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Characterization of Thyroid Disorders Using Doppler Ultrasonography & Thyroid Uptake Scan

توصيف أمراض الغدة الدرقية بإستخدام التصوير الطبي بالموجات فوق الصوتية وفحص إمتصاص الغدة الدرقية

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الآية

قَالَ تَعَالَىٰ:

﴿ يَرْفَعِ ٱللَّهُ ٱلَّذِينَ ءَامَنُوا۟ مِنكُمْ وَٱلَّذِينَ أُوتُوا۟ ٱلْعِلْمَ دَرَجَٰتٍۚ ﴾

صدق الله العظيم

سورة المجادلة، الآية (11)

Dedication

Every challenging work need self-efforts as well as
guidance of elder especially those who are very c
lose to our heart.
My humble effort I dedicate it to my sweet and loving:
Father and Mother
My lovely sisters
My husband
My sons
To everyone who supported me

Acknowledgment

In the beginning and the end, all thanks to almighty Allah for giving me strength and ability to understand and learn.

I would like to express my deep gratitude to my research supervisor **Professor. Mohamed Elfadel Gar Alnabe** for his friendship, empathy, great sense of humor and giving me invaluable guidance, it was a great privilege and honor to work and study under his guidance and cannot forget to thank all the nuclear medicine department staff for their help.

I am extremely grateful to my father **Mohamed Taha** and my mother **Seham Mahjoub** for prayers, caring and sacrifices to educate me .All my love to my amazing four sisters for their love and support.

Thousands of thank to the person who always beside me and encourages me **Mohamed Abdelbasit Elsawi**.

All my love to my beautiful sons **Hazem & Fares.**

Abstract

The aim of this study is characterizing the thyroid gland using Doppler Ultrasonography and Thyroid Scintigraphy using GE introduces Discovery NM-CT 670 pro and Q.Merix at nuclear medicine department and GE Logiq E9 equipment at ultrasound department at King Saud Medical Center (KSMC) in Saudi Arabia. The total number of patients was 144 where the males were 33 with percent 22.9 and the number of females was 111 with percent 77.1. The results showed that the group statistics for patients according to their gender. For TSH the mean ± standard deviation for female was 0.88 ± 1.89 and for male was 1.377 ± 3.82, for T4 female was 32.47 ± 31.51 and for male was 31.39 ± 19.77, for right lobe length female was 4.99 ± 1.79 and for male was 5.77 ± 1.75, right lobe width for female was 2.99 ± 1.47 and for male was 3.09 ± 1.52, right lobe size female was 14.53 ± 7.37 and for male was 17.83 ± 8.75, right lobe volume for female was 14.95 ± 12.999 and for male was 19.41 ± 17.77. For left lobe length for female was 4.55± 1.87 and for male was 5.64 ± 2.14, left lobe width for female was 2.74 ± 1.44 and for male was 3.17 ± 153, left lobe size for female 12.71 ± 7.65 and for male was 18.92 ± 10.83, left lobe volume for female was 11.35 ± 9.97 and for male was 17.55 ± 16.10, for thyroid uptake for female was 7.43 ± 9.21 and for male was 8.74 ± 9.89. Analysis of variance for thyroid uptake with other variables, where the p-value show no significant difference between the thyroid uptake with right lobe length, right lobe width, right lobe size, right lobe volume and left lobe volume were the p-value was 0.550, 0.105, 0.992, 0.965 and 0.938 respectively. While show significant difference between the thyroid uptake with left lobe length, left lobe width and left lobe size were the p-value was 0.047, 0.000 and 0.004 respectively. Correlation between the thyroid uptake with t4 hormone were the rate of change for thyroid uptake increase by 0.1172 with each value for T4 hormone.

المستخلص

الهدف من هذه الدراسة هو توصيف الغدة الدرقية باستخدام برنامج ديسكفري ستي 670 و كيوماتركس في قسم الطب النووي ومعدات جنرال الكتريك لوجيك 9 في قسم الموجات فوق الصوتية في مركز الملك سعود الطبي في المملكة العربية السعودية. بلغ العدد الإجمالي للمرضى 144 مريضا حيث كان عدد الذكور33 بنسبة 22.9 في المائة وعدد الإناث 111انثى بنسبة 77.1 في المائة. إحصائيات المجموعة للمرضى حسب جنسهم: بالنسبة للهرمون المحفز للغدة الدرقية، كان الانحراف المعياري المتوسط للإناث 0.88 ± 1.89 وللذكور 1.377 ± 3.82 ،إحصائية T4 بالنسبة للإناث كان 32.47±31.51 وللذكور 31.39 ± 19.77 ، طول الفص الأيمن للإناث كان 4.99 ± 1.79 وللذكور كان 5.77 ± 1.75 ، عرض الفص الأيمن للإناث 2.99 ± 1.47 وللذكور 3.09 ± 1.52 ، مساحة الفص الأيمن للإناث 14.53 ± 7.37 وللذكور 17.83 ± 8.75 ، وكان حجم الفص الأيمن للإناث 14.95 ± 12.999 وللذكور كان 19.41 ± 17.77. بالنسبة لطول الفص الأيسر للإناث كان 4.55 ± 1.87 وللذكور كان 5.64 ± 2.14 ، وكان عرض الفص الأيسر للإناث 2.74 ± 1.44 وللذكور 3.17 ± 153 ، وكان حجم الفص الأيسر للإناث 12.71 ± 7.65 وللذكور كان 18.92 ± 10.83 ، وكان امتصاص الغدة الدرقية للإناث 7.43 ± 9.21 وللذكور 8.74 ± 9.89. تحليل التباين لامتصاص الغدة الدرقية مع المتغيرات الأخرى ، حيث لا تظهر القيمة المعنوية أي فرق كبير بين امتصاص الغدة الدرقية بطول الفص الأيمن وعرض الفص الأيمن ومساحة الفص الأيمن وحجم الفص الأيمن وحجم الفص الأيسر وكانت القيمة المعنوية هي 0.550 و 0.105 و 0.992 و 0.965 و 0.938 على التوالي. بينما أظهرت فروق معنوية بين امتصاص الغدة الدرقية وطول الفص الأيسر وعرض الفص الأيسر وحجم الفص الأيسر كانت القيمة المعنوية هي 0.047 و 0.000 و 0.004 على التوالي. كان الارتباط بين امتصاص الغدة الدرقية لهرمون الثيروكسين بقيمة 0.1172

