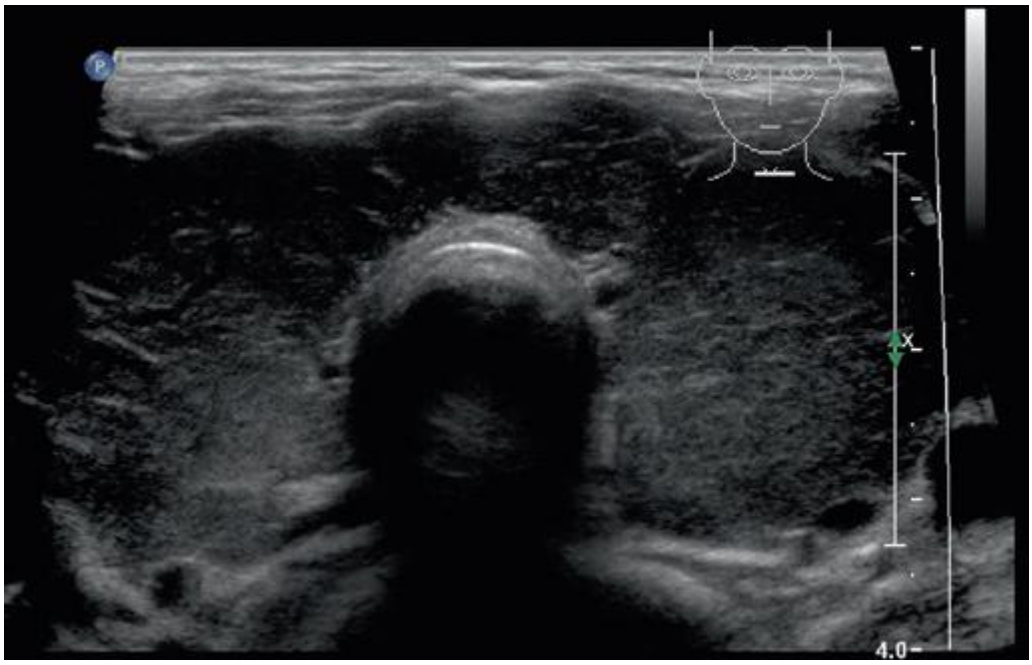

Figure17: Classical Ultrasound Appearance of Diffuse Thyroid Enlargement (Goiter).

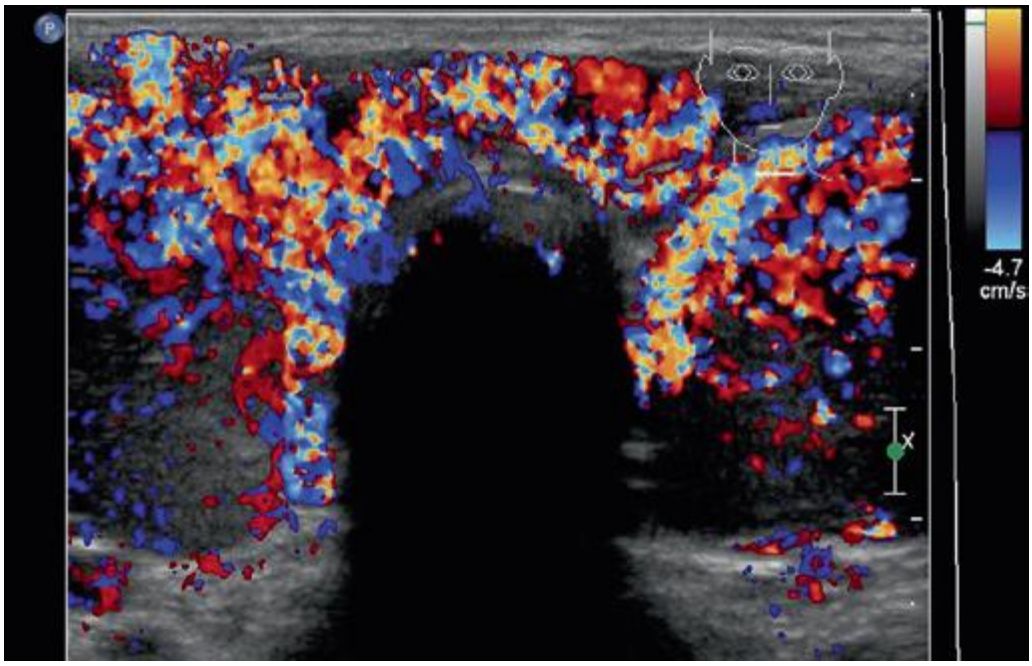

Figure 18: CFDS Demonstrated Qualitative Assessment Of Vascular Pattern Demonstrated Grade III Vascularity (Thyroid Inferno).

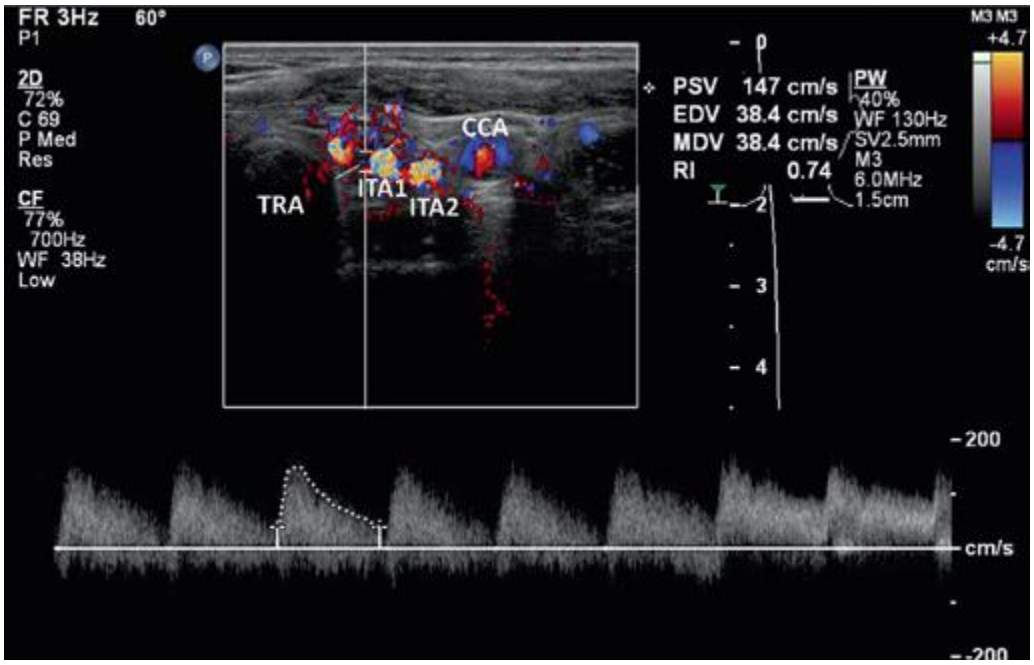

Figure 19: Quantitative Doppler Assessment of Right Superior Thyroid Artery (STA), Intense Shunting Flow with Increase Velocity (PSV).