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List of Abbreviations

BMR	Basal metabolic rate
T4	Thyroxine
T3	Triiodothyronine
US	Thyroid ultrasonography
DE	Doppler Effect
TSH	Thyroid stimulating hormone
TRH	Thyrotropin releasing hormone
MIT	Monoiodotyrosine
DIT	Diiodotyrosine
FSH	Follicle-stimulating hormone
USG	High-resolution ultrasonography
TFT	Thyroid function test
THs	Thyroid hormones
MNG	Toxic Multinodular Goiter
GD	Graves' disease
AIT	Autoimmune thyroiditis
TS	Thyroid Scintigraphy
CFDS	Color flow doppler sonography
RAIU	Radio Active Iodine Uptake

Chapter One
Introduction

1.1 Thyroid Gland:

The thyroid gland is a vital butterfly-shaped endocrine gland situated in the lower part of the neck, presents in front and sides of the trachea, inferior to the larynx. It plays an essential role in the regulation of the basal metabolic rate (BMR), and stimulates somatic and psychic growth(Khan YS et al.,2020), besides having a vital role in calcium metabolism. The thyroid produces approximately 90% inactive thyroid hormone, or thyroxine (T4) and 10% active thyroid hormone, or triiodothyronine (T3). Inactive thyroid hormone is converted peripherally to either activated thyroid hormone or an alternative inactive thyroid hormone(Armstrong M et al., 2018). Thyroid disorders are amongst the most prevalent of the medical condition. Their manifestations vary considerably from area to area and are determined principal by the availability of iodine in the diet According to the World health organization (WHO) more than 190 million suffer from iodine deficiency disorders(Saeed MI et al.,2018), thyroid gland disorders are the most common endocrine abnormalities in Kingdom of Saudi Arabia (KSA) as well as in the Middle East region (Saleh A et al., 2021) Common thyroid disorders - such as hypothyroidism, hyperthyroidism and thyroid nodules require different sequences of investigations to assist with formulating a diagnosis and plan. Rational investigation of thyroid disease requires careful avoidance of over-investigation of minor abnormalities balanced with prompt diagnosis of serious health conditions. An awareness of which thyroid tests are appropriate or not indicated in different contexts will improve patient care and health resource utilization.(Croker EE et al., 2021).

Thyroid ultrasonography (US) is the most common, extremely useful, safe, does not cause damage to tissue and cost-effective way to image the internal structure of the thyroid gland and its pathology without using ionizing radiation or iodine containing contrast medium. Rather, high frequency sound waves in the megahertz range (ultrasound), are used to produce an image. Although each image is a static picture Color Flow Doppler enhancement of the US images, that delineates the vasculature, is essential. Dynamic information such as blood flow can be added to the standard US signal by employing a physics principle called the Doppler Effect (DE). The frequency of a sound wave increases when it approaches a listener (and decreases as it departs. The Doppler signals, which are superimposed on real time gray scale images, are extremely bright in black and white images and may be color coded to reveal the velocity (frequency shift) and direction of blood flow (phase shift), as well as the degree of vascularity of an organ . Flow in one direction is made red and in the opposite direction, blue. The shade and intensity of color can correlate with the velocity of flow. Thus, in general terms, venous and arterial flow can be depicted by assuming that flow in these two kinds of blood vessels is parallel, but in opposite directions. Since portions of blood vessels may be tortuous, modifying orientation to the probe, different colors are displayed within the same blood vessel even if the true direction of blood flow has not changed. Thus, an analysis of flow characteristics requires careful observations and cautious interpretations. The absence of flow in a fluid-filled structure can differentiate a cystic structure and a blood vessel (Blum M et al., 2020).

The thyroid uptake and scan play a central role in the diagnosis of thyroid disease and abnormalities in thyroid function as it provides detailed information on the functions and anatomy of the thyroid gland. Different radioactive tracers function to detect or diagnose various thyroid diseases, such as Iodine, technetium pertechnetate, gallium-67, and fluoro-deoxy-glucose, Relative uptake of iodine and technetium pertechnetate by focal thyroid nodule is labeled as warm, cold, or hot. Other uses of iodine include treatment of thyroid cancer, evaluation of residual/recurrent disease, evaluation of distant metastasis, and follow up of patients after thyroidectomy. Never the less there is some obstacles like pain at the injection site , hypersensitivity and anaphylaxis to radiotracer and women of childbearing age.(Iqbal A et al.,2020).

This study will play an active role in predicting the thyroid patients who truly need to do thyroid scan, and hence it will minimize the number of patient send to nuclear medicine department.

1.2 Problem of the study:

Due to the presence of risks in Radioactive Iodine uptake and thyroid scintigraphy, the reduction in its use in the cases that truly need it requires accurate scientific study that may lead to the use of a safer method, taking into account the accuracy and sensitivity.

1.3 Justification of the study:

Ultra sound is usually one of the first lines of thyroid examination because it is widely available, affordable, and does not adopt ionizing radiation; on the other hand it is not reliable method to assess functional changes. The patient who needed further test" will request to perform Radioactive Iodine uptake & thyroid scintigraphy, which it has limitation such as high risks of radiation that cannot be ignored, the financial cost and accessibility. The purpose of this study to assist imaging specialists and clinicians in recommending, performing, and interpreting the results of thyroid scintigraphy and Doppler ultrasonography in patients with different thyroid disease.

1.4 Objectives:

1.4.1: General objective:

- To characterize the thyroid gland disorders using Doppler Ultrasonography and Thyroid Scintigraphy.

1.4.2: Specific objectives:

- To cross-correlate between ultrasound finding to nuclear medicine finding.
- To correlate between the results of thyroid function test to thyroid scintigraphy.
- To correlate between right and left lobe size, volume, width and length to nuclear medicine finding.
- To correlate the percentage of thyroid uptake to thyroid scintigraphy finding.
- To correlate between right and left lobe size, volume, width and length to ultrasound finding.
- To correlate between right and left lobe size, volume, width and length to thyroid uptake results.
- To correlate between nuclear medicine finding to background uptake ratio.
- To evaluate the thyroid abnormalities according to age of the patients.
- To evaluate the thyroid abnormalities according to blood flow into thyroid gland.
- To generate equation from thyroid function test finding to estimate the patient who truly need to send to nuclear medicine scan.

1.5 Overview of the study:

This study was concern with characterization of thyroid gland using Doppler ultrasonography and thyroid scintigraphy; it was fall into five chapters. Chapter one is an introduction about thyroid disorders also concluded by objectives, problem as well as significance of the study, Chapter two; included a comprehensive literature review in addition to the previous studies, While Chapter three was described the materials and method that was followed in data collection, Chapter four presented the results included in frequency tables, scattering plot and their discussion. Finally, chapter five was included the conclusions and further recommendations.

Chapter Two

Theoretical background

2.1 Thyroid function:

The thyroid gland is a midline structure located in the anterior neck. The thyroid functions as an endocrine gland and is responsible for producing thyroid hormone and calcitonin, thus contributing to the regulation of metabolism, growth, and serum concentrations of electrolytes such as calcium (Ilahi A et al.,2020) (Fitzpatrick TH et al.,2020). Many disease processes can involve the thyroid gland, and alterations in the production of hormones can result in hypothyroidism or hyperthyroidism. The thyroid gland is involved in inflammatory processes (e.g., thyroiditis), autoimmune processes (e.g., Graves disease), and cancers (e.g., papillary thyroid carcinoma, medullary thyroid carcinoma, and follicular carcinoma). In addition to considering its role in metabolism, growth, regulation of certain electrolytes, and its involvement in many disease processes, the thyroid gland deserves consideration for its anatomical location and its close relationship to important structures including the parathyroid glands, recurrent laryngeal nerves, and certain vasculature.(Allen E e al.,2021)

2.2 Embryology:

The pharyngeal apparatus is responsible for the formation of numerous parts of the head and neck region . During the 3rd gestational week, there is hypertrophy of the endoderm in the midline of the primitive pharynx, arising from the first pharyngeal arch between the tuberculum impar and copula; at a point later referred to as the foramen caecum. This thyroid primordium subsequently enlarges and is attached to the floor of the primitive pharynx by a hollow tube known as the thyroglossal duct. The duct communicates with the foramen caecum, which is caudal to the tuberculum impar (median tongue bud) and rostral to the copula (hypobranchial eminence). The thyroid primordium progresses to a thyroid placode located at the base of the tongue ; which subsequently forms the thyroid diverticulum near the apical pole of the aortic sac. The thyroid diverticulum then begins its descent towards its final pretracheal destination, passing anterior to the laryngeal cartilages and hyoid bone . During this course, it maintains connection with the floor of the primitive pharynx via the thyroglossal duct. Under normal circumstances, the thyroglossal duct will degenerate and the diverticulum remains suspended in mesenchyme. The solid structure is invaded by vascular mesenchyme, which results in disruption of the solid cellular arrangement. Subsequently, the cells arrange themselves into a web of epithelial cords. The gland regains contact with the aortic sac and subsequently bifurcates. This process is associated with rapid, thyroid stimulating hormone (TSH)-independent, proliferation of the thyroid progenitor cells. During the 5th week of gestation, the ultimobranchial body (arising from the 4th pharyngeal arch) fuses with the thyroid gland. Prior to this, the ultimobranchial body, which is an endodermal derivative, is invaded by neural crest cells. These cells give rise to the C-cells that participate in calcium homeostasis by producing calcitonin under hypocalcemic circumstances. A structure known as the tubercle of Zuckerkandl is the only remaining structure at the point where the two primitive structures merged. This tubercle can be seen in most adults at the posterior aspect of the gland. It is of clinical significance during thyroidectomies, as the nerve has a close relationship to the recurrent laryngeal nerve.(Roman BR et al.,2019)

2.3 Anatomy of thyroid gland:

The thyroid gland is a largest gland that is located in the lower part of the neck anterolateral to the trachea , it is extend from the oblique line of thyroid cartilage to the 5^{th} -6^{th} tracheal cartilage ring(lie opposite to the C5, C6, C7 and T1 vertebrae). (Fitzpatrick TH et al.,2020)