CHAPTER 2

LITERATURE REVIEW

2. Literature review

Limited studies have reported the role of quantitative Doppler assessment to differentiate between Graves` disease and hashimotos thyroiditis.

2.1. Study of Unchida Toyoyoshi et al. (2010):

Aim of study to assessed the ability of peak systolic velocity of superior thyroid artery to discriminate untreated Graves` disease from treated graves` disease and Destructive thyroiditis in Japanese patients with thyrotoxicosis. Unchida Toyoyoshi et al. in (2010) studied 57patients with thyrotoxicosis. The results found that, the mean STA-PSV was the highest in the untreated GD groups, followed by treated GD patients and then those with destructive thyroiditis (DT) (55).

2.2. Zhao xialong et.al. (2012):

Aim: The differentiation of destruction-induced thyrotoxicosis and Graves' disease (GD) is of great importance for selection of proper therapy. Radioactive iodine uptake (RAIU) is the gold standard for differentiating these two conditions but its application has remained somewhat limited. Thyroid color Doppler flow sonography (CDFS) is a potential alternative of RAIU but more supporting evidence warranted. In the present study in china, a standard operative procedure developed to measure the mean peak systolic velocity of superior thyroid artery (STA-PSV) and evaluate its role in the differential Diagnosis of thyrotoxicosis. Out of 135 patients with untreated thyrotoxicosis were enrolled into one retrospective study (GD, n = 103; Thyroiditis, n = 32) and another prospective study recruited 169 patients (GD, n = 118; thyroiditis, n = 51). Thirty normal controls also enrolled. Results: STA-PSV of GD was significantly higher than that of thyroiditis in both retrospective and prospective studies (56).

2.3. **Study of Sarikaya B. et al. (2012):**

Objective: the role of Doppler ultrasonography in the diagnosis of diffuse thyroid disease is not well established.in particular Doppler ultrasonography findings in children with hashimotos thyroiditis are very limited. We examined gray- scale and Doppler findings in hashimotos thyroiditis in children in an attempt to understand the feasibility of future prospective controlled studies. Pilot study by Sarikaya B. et al. (2012) studied the mean resistive index values between patients normal gray scale or near normal gray scale finding. This study in turkey with 21 pediatric patients. The results found that the mean RI value, calculated as the mean of the RI values of both lobes obtained from each patient, found to be 0.57±0.05. The results indicated that the

RI might be more sensitive than other ultrasound parameters for the diagnosis of Hashimoto's thyroiditis. The distribution of thyroid classifications was as follows: pattern 0, n=7; pattern 1, n=six; pattern II, n=four and pattern III (thyroid inferno), n=four. The major conclusion of study is that, despite variations in color Doppler patterns, there was no statistically significant difference in the mean RI values between patients with normal or near-normal gray-scale findings and patients with marked Gray-scale changes (57).

2.4. *Study* of Donkol et al. (2013):

Aim of study, to evaluate the role of Thyroid blood flow assessment, by color – flow Doppler ultrasonography in the differential diagnosis of thyrotoxicosis and compare it to technetium pertechnetate thyroid scanning. Donkol et al. (2013) studied 26 patients with thyrotoxicosis in Cairo. The study results it was identified the peak systolic velocity in the inferior thyroid arteries were significantly higher in patients with graves` than in patients with thyroiditis (p=0.004in the rt. Inferior thyroid artery and p=0.001in left inferior artery).color flow Doppler ultrasonography parameters demonstrated a sensitivity 88.9% and specificity of 87.5% in the differential diagnosis of thyrotoxicosis (58).

2.5. **Banaka Ioanna et al. (2013**):

Objectives—the purpose of this study was to calculate a number of thyroid gray scale And Doppler sonographic parameters in healthy individuals and patients with Hashimoto thyroiditis or Graves' disease and assess their sensitivity and specificity for The diagnosis of autoimmune thyroid disease using receiver-operating characteristic Curves. This study in (greec), **Banaka Ioanna et al. In (2013**) carried out 153 patient the results reported that the patients with graves` disease had higher mean PSV. On the contrary, no statistically significant differences observed in the RI between hashimotos thyroiditis and graves` disease (59).

2.6. Hiraiwa Testsuya et.al. (2013):

The aim was to determine whether the measurement of peak systolic blood-flow velocity in the superior thyroid artery (STV) and thyroid tissue blood flow (TBF) using CDU could differentiate Graves' disease (GD) from painless thyroiditis (PT). The second objective was to examine the factors mediating increased blood flow to the thyroid gland in GD. In japan; Hiraiwa Testsuya et.al. (2013) carried out 68 patients in the GD group, 33 in the PT group, and 25 in the normal control group. Six out of 27female patients with PT had postpartum thyroiditis. The results found that peak

systolic velocity at superior thyroid artery measurements successfully differentiated GD from PT (60).

2.7. Kim Tea Kayoo et al. (2015):

The aim of this study was to validate the superior thyroidal artery mean peak systolic velocity (STA-m PSV) as an alternative to other diagnostic parameters in the differentiation of the causes of thyrotoxicosis in Korean patients**.**The study conducted with newly diagnosed and untreated thyrotoxic patients. Forty patients diagnosed with Graves' disease (GD) and 20 patients with destructive thyroiditis (DT). Another 60 healthy subjects without thyroid disease participated as the control group. The results: The STA-mPSV was significantly higher in the untreated GD group than in the DT group (GD, 78.96±29.04 cm/sec; DT, 29.97±14.67 cm/sec; control, 17.55±4.99 cm/sec; P<0.001) (61).

2.8. Study of Sundarram Ks Thalavai et al. (2017):

Aim of study to evaluate the role of color Doppler ultrasonography in differentiation of Graves ' disease from thyroiditis: A prospective cohort study in India out of 120 newly diagnosed thyrotoxicosis patients, 54 were GD and 66 were DT. Patient's .totally, 55 euthyroid patients served as controls, results of study: both groups were age and sex matched. the mean peak systolic velocity of superior thyroid artery (cm/s) was statistically higher in group (graves` disease)(54.09±4.67) than group II(hashimotos thyroiditis (28.92±4.39) ($p \leq 0.001$) . mean PSV-ITA(cm/s) was higher in group I (graves`)(32.11±2.45)than group II (25.23 ±3.45)(p=0.006). In the same study, they found that bilateral mean RI-STA in GD was not statistically higher than in hashimotos disease, and the mean RI-ITA in GD. Was not statistically higher than HT (62).

CHAPTER3

AIM OF STUDY

AIM OF THE STUDY:

1. The Aim of the present study to evaluate the usefulness of quantitative assessment of resistive index (RI) and peak systolic velocity(PSV) in the differentiation between the Graves' disease and Hashimoto`s Thyroiditis among patient from endocrine clinic at Benghazi 2018.
2. To assess the overlapping in the sonographic features between some cases of Graves` disease and hashimotos thyroiditis, when they are in Hashitoxicosis stage ,on other hand there is some cases of Graves` disease they had the same ultrasound features of Hashimotos Thyroiditis as (Micronodulation & fibrous septations).