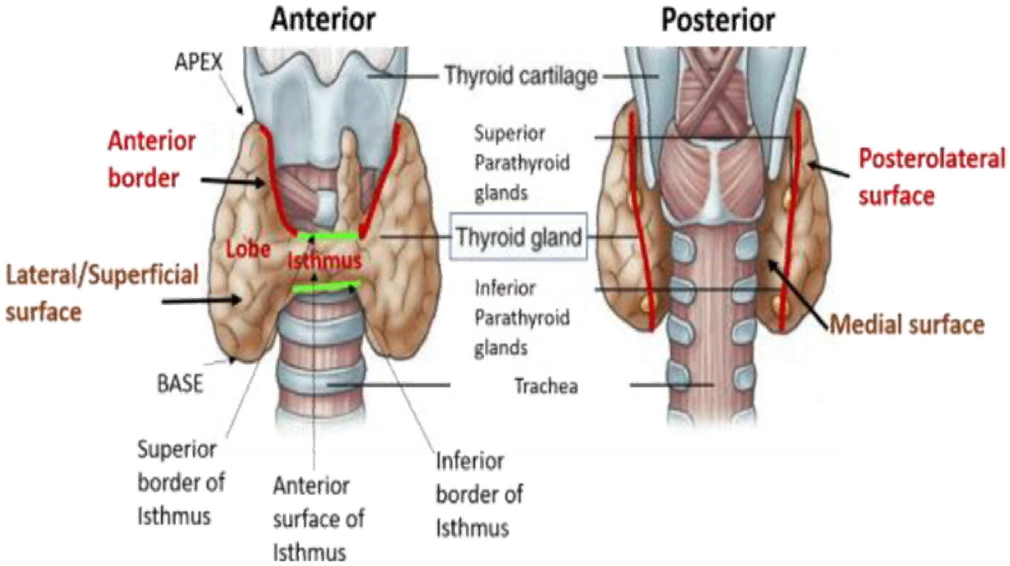


Figure (2.1): Anatomy of thyroid gland

It attaches to the trachea via a consolidation of connective tissue, referred to as the lateral suspensory ligament or Berry's ligament. This ligament connects each of the thyroid lobes to the trachea. The thyroid gland, along with the esophagus, pharynx, and trachea, is found within the visceral compartment of the neck which is bound by pretracheal fascia.(Ilahi A et al.,2020)

It has H- shape and lateral lobes that are symmetrical with a well-marked centrally located isthmus. The thyroid gland typically contains a pyramidal extension on the posterior-most aspect of each lobe, referred to as the tubercle of Zuckerkandl. Despite these general characteristics, the thyroid gland is known to have many morphologic variations. The position of the thyroid gland and its close relationship with various structures brings about several surgical considerations with clinical relevance. (Ilahi A et al.,2020).

2.4 Blood Supply and Lymphatic:

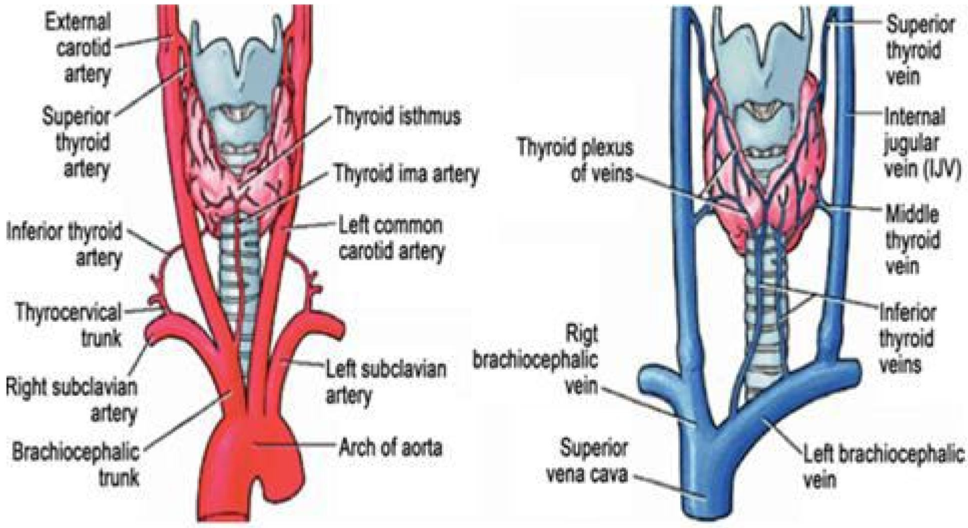


Figure (2.2): Arterial supply and venous drainage of the thyroid gland

The thyroid gland has an extremely rich blood supply and is estimated to be six times as vascular as the kidney and relatively three to four times more vascular than the brain. It receives blood from the superior and inferior thyroid arteries. These paired vessels supply the superior and inferior aspect of the gland. The superior thyroid artery is the first branch of the external carotid artery as it arises near the level of the superior horn of the thyroid cartilage. The superior thyroid artery then moves anterior, inferior, and towards the midline behind the sternothyroid muscle to the superior pole of the lobe of the thyroid gland. From this point, the superior thyroid artery branches off. One branching point runs down the dorsal aspect of the thyroid gland. The other superficial branch runs along the sternothyroid muscle and thyrohyoid muscles, supplying branches to these muscles as well as the sternohyoid. The superficial branch continues downward to further give off the cricothyroid branch and to supply the isthmus, inner sides of the lateral lobes, and when present the pyramidal lobe.

The thyrocervical trunk arises from the anterosuperior surface of the subclavian artery and gives rise to three branches, one being the inferior thyroid artery. The inferior thyroid artery branches from the thyrocervical trunk at the inner border of the anterior scalene muscle and advances medially to the thyroid gland. The artery reaches the posterior surface of the lateral lobe of the thyroid gland at the level of the junction of the upper two thirds and lower third of the outer border. The largest branch of the inferior thyroid artery is the ascending cervical branch, and it is important not to mistake this branch for the inferior thyroid artery itself. (Roman BR et al.,2019). In 10% of the population, there is an additional artery known as the thyroid ima artery. This artery most commonly originates from the brachiocephalic trunk and supplies the isthmus and anterior thyroid gland. (Roman BR et al.,2019).

The thyroid gland is drained via the superior, middle, and inferior thyroid veins. The middle and superior thyroid veins follow a tortuous route and eventually drain into the internal jugular vein on either side of the neck. The drainage of the inferior thyroid vein may enter either the subclavian or brachiocephalic veins, located just posterior to the manubrium. (Roman BR et al.,2019)

Lymphatic drainage of the thyroid gland involves the lower deep cervical, prelaryngeal, pretracheal, and paratracheal nodes. The paratracheal and lower deep cervical nodes, specifically, receive lymphatic drainage from the isthmus and the inferior lateral lobes. The superior portions of the thyroid gland drain into the superior pretracheal and cervical nodes. (Roman BR et al.,2019)

2.5 Hormone synthesis:

Thyroid hormone synthesis is governed by the hypothalamus . When circulating levels of thyroid hormone is low, the hypothalamus releases thyrotropin releasing hormone (TRH). This hormone then travels to the anterior pituitary glan , where it promotes the release of thyroid stimulating hormone (TSH). TSH enters the bloodstream and travels to the thyroid gland, where it upregulates the transcription and translation of thyroglobulin. The thyroglobulin is packaged by the Golgi body in vesicles, which are exocytosed. The compound is then temporarily stored in the follicular lumen.(Muhammad A.,2021)

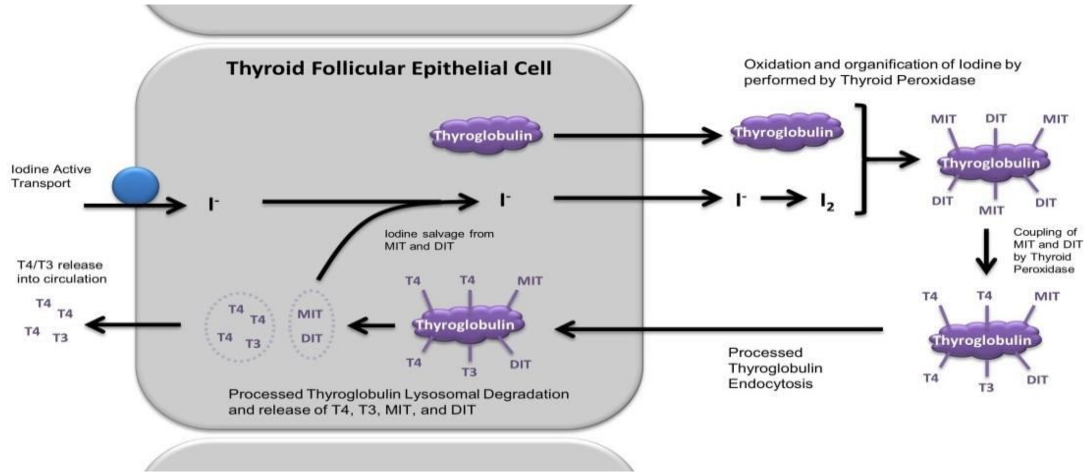


Figure (2.3) thyroid hormones synthesis

Iodine is also important for the production of thyroid hormones. Iodine is provided by dietary means and is concentrated within the cells via basolateral sodium-iodide (Na+-I-) symporters. Iodide within the thyrocytes are then pumped into the follicular lumen via pendrin pumps (apically located iodide-chloride (I--Cl-) pumps). Also, the excess sodium is pumped back into systemic circulation by Na+-K+ ATPase pumps.

At the luminal surface of the follicular cells, iodide is oxidized by peroxidase bound to the microvilli to iodine; which is then used for the organification of the tyrosine moiety of the thyroglobulin protein. The resulting monoiodotyrosine (MIT) can be further organified to diiodotyrosine (DIT). In the presence of thyroperoxidase, MIT and DIT, or two DIT molecules react to form triiodothyronine (T3) or thyroxine (T4), respectively. The newly synthesized thyroid hormones are still bound to thyroglobulin. This allows the hormones to re-enter the cells by receptor mediated endocytosis. When the serum levels of thyroid hormones increase, they act at the level of the pituitary gland and hypothalamus to inhibit release of TRH and TSH. Therefore, the hypothalamic-pituitary-thyroid axis operates under a negative feedback mechanism in order to maintain homeostasis. Majority of the hormone released from the gland is in the T4 form. However, at the level of the target cells almost all of the T4 is converted to T3, which is utilized for various metabolic processes. (Muhammad A.,2021)

2.6 Organ Systems Involved:

Thyroid hormone affects virtually every organ system in the body, including the heart, CNS, autonomic nervous system, bone, GI, and metabolism. In general, when the thyroid hormone binds to its intranuclear receptor, it activates the genes for increasing metabolic rate and thermogenesis. Increasing metabolic rate involves increased oxygen and energy consumption.(Muhammad A.,2021)

Heart: thyroid hormones have a permissive effect on catecholamines. It increases the expression of beta-receptors to increase heart rate, stroke volume, cardiac output, and contractility.

Lungs: thyroid hormones stimulate the respiratory centers and lead to increased oxygenation because of increased perfusion.

Skeletal muscles: thyroid hormones cause increased development of type II muscle fibers. These are fast-twitch muscle fibers capable of fast and powerful contractions.