CHAPTER4

SUBJECT AND METHODS

4. SUBJECT &METHODS:

4.1. SUBJECT:

Sixty-nine patients with hyperemic enlarged gland were included in the study. The diagnosis of Graves ' disease and hashimoto thyroiditis was supported by clinical picture and biochemical results. The known cases referred from endocrinologist at Al-hawari General Hospital and Benghazi medical center (BMC) department to ultrasound unit at Benghazi Radiology Center (BRC). The thyroid glands of all patients were been evaluated by gray scale ultrasonography for size, shape and echo texture, presence of echogenic fibrous septations and paratracheal lymph nodes. Color-flow Doppler ultrasonography of the thyroid tissue was performed and spectral flow analysis of superior or inferior thyroid arteries it assessed. The patients divided into two groups: 30 cases with Graves' disease (3 male and 27 female) and 39 cases with Hashimoto's thyroiditis (4males and 35 female). The Inclusion criteria of the two groups of cases depend on the clinical and laboratory investigation presenting in the endocrine clinic with goiter and hormonal disturbance , Exclusion criteria included toxic nodule, multinodular goiter, history of thyroid surgery, radioiodine therapy or radiation exposure to neck. The study done in the Benghazi from 4 April 2018 to 1-January-2019**.**

4.2. METHODS:

Sonographic examination is a noninvasive, relatively inexpensive, and objective diagnostic test for diffuse thyroid diseases. Begin the examination by review the medical history from the referring physicians and obtain information from the patient. Information about symptoms, duration, current treatment. No patient preparation is required for these groups of patients for thyroid ultrasonography, the patient in a supine position, hyperextending the neck. This will permit easier access to the thyroid gland. Each subject underwent ultrasound examination using A Hitachi sonographic machine with a 7.5-MHz transducer. Ultrasound examination performed by the same researcher for all patients. Gray-scale ultrasonography parameters included echogenicity and size of the thyroid gland as well as the presence or absence of nodules and fibrous septea .In addition, the thyroid enlargement (goiter) was evaluated. Staying alert for any extra thyroid masses, such as enlarged lymph nodes. Panoramic imaging used when scanning enlarged glands; some cases the only way to demonstrate the thyroid gland in its entirety.

Color flow Doppler, pulsed wave Doppler imaging contribute to the thyroid sonography examination by revealing internal vascular detail.

The color flow mapping and spectral analysis evaluation of the thyroidal arteries peak systolic velocity (PSV) using small sample volume 1-2 mm adjustment, in vessel center with insonation angle should be 0º-60º, and adjust the angle correction parallel to the vessel wall,. The measurement of RI either in thyroidal arteries or in the intraparenchymal thyroid arterioles with smallest sample volume 1-2 mm. was calculated using the software built in the used ultrasound equipment.

The vascularity pattern of both lobes was determined based on a visual scale (Qualitative assessment of thyroid vascularity) according to the classification previously created by Schulz et al.

Table4.1: Color Doppler Classification in Hypothyroidism, By Schulz Et Al.

Pattern 0	**Blood flow limited to the peripheral thyroid arteries, while parenchymal flow is absent**
Pattern I	Presence of mildly increased parenchymal flow
Pattern II	Clearly increased color flow with a diffuse homogenous distribution
Pattern III	Markedly increased color flow with a homogenous distribution, including the so-called ‘‘thyroid inferno

PSV and RI measurements performed within each lobe of the thyroid at a location close to the center, where vascularity still observed. In addition, a mean RI value for the entire patient group was calculated. The Doppler spectral analysis of the inferior or superior thyroid arteries in the transverse scanning, in which the ITA It supply the postero-inferior aspect of thyroid lobe, The inferior thyroid artery was examined in the oblique transversal plane, close to the transition between the medium and the inferior third of the thyroid lobe(63) . The STA it supplies the superior and

anterior aspects of the thyroid gland STA identified as the first branch of external carotid artery that arises anteriorly at the level of hyoid bone (64).

RI values, calculated using the formula of Pourcelot:

$$\text{Resistive Index} = \frac{(\textbf{\textit{systolic velocity} – \textit{diastolic velocity}})}{\textbf{\textit{systolic velocity}}}$$

Resistive index (RI) can be calculate using the formulas above, or by the ultrasound machine. The peak systolic flow velocity and resistive index they are provide a vascular quantification of thyroid tissue. Analysis of the Doppler spectrum allows determining the velocity of flow and the calculation of the resistance to flow. By analyzing the waveform, the peak systolic and diastolic velocities can be calculating.

DESCREPTION:

RI	
0	Continuous flow
1	Systolic flow, but no diastolic flow
>1	Triphasic flow

The RI is altering by the combination of vascular resistance and vascular compliance. Normal mean artery RI for an adult is 0.6 with 0.7 the upper limit of normal. Data were analyzed using statistical package for the social sciences software (SPSS STATISTICS 21) for comparison of continues variables between different groups, Data analysis was done using chi-square test (x^2) &T-test. In addition, measured the level of significantly by P –value.

CHAPTER 5

RESULTES

5. RESULTS:

69 patients with thyrotoxicosis and goiter referred from endocrine department as known cases differentiated by clinical, biochemical data. A 30 cases with Graves' disease (3males & 27 female) and 39 cases of thyroiditis (4males & 35 female), were examined.

1. Age differences between HT and GD the study found no significant differences between hashimotos and Graves` disease were the (*T-test =0.023), (P =0.9).* The mean age of HT cases (*37.8±9.5*) & the mean age of GD was (*37.7±12.7*) (table 2).
2. Resistive index differences between HT and GD the study found no significant differences between HT and GD were the (*T- test = 0.37), (P =0.72*). The mean resistive index of HT cases were (*8.8±8.8)* & the mean resistive index of GD was (*7.9±11.7*) (Table 2).
3. Peak systolic velocity of thyroidal arteries differences between HT and GD The study found that significantly higher differences between HT and GD where the *(T-test -7.9), (P =0.001).* The mean peak systolic velocity of HT was (*23.5±10.8)* and the mean of GD. was (*73.8±6.10*) (table2).
4. Vascular grading differences between HT &GD There is significantly higher differences between two entities were the (*T-test value -7.5*), (*P value =0.001*).The mean vascular grading of HT *(1.97±0.4*) and the mean of GD (2.8± *0.5*) (table2).
5. Sex: we found there no significant differences between HT and GD. the disease affect the females more than males where X^2_1=0.01 & Fishers 'Exact Test (P = *0, 65*). In addition, found that in HT 4 (10.2%) were males and 35(89.7%) were females in comparable with GD we found that three (10%) were males and 27(90%) were females (table3).
6. The present study reported highly significant differences between HT&GD regarding thyroid nodules were ($x^2_{1=}$*11.2&p=0.001**),* We found in HT 12(30.7%) were thyroid nodules present and *27(69.2%)* were thyroid nodules absent in comparable with GD (0) were thyroid nodule present, 30(100%) were thyroid nodule absent (table 3).
7. The present study reported highly significant differences between HT& GD regarding the size of thyroid gland (x^2_2*=11.64 &p=0.003*).The current study found that in HT cases five (12.8%) were normal size of thyroid gland,

24(61.5%) were mildly enlarged thyroid gland &*10(25.6%*) were markedly enlarged thyroid gland. In comparable with GD we found two (6.66%) were normal, eight (26.6%) were mildly enlarged and 20(66.6%) were markedly enlarged gland.