Metabolism: thyroid hormone increases the basal metabolic rate. It increases the gene expression of Na+/K+ ATPase in different tissues leading to increased oxygen consumption, respiration rate, and body temperature. Depending on the metabolic status, it can induce lipolysis or lipid synthesis. Thyroid hormones stimulate the metabolism of carbohydrates and anabolism of proteins. Thyroid hormones can also induce catabolism of proteins in high doses. Thyroid hormones do not change the blood glucose level, but they can cause increased glucose reabsorption, gluconeogenesis, glycogen synthesis, and glucose oxidation.

Growth during childhood: In children, thyroid hormones act synergistically with growth hormone to stimulate bone growth. It induces chondrocytes, osteoblasts, and osteoclasts. Thyroid hormone also helps with brain maturation by axonal growth and the formation of the myelin sheath.

2.7 Function of thyroid hormone:

Physiological effects of thyroid hormones are listed below:

Increases the basal metabolic rate, Depending on the metabolic status it can induce lipolysis or lipid synthesis, Stimulate the metabolism of carbohydrates, Anabolism of proteins. Thyroid hormones can also induce catabolism of proteins in high doses, Permissive effect on catecholamines, In children, thyroid hormones act synergistically with growth hormone to stimulate bone growth, The impact of thyroid hormone in CNS is important. During the prenatal period, it is needed for the maturation of the brain. In adults, it can affect mood. Hyperthyroidism can lead to hyperexcitability and irritability. Hypothyroidism can cause impaired memory, slowed speech, and sleepiness, Thyroid hormone affects fertility, ovulation, and menstruation (Muhammad A.,2021).

2.8 Pathophysiology of thyroid gland:

The follicular cells take up the iodinated thyroglobulins from the colloid present within the lumen of the thyroid follicle. This process is under the influence of follicle-stimulating hormone (FSH). Afterward, lysosomal digestion and intracellular proteolysis release the thyroid hormone in the form of T3 and T4. These amino acid derivates are so small that they can easily escape the follicular cells and enter the bloodstream through fenestrations present in the capillaries.

The thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland not only affects the changes in the follicular cells but also the thyroid follicles and the activity of the gland itself. TSH stimulation occurs when there is a low level of iodine in the diet by a negative feedback mechanism on pituitary thyrotrophs. TSH not only increases the size of the follicular cells (hypertrophy) but also increases the number of follicular cells (hyperplasia). Thus under the influence of the TSH, the follicular cells become tall and columnar, demonstrating the heavy activity of the follicular cells and the follicles. The TSH also enhances the exocytosis, synthesis, and iodination of thyroglobulin. It also enhances endocytosis and intracellular breakdown of colloid. Thus the intraluminal colloid is greatly reduced, which manifests externally by the enlargement of the thyroid gland. Usually, enlargement of the thyroid gland is called goiter, which is a diseased state. But in this condition, the enlargement of the thyroid gland is because of the hypertrophy and hyperplasia of the parenchyma. Hence it is called parenchymatous goiter. This condition differentiates from another type of goiter where the enlargement is not because of the hypertrophy and hyperplasia of the parenchyma but due to an increase in the production of colloid within the thyroid follicle. This condition is known as colloid goiter. If this condition becomes longstanding with recurrent stages of hyperplasia and involution, it leads to a more irregular enlargement as a multinodular goiter . They later also show fibrosis, calcification, cystic changes, and hemorrhagic spots. If there is no stimulation of TSH, it leads to a decrease in the size of follicular cells to the cuboidal and later squamous cells.

In Graves's disease, the follicular cells are tall, columnar, overcrowded, which results in the formation of small papillae. These papillae will project into the follicular lumen. The colloid is pale and shows scalloped margins. The interstitium becomes infiltrated with T lymphocytes. In the case of adenoma, the follicular cells are uniform and contain colloid in the lumen. They show atypia and prominent nucleoli and focal nuclear pleomorphism. They are well encapsulated in an intact capsule, which distinguishes them from follicular carcinoma. The papillary carcinoma shows typical "Orphan Annie eye" nuclei, which are due to finely dispersed chromatin. It also shows a papillary architecture with psammoma bodies (calcified concentric structures) with the papillae. The cytoplasm of follicular cells also show invaginations, which give intranuclear inclusions like appearance. Anaplastic carcinomas present themselves with large, pleomorphic giant cell lesions, spindle cells, etc.

The parafollicular cells secrete calcitonin whenever the plasma calcium level exceeds its normal limit. The target site for calcitonin in the bone is the osteoclast cells, thus reducing their number and action. Calcitonin also promotes excretion of phosphate and calcium through urine. No significant clinical manifestations have been observed due to an increase or decrease of the calcitonin, and hence, its role in humans is debatable. (Khan.,2020)

2.9 Clinical Significance (Khan.,2020)

Goiter: It is a condition where the thyroid gland shows an abnormal enlargement. Goiters broadly classify into uni-nodular, multinodular, and diffuse types. Each further includes many different types of goiters. Some of the commonest with some of their important features are described below.

Colloid nodular goiter: This is the commonest of the non-neoplastic lesions of the thyroid. In these types of goiter, the thyroid follicles are filled with an abundant amount of colloid in their lumens and lined by squamous follicular cells.

Hyperthyroidism (Thyrotoxicosis): It is a condition of hypermetabolic state and hyperfunctioning of the thyroid gland resulting in increased T3 and T4 levels. Some symptoms included palpitations, tachycardia, nervousness, etc.

Graves disease: This disease is a combination of thyrotoxicosis, exophthalmos, and dermopathy (myxedema). It is especially seen in women in the age group of 20 to 40 years, manifesting in the form of prolonged and violent palpitations.

Hypothyroidism: This condition develops due to any functional and structural derangement that leads to decreased production of thyroid hormone. This condition clinically manifests as cretinism in infants and myxoedema in adults. Cretinism presents itself as short stature, coarse facial features, mental retardation, protruding tongue, etc.

Thyroid cancer: Thyroid carcinomas arise either from the follicular epithelium or parafollicular C-cells. They are painless nodules and compression, displaces the adjacent structures. The carcinomas of the thyroid can manifest in the form of papillary carcinoma, follicular carcinoma, anaplastic carcinoma, and medullary carcinoma.

2.10 Thyroid gland ultrasonography:

High-resolution ultrasonography (USG) is the most sensitive imaging modality available for examination of the thyroid gland and associated abnormalities. Ultrasound scanning is non-invasive, widely available, less expensive, and does not use any ionizing radiation. Further, real time ultrasound imaging helps to guide diagnostic and therapeutic interventional procedures in cases of thyroid disease. The major limitation of ultrasound in thyroid imaging is that it cannot determine thyroid function, i.e., whether the thyroid gland is underactive, overactive or normal in function; for which a blood test or radioactive isotope uptake test is generally required(Solbiati.,2005).

Thyroid ultrasound with gray-scale and color Doppler is the most helpful imaging modality to differentiate normal thyroid parenchyma from diffuse or nodular thyroid disease by evaluating glandular size, echogenicity, echotexture, margins, and vascularity. The various causes of diffuse thyroid disease often have overlapping sonographic imaging features. Thyroid nodules may be hyperplastic or neoplastic, with most due to benign hyperplastic changes in architecture and benign follicular adenomas; only a small percentage are malignant. A systematic approach to nodule morphology that includes evaluation of composition, echogenicity, margin, shape, and any echogenic foci can guide decision to biopsy or follow nodules (Alexander t al.,2020).

Routine sonography can be useful in distinguishing different types of thyroid disorders, the sonography of the normal thyroid is slightly more echo-dense than the adjacent structures because of its high iodine content. It has a homogenous ground glass appearance. Each lobe has a smooth globular-shaped contour and is no more than 3 - 4 centimeters in height, 1 - 1.5 cm in width, and 1 centimeter in depth. The isthmus is identified, anterior to the trachea as a uniform structure that is approximately 0.5 cm in height and 2 - 3 mm in depth.

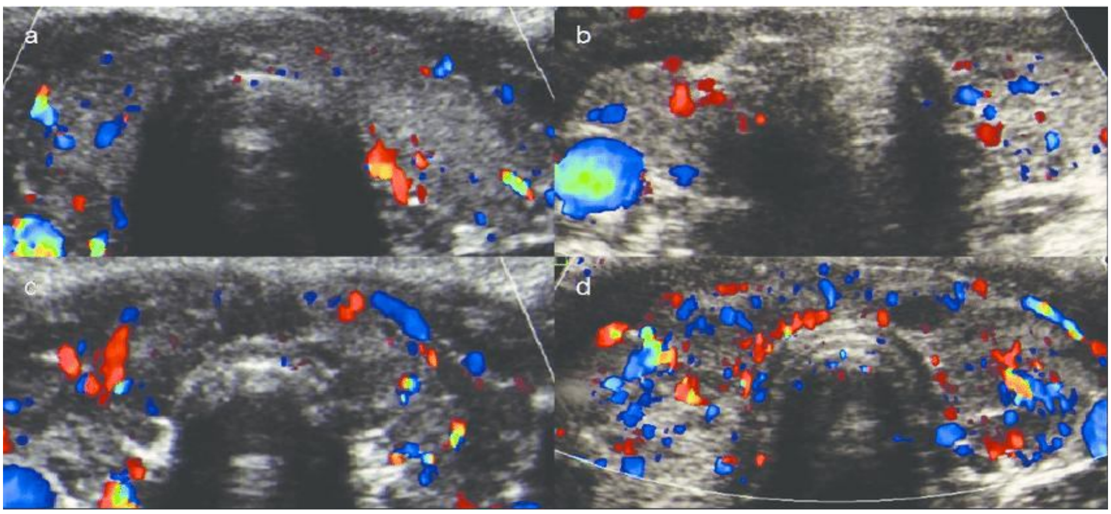


Figure (2.4): Color Doppler patterns.

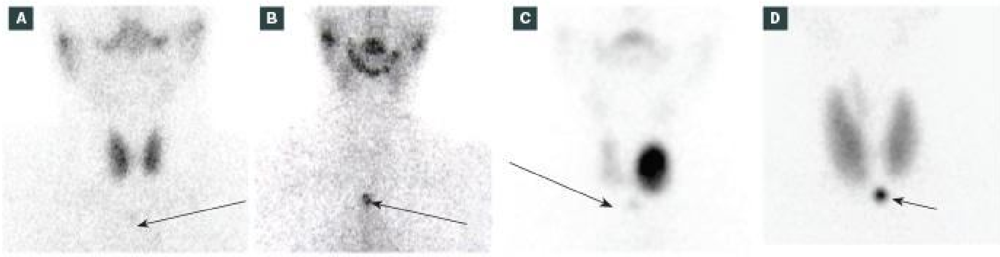
Pattern 0 (normal thyroid vascularity); b. color Doppler Pattern I (minimally increased thyroid vascularity); c. color Doppler Pattern II (increased blood flow with a diffuse homogenous distribution); and d. color Doppler Pattern III ("thyroid inferno").