8. The present study reported highly significant differences between HT. and GD regarding Echopattern (x^2_2*=22.8, p=0.001**), the* current study found that in HT cases two (5.12%) were homogenous Echopatteren, *32(82%*) were micro nodular echo pattern & *five (12.8%)* heterogeneous Echopatteren.in GD cases 13(43.3%) were homogenous Echopatteren, 8(26.6) were micronodular Echopatteren, 9(30%) were heterogeneous Echopatteren.
9. The present study reported significant differences between HT and GD as fibrous septations are concerned (x^2_1*=5.3&p=0.21*).*the current study found that in HT cases 10(25.6%) were few septations, *29(74.3%)* were numerous septations & *(0)* were absent septations.in GD cases eight (27.58%) were few septations, 10(34.48%) were numerous septations and 12(37.9%) were absent septations.
10. The current study reported significant differences between HT and GD as Delphian lymph nodes are concerned. *(X^2_1=5.33&p=0.035*) the current study found that in HT cases *nine (23%)* there was of Delphian lymph nodes present & *30(77%*) there was no Delphian lymph nodes, there was no any Delphian lymph nodes seen in graves` disease cases were ,29(97%) were absent Delphian lymph nodes.

Table 5.1: Comparing Quantitative Parameters between Hashimotos and Graves Thyroiditis among Patients from Endocrine Clinic at Benghazi.

Items	Hashimotos	Graves	T-Test	P-Value
Mean Age± SD	37.8±9.5	37.3±12.7	0.023	0.98
Mean RI± SD	8.8±8.8	7.9 ± 11.7	0.37	0.72
Mean PSV±SD	23.5±10.8	73.8±6.10	-7.9	0.001**
Mean Vascular Grading± SD	1.97±0.4	2.8± 0.5	-7.5	0.001**

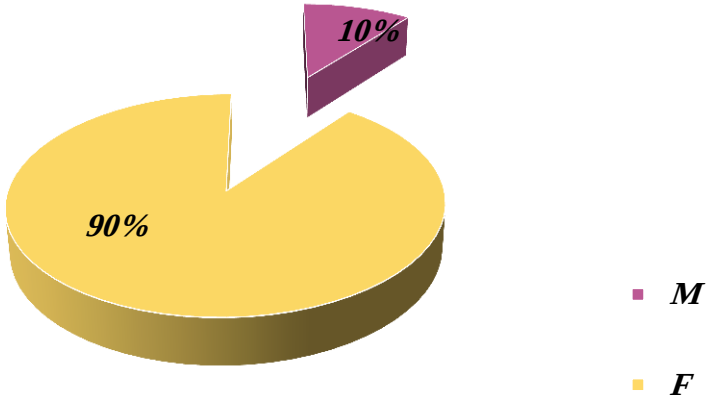

Figure 20 :Sex Distribution Among Thyroid Diseases

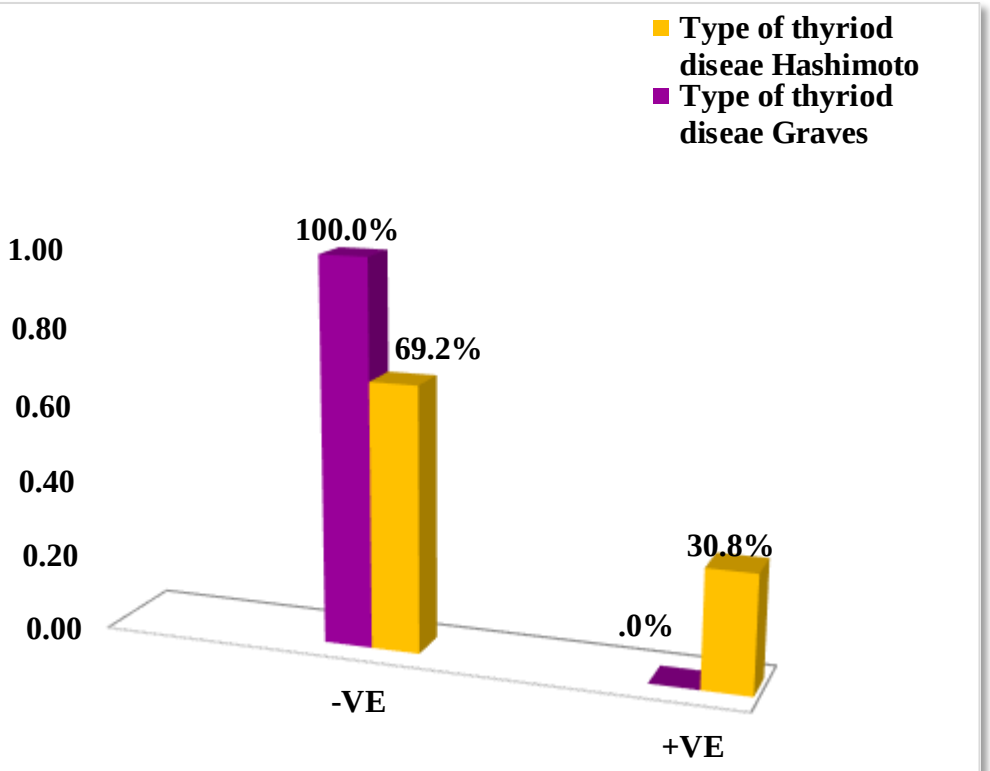

Figure 21: Comparison between Hashimotos Thyroiditis and Graves`Disease According to the Thyroid Nodule.
p=0.001 **

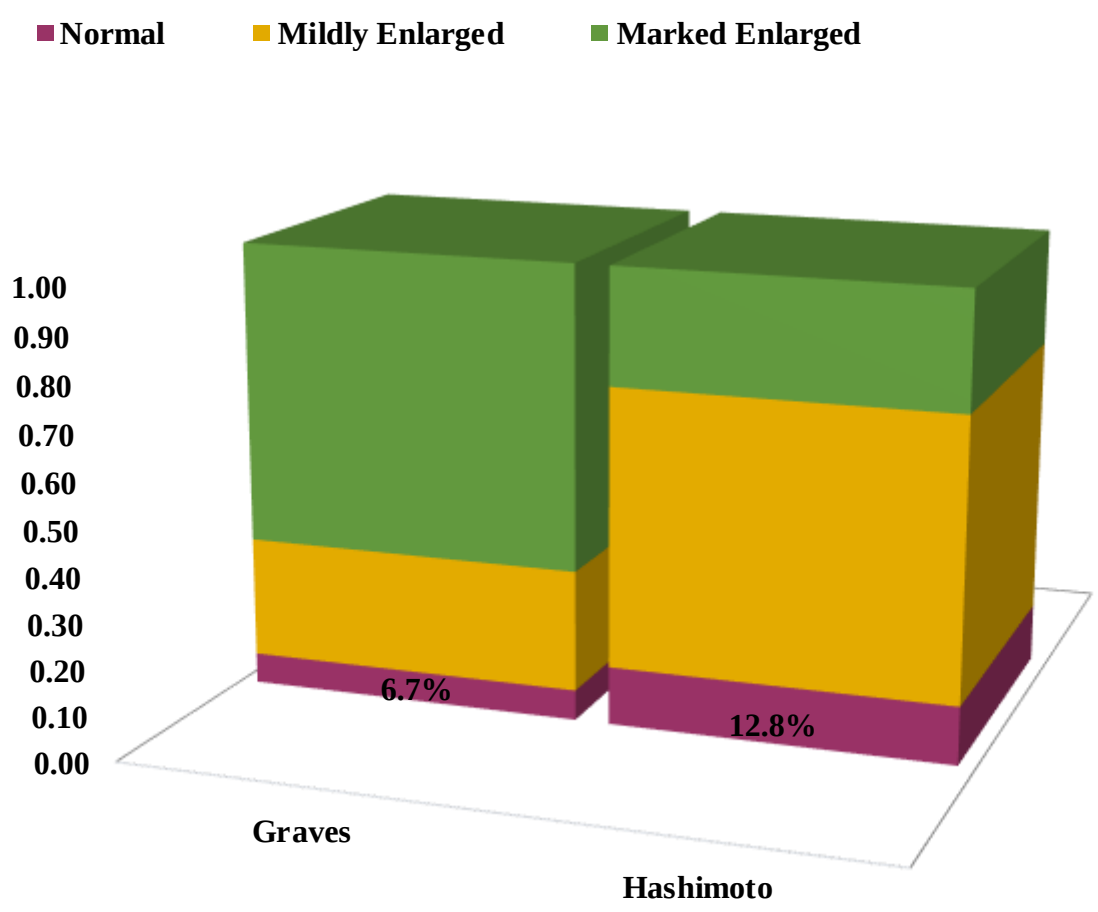

Figure 22 :Differences between Hashimotos Thyroiditis and Graves`Disease According to Size of Thyroid Gland p=0.003**

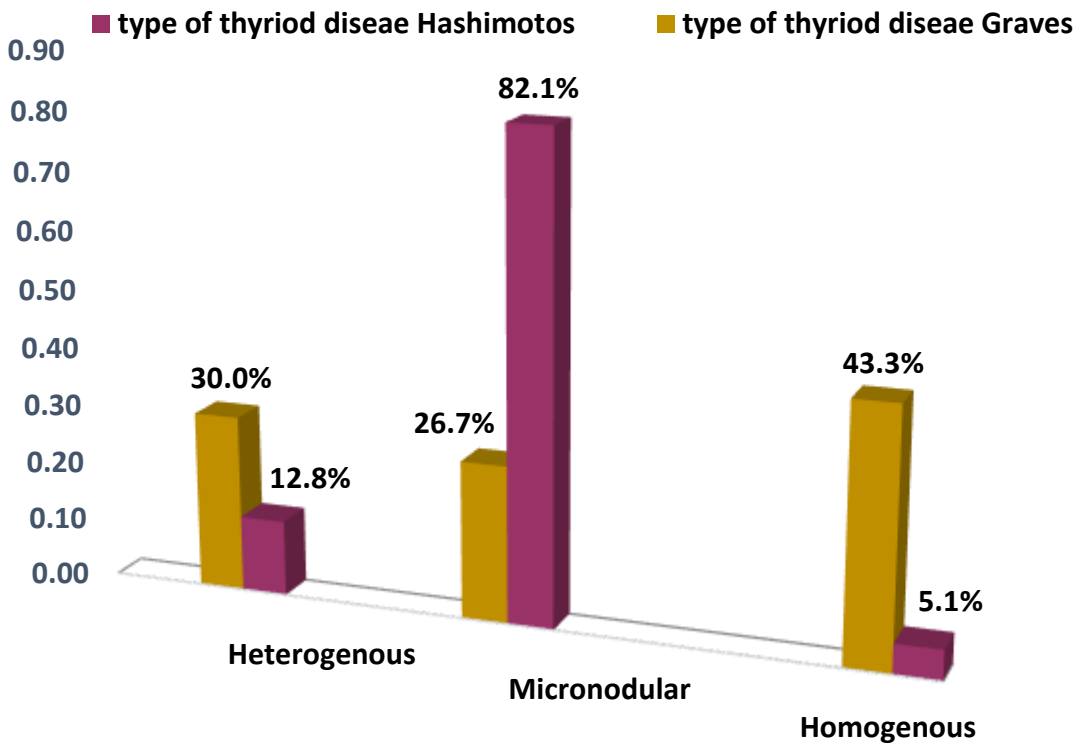

Figure 23:Differences Between Hashimotos Thyroiditis and Graves` Disease According to Echopattern P=0.001**

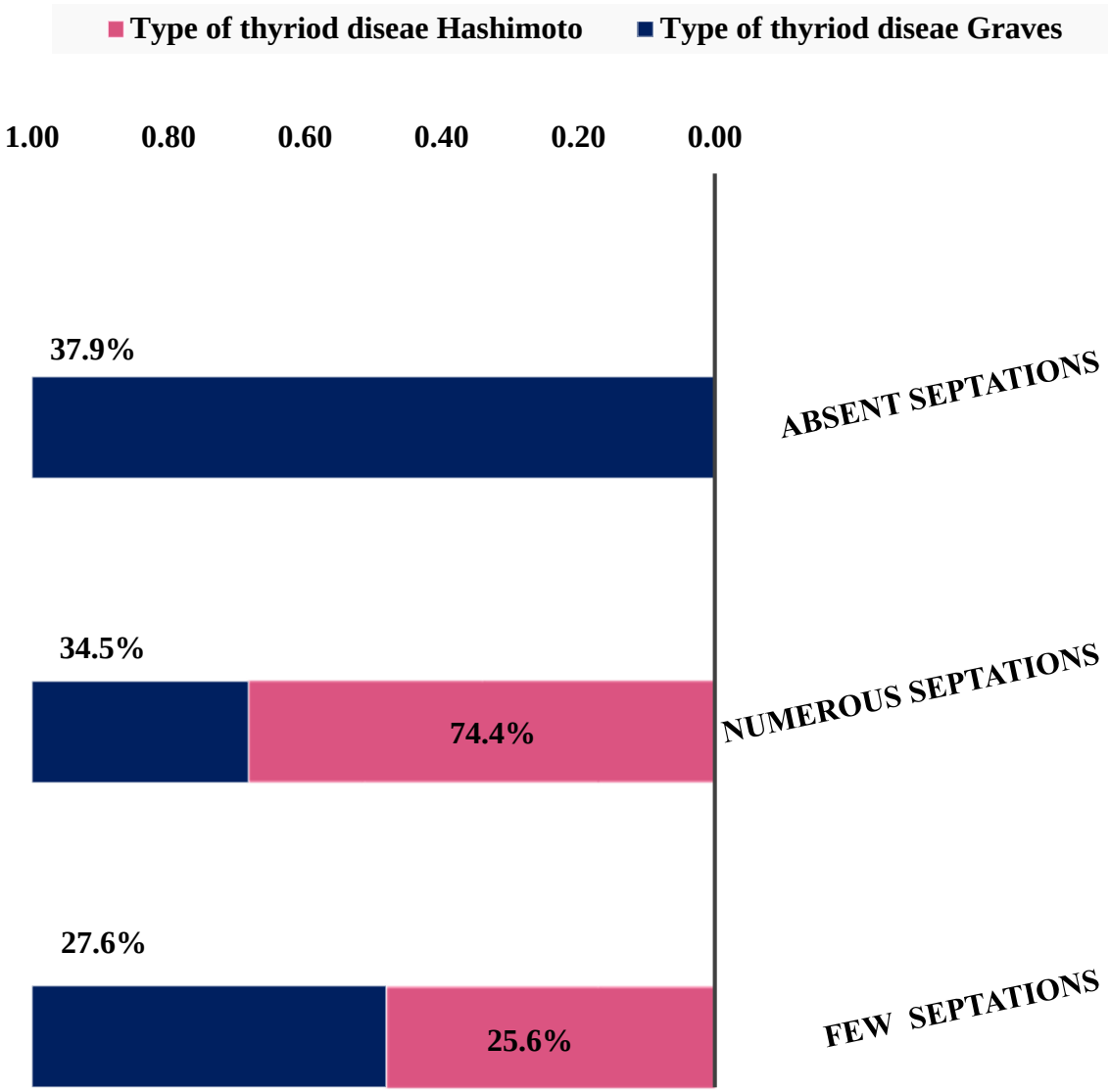

Figure 24:Comparison Between hashimotos Thyroiditis and Graves` Disease According to Fibrous Septation P=0.21*

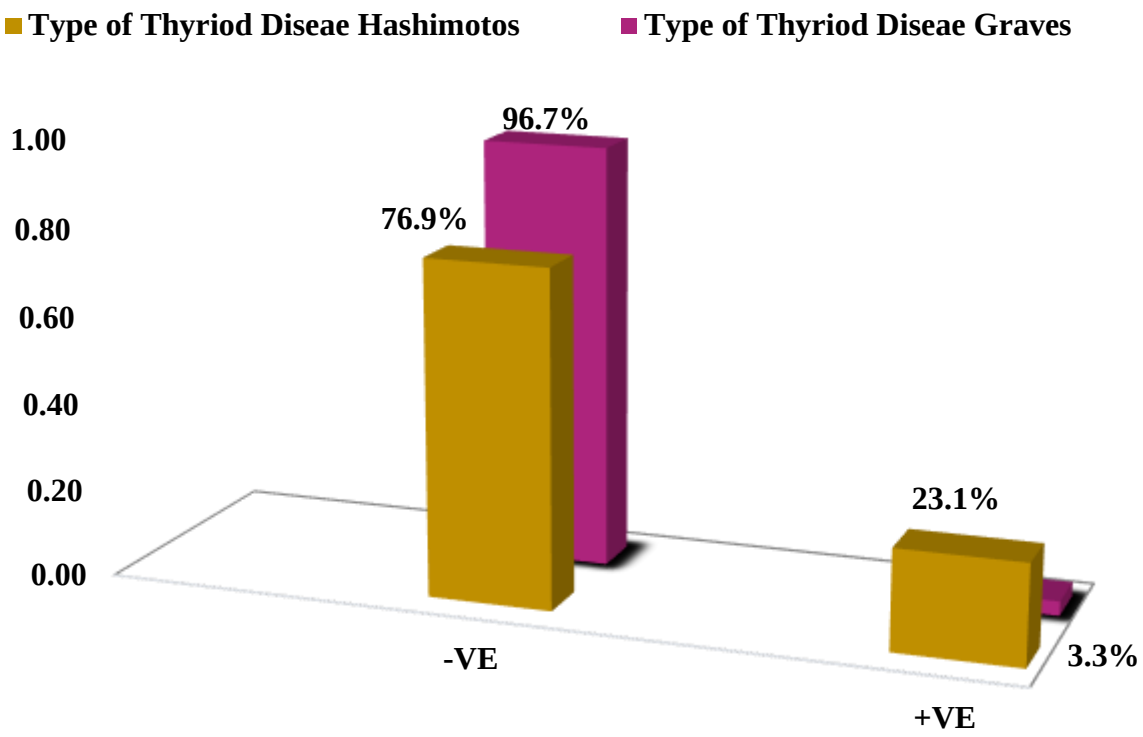

Figure 25:Comparison between Hashimotos Thyroiditis and Graves` Disease According to Presence of Lymph nodes. p=0.035*

CHAPTER 6

DISSCUSION

6. DISCUSSION:

In the present prospective case series study of 30 patient Graves` disease and 39 hashimoto`s thyroiditis depend on clinical and biochemical investigation for differentiate between graves` disease and hashimotos thyroiditis at endocrine department, the thyroid blood flow was evaluated by color Doppler and quantitative Doppler assessment where used to differentiate between Graves` disease and hashimotos thyroiditis. Despite the gold standard to differentiate between the two types of thyroiditis (thyroid T99pertechnetate scan). However, limited availability, high cost and contraindications to a radioisotope scan during pregnancy and lactation may restrict its application. CDFS is more accessible and available than radioisotope scan.

The present study estimate the reliability of PSV and RI to the differentiation between Graves` disease and hashimotos thyroiditis among Libyan patients in Benghazi. To assess the overlapping in the sonographic features between some cases of Graves` disease and hashimotos thyroiditis, when they are in Hashitoxicosis stage ,however there are some cases of graves` disease had the same ultrasound features of hashimotos thyroiditis as (Micronodulation & fibrous septations).
However, the Differentiation is difficult.

The advantages of measuring peak systolic velocity (PSV), resistive index (RI) are simple procedures, and the results confirmed immediately. However, the disadvantages of PSV and RI. The measurement of blood-flow velocity & index is difficult without a high-performance ultrasound device. Furthermore, peak systolic velocity with resistive index measurement requires technical expertise. The quantitative Doppler assessment ultrasound is not invasive and performed repeatedly. In addition, the lack of exposure to radioactivity and the low cost are major advantages over the scintigraphy.

6.1. *Regarding To Peak Systolic Velocity:*

The present study indicated that superior and / or inferior thyroid arteries / peak systolic velocity obtained by quantitative color Doppler assessment are useful in the differentiation between Graves` disease and hashimotos thyroiditis. Where the mean peak systolic velocity of hashimotos thyroiditis was (23.5±10.8) and the mean peak systolic velocity of Graves` disease was (73.8±6.10) (table 2)**. Donkol et al.** ***(2013)*** reported that the peak systolic velocity in the inferior thyroid arteries were significantly higher in patients with Graves 'disease than in patients with thyroiditis (Donkol et al.), the mean PSV of 40.0cm /s. in ITA was higher and suggestive of GD (58) . While, other

studies reported a PSV of above 50.0cm/s, values above 100 cm/s reached in newly diagnosed patients or patients not responsive to treatment (58).sensitivity and specificity for the diagnosis of autoimmune thyroid disease. They found no statistically significant differences observed in the RI between the groups (59).**Unchida Toyoyoshi et al. in (2010)** studied 57 patients with thyrotoxicosis. They attempted to differentiate Graves' from destructive thyroiditis, using spectral analysis of the superior thyroid artery mean peak systolic velocity. Also demonstrating a statistical difference between 44 patients with untreated Graves' disease and 13 with destructive thyroiditis, the mean STA-PSV was the highest in the untreated GD group, Followed by treated GD patients and then those with destructive thyroiditis (55).

Sundarram Ks Thalavai et al. (2017) reported that the mean peak systolic velocity of superior thyroid artery (cm/s) was statistically higher in-group I (graves` disease) (54.09±4.67) than group II (hashimotos thyroiditis) (28.92±4.39) ($p \leq 0.001$). Mean PSV- ITA (cm/s) was higher in-group I (graves`) (32.11±2.45) than group II (25.23 ±3.45) (p=0.006) (62). **Hari Kumar et al.** reported the ability to distinguish GD from destructive thyroiditis using color-flow Doppler imaging and peak systolic velocity (PSV) of the inferior thyroid artery (65).They reported a small overlap between the groups using both modalities (65)

In our study, the mean PSV in the thyroid arteries in GD group was **73.8** cm/s. and in hashimotos thyroiditis patient's was 23.5 cm/s. Therefore, the high PSV in graves` disease correlates with increased cardiac output due to hyperdynamic status secondary to thyrotoxicosis. There is significant increases in systolic BP (blood pressure), PR (pulse rate) and CCV (common carotid artery velocity) on both sides in GD group compared with HT (60).

6.2. Regarding to Resistive Index of Thyroid Arteries:

The current study reported that there were no significant differences between Graves` disease and hashimotos thyroiditis in resistive index (RI). Were the mean resistive index of hashimotos thyroiditis was (8.8±8.8) & the mean resistive index of Graves` disease was (7.9±11.7) (table 2) .there where limited studies had described quantitative assessment Doppler US (RI) findings to differentiate between hashimoto's thyroiditis and graves` disease. **Sarikaya B. et a**l. **(2012)** reported that, the RI more sensitive than other ultrasound parameters for the diagnosis of Hashimoto's thyroiditis. **Sundarram Ks Thalavai et al. (2017)** found that the bilateral mean RI-STA and the mean RI-ITA were not statistically significantly differences between hashimotos thyroiditis and

graves` disease (62). These results are comparable to the results of a study carried out by **Banaka et al (2013)** studied the Doppler sonographic parameters in healthy individuals and patients with Hashimoto thyroiditis or Graves` disease and assess their Sensitivity and specificity for the diagnosis of autoimmune thyroid disease. They found no statistically significant differences observed in the RI between the groups (59).

Doppler techniques, whether qualitative or quantitative, show statistical significance differences in differentiating Graves' disease from hashimotos thyroiditis but suffer a limitation of overlap of values between the two entities. Since Graves' disease typically has the *very intense flow, the absence of flow in a thyrotoxic patient is strongly suggestive of* thyroiditis, and the presence of the "thyroid inferno" is highly suggestive of Graves' disease. In current study, we found there is clearly overlap in the quantitative color Doppler assessment imaging (resistive index) between Graves' disease and hashimoto's thyroiditis and there is significantly differences in peak systolic velocity between graves` disease and hashimotos thyroiditis.

6.3. Regarding the Vascular Grading (Qualitative Vascular Pattern):

In this study, we found There is significantly higher differences between two entities as vascular grading of patients is concerned where the mean vascular grading of HT. 1.97±0.4 and the mean of GD. 2.8± 0.5(table2).

Hiraiwa T.et al (2013) reported that the TBF (total blood flow) measurements also successfully differentiated GD from HT. The $p < 0.05$ (60). **Vitti P. et al (1995)** founded that diffusely increased thyroid blood flow is pathognomonic of untreated Graves' disease and an abnormal CFD pattern identifies the majority of Graves' patients with a normal thyroid ultrasound pattern. Thus, CFD sonography may be useful in distinguishing patients with Graves' disease and Hashimoto's thyroiditis having a similar thyroid echo pattern at ultrasound (66).

> The thyroid gland vascularization correlates to the underlying functional status, decreases with the disease under control and can rise again in cases of recurrence. Many authors observed that GD vascularity decrease occurred in parallel to the biochemistry remission and disease control, ratifying that thyroid US Doppler has the potential to monitor therapy response in patients with GD, as well as distinguish GD patients from Hashimoto thyroiditis, with similar B-mode pattern, without the use of expensive laboratory assays (65).

6.4. Regarding the Presence of Thyroid Nodules:

The present study reported highly significant differences between hashimotos thyroiditis and Graves` disease regarding thyroid nodules ($x^2_{1=}$11.2&p=0.001**) .The thyroid nodules were more common in patients with hashimotos thyroiditis. This finding similar to **Anderson l ET. al. (2009)** reported Nodular Hashimoto thyroiditis occurred as a solitary nodule in (36%) of cases and in the setting of five or more nodules in 23% of cases. More than half percent (55%) of the cases of nodular Hashimoto thyroiditis occurred within a sonographic background of diffuse Hashimoto thyroiditis, and (45%) of cases occurred within normal thyroid parenchyma (68). **Pishadad p. et al (2017)** reported that the frequency of nodularity was 28.18 % in hashimotos thyroiditis (69). **Langer et al.** Showed that focal lymphocytic thyroiditis can present as hyperechoic nodules with ill-defined margins on sonography among hashimotos thyroiditis patients (70) (71).

6.5. Regarding the Size of Thyroid Gland:

The present study reported highly significant differences between hashimotos & Graves` disease regarding the size of thyroid gland ($x^2_2$=11.64 &p=0.003).The current study found that mildly enlarged gland more common among hashimotos thyroiditis cases; however the markedly enlarged thyroid gland were more common among graves` disease cases. In comparable with **Dos Santos TA et al. (2014)** reported that the markedly increased size of the gland (goiter) more in graves` disease patients` however decreased, normal or increased (goiter) in HT. patient (67) . In another previous study, **Zhang J. W. et al. (2016)** Twenty-one patients (87.5%) of hashimotos thyroiditis had an enlarged thyroid gland (antero-posterior diameter more than18mm) at ultrasound, while the rest had a normal-sized thyroid gland (72).

6.6. Regarding the Echopatteren of Thyroid Parenchyma:

The present study reported highly significant differences between hashimotos thyroiditis and Graves` disease as Echo pattern is concerned (x^2_2=22.8&p=0.001**). The micronodular Echo pattern seen more common among the HT cases than GD cases. A micro nodular pattern on ultrasound is highly diagnostic of Hashimoto thyroiditis with a positive predictive value of 95% (68).In comparable with results of **Patel S. et al. (2018)** Parenchymal heterogeneity and hypoechoic micronodular echotexture were more common in patients with HT with p value <0.001 (73). Hypoechoic micro

nodularity it is recognized as a key diagnostic feature with a PPV up to 95% (68) (50). **Yeh et al. (1996)** showed that Micronodulation on sonography is useful for diagnosing diffuse lymphocytic thyroiditis because of a high positive predictive value (94.7%) (50).

6.7. Regarding the echogenic fibrous septations:

The present study reported significant differences between hashimotos thyroiditis and Graves` disease as fibrous septations as concerned (x^2_1=5.3&p=0.21*). In the current study, we found that the echogenic fibrous septations are more common among the HT cases than GD cases. **Patel S. et al (2018)** reported that among 101 patients, (84%) demonstrated sonographic evidence of HT. The echogenic septations is one of the most important of sonographic features used for the identification of HT (73). **Anderson et al (2010)** reported that on sonography, a thyroid gland affected by Hashimoto thyroiditis typically has an echogenic septations, which is significant sonographic features in the diagnosis of hashimotos thyroiditis (68).Sonographically, numerous imaging features have been described with HT including diffusely hypoechogenicity, coarse and heterogeneous parenchymal echotexture, echogenic septations, hypoechoic micronodularity, and hypervascularity (73)(74).

6.8. Regarding the Presence of Paratracheal Lymph Nodes:

Our study explains the differences between hashimotos thyroiditis and Graves` disease through Delphian lymph nodes (X^2_1=5.33&p=0.035). These Delphian lymph nodes only seen more in HT cases than GD cases. **Kosiak W. et al (2015)** reported that a strong correlation between the presence of lymph nodes adjacent to the thyroid gland, and hashimotos thyroiditis (75). **Solivetti et al. (1998)** indicate that enlargement of para-isthmian lymph nodes appears to be one of the signs of hashimotos thyroiditis (76). In 2008, a report it was published on the presence of paratracheal lymph nodes in adult autoimmune thyroiditis. The authors estimated the sensitivity of that sign in diagnosing autoimmune thyroiditis at 93.4%, and its specificity at 74.5% (77).

CHAPTER 7

CONCLUSION AND RECOMMENDATION

7.1. CONCLUSION:

1. We concluded that there is significant differences in the peak systolic velocity between hashimotos thyroiditis and graves` disease where p=0.001**. The peak systolic velocity higher in graves` disease (73.8±6.10) as compared to (23.5±10.8) in the hashimotos thyroiditis.

2. Regarding the mean of vascular grading there is significant differences between hashimotos thyroiditis and graves` disease p=0.001**

3. There is significant differences between hashimotos thyroiditis and graves` disease as regarded thyroid nodule, thyroid size, Echopatteren, fibrous septations and Delphian lymph nodes.

4. No significant differences between hashimotos thyroiditis and graves` disease as age, sex and resistive index are concerned

7.2. RECOMMENDATION:

1. Use of peak systolic velocity assessment in the differentiation between the two types of these thyroid diseases.

2. More researches on larger scale to confirm the radiological differentiation between the two pathological entities.

CHAPTER 8

REFFERENCES

8. REFFERENCES:

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CHAPTER 8

APPENDICES

APPENDIX –I-DATA COLLECTION SHEATH:

Name:

Age:

Clinical data: (Euthyroidism, Hypothyroidism, Hyperthyroidism)

Ultrasonography data:

Both Thyroid Lobes and isthmus:

1. Size :(Normal, Mildly enlarged, Marked enlarged)

2. Echogenicity: compare to strap muscles (iso echogenic, high echogenicity, low echogenicity)**.**

3. Echo-pattern :(Homogenous, Heterogeneous, and Micro-nodulation).

4. Fibrous septations :(Absent, Few, Numerous septations).

5. Grade of vascularity: (Pattern 0, Pattern I, Pattern II, Pattern III).

6. Quantitative Doppler assessment of **thyroidal vasculature** :(RI=) and (PSV=).

7. Thyroid nodules: (Present, absent).

8. Paratracheal Lymph nodes :(Present, Absent)

APPENDIX –II-INFORMED CONSENT FORMS:

This Informed Consent Form is for graves` disease patient and hashimotos thyroiditis patients who attend ultrasound unit at radiology department, and who we are inviting to participate in research on diffuse thyroid disease. The title of our research project is "role of quantitative doppler assessment in the differentiation between graves` disease and hashimotos thyroiditis".

The consent was verbal consent from two groups of patients.

The consent forms the world health organization (WHO).

دور مؤشر مقام في التمايز بين مرض قرافيز التهاب هاشيموتوس في الغدة الدرقية

قدمت من قبل:

سهام ادم سالم المغربي

المشرف: د. فيصل محمد شمبش

المشرف المساعد: د. فايزة محمد القطراني

الخلاصة

الكلمات المفتاحية: مرض قرايفز، التهاب الغدة الدرقية هاشيموتوز، تقييم دوبلر الكمي الأشكال

الأكثر شيوعا من مرض الغدة الدرقية المنتشر ومرض قرافيز GD ومتلازمة التهاب هاشيموتوز في الغدة الدرقية HT. يمكن أن يظهر كل من قرايفز ومتلازمة التهاب هاشيموتوز كغدة درقية متضخمة وارتفاع هرمون الثيروكسين في الدم، ولكنهما يحتاجان إلى التمايز، حيث تختلف استراتيجية العلاج.

في دراستنا لسلسلة الحالات المحتملين لمراحل مختلفة من استهداف الغدة الدرقية لتحديد مدى فائدة تقييم دوبلر الكمي في الأوعية الدرقية في هذه المجموعة الخاصة من المرضى، والتفريق بين المرضين. وقد أجريت دراسة لتقييم الدوبلر الكمي للفصل بين هذين الكيانين في هذه المجموعات من المرضى. المرضى والقياسات تم فحص 69 مريضا يعانون من زيادة الغدة الدرقية المفرطة (30 مرض قرايفز، 39 التهاب الغدة الدرقية) في (3دكور و27 أنثى) من مرض قرليفز ومع ذلك، (4 ذكور و35 أنثى) من حالات التهاب الغدة الدرقية، تم فحصها. تم تشخيص هذه المجموعات من المرضى سريرياً وبيوكيميائيًا، وتمت إحالتهم من أخصائي الغدد

الصماء في مستشفى الهواري العام ومركز بنغازي الطبي (BMC) إلى مركز بنغازي للأشعة (BRC). تم قياس معلمة دوبلر الدائرية كمياً بواسطة التصوير بالموجات فوق الصوتية.

في هذه الدراسة، وجدنا اختلاف ملحوظ في قمة سرعة انقباض الأوعية الدموية للغدة الدرقية، ولم نجد اختلافات ملحوظة في مؤشر مقاوم بين التمييز بين GD وHT على خلاف ذلك توجد فروق ذات دلالة إحصائية بين GD. و HT. مطلوب مزيد من الدراسات لتأكيد هذا التمايز.

دور مؤشر مقام في التمايز بين مرض قرافيز والتهاب هاشيموتوس في الغدة الدرقية

قدمت من قبل:

سهام ادم سالم المغربي

اشراف:

د. فيصل محمد شمبش

د. فايزة محمد القطراني

قدمت هده الرسالة استكمالا لمتطلبات الحصول على درجة الماجستير في الاشعة التشخيصية.

جامعة بنغازي

كليه الطب

2019