2.11 Thyroid scintigraphy and uptake:

Thyroid scintigraphy and uptake examination is a simple, non-invasive and safe method for evaluation of thyroid gland function and structure. It play a central role in the diagnosis of thyroid diseases and abnormalities in thyroid function as it provides detailed information on the functions and anatomy of the thyroid gland For a standard estimation of thyroid hormonogenesis in clinical practice, radiopharmaceuticals (i.e., 131Iodine, 123Iodine, 99mTechnetium) have been commonly quantified for thyroid gland uptake through determining the degree of trapping or organification in the thyroid gland for more than five decades. Relative uptake of iodine and technetium pertechnetate by focal thyroid nodule is labeled as warm, cold, or hot (Broos et al.,2020).

Thyroid scintigraphy and uptake used for Differential diagnosis of hyperthyroidism, confirmation of suspected thyroid cancer and metastasis of thyroid cancer, detection of thyroid nodule and inflammation, determine the efficacy of radioactive iodine therapy, detection of organification (incorporation of iodine into thyroglobulin) defects and Determine congenital thyroid defects.(Arciero et al.,2012).

The test uses a radioactive tracer, which is a protein or a molecule attached to radioactive material. The radioactive tracer is administered into the patient, and a probe measures the amount of iodine uptake by the thyroid gland. The normal values of thyroid uptake of radiotracer are 3 to 16% at 6 hours and 8 to 25% at 24 hours. These values may change according to laboratory standard techniques or patient dietary habits. The thyroid gland can uptake more or less than normal. More than normal uptake of radioactive iodine by the thyroid gland indicates hyperactive thyroid like : (Hyperthyroidism due to Graves, multinodular goiter or thyroid adenoma , Goiter , Early-stage of Hashimoto thyroiditis ,Iodine deficiency ,The recovery phase from subacute, silent, or postpartum thyroiditis ,Pregnancy ,Lithium carbonate therapy ,Withdrawl of antithyroid medication ,Rebound after the suppression of thyrotropin ,Congenital defects of thyroid hormone synthesis) and less than normal uptake like (Primary hypothyroidism ,Central hypothyroidism ,Destructive thyroiditis , Excess iodine ,Dietary supplements ,Radiological contrast , some Medications , Post-thyroidectomy and External neck radiation)(Iqbal et al., 2020).

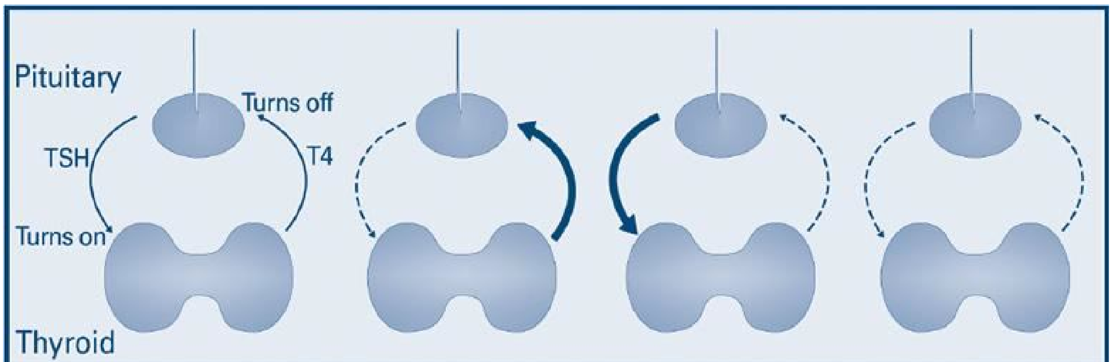


Diagnosis	Normal thyroid	Thyroiditis	Left toxic adenoma	Graves' disease
Thyroid uptake	Diffuse, symmetrical	Low or absent	Increased in nodule Contralateral reduced	Diffuse, symmetrical
Salivary gland uptake	Normal	Appears prominent	Appears reduced	Appears reduced

Figure (2.5): Thyroid scintigraphy and uptake

2.12 Thyroid function test (TFT):

Thyroid hormones (THs) and thyroid-stimulating hormone (thyrotropin, TSH) laboratory tests are commonly used worldwide for the assessment of thyroid function. According to data from 2013, TSH tests were ordered 59 million times in the US during a year. The results of thyroid function tests have an important influence on decisions about treatment and further diagnostic processes. When results are combined with symptoms, determination of whether a patient is euthyroid or suffers from hypo- or hyperthyroidism is usually simple for clinicians. However, there are a group of patients whose diagnostic process is challenging due to the discrepancies between the results of hormone tests and symptoms or because results are inconsistent with each other. Inconsistencies in hormone tests might be a result of physiological changes in hormonal balance (e.g. pregnancy), a disease (non-thyroidal or thyroid disorders), drug intake (e.g. amiodarone, contrast agents), or laboratory interference (e.g. with heterophilic antibodies). An assessment of thyroid function is mainly based on the measurement of free thyroid hormones and thyrotropin concentrations, in the form of thyroid function tests (TFTs). These hormones are most often determined by immunochemical methods, in which an antigen-antibody interaction is used. Affinity be- tween a paratope of the antibody Fab fragment and a unique determinant of the antigen molecule leads to form an antigen-antibody complex (Ag-Ab) . The immunochemical methods, depending on the principle of the test, may be divided into two groups: competitive and non-competitive (Paczkowska et al.,2020).



CONDITION:	Normal	Hyperthyroidism	Hypothyroidism Primary	Hypothyroidism Secondary
TSH	Normal	Low	High	Low
T4	Normal	High	Low	Low

Figure (2.6): Thyroid hormone function test interpretation

2.13 previous study:

Anil Kumar Avs et al(2017) evaluated the scintigraphic profile of thyrotoxicosis patients and correlate biochemical and USG findings with scintigraphy. A total of 60 newly diagnosed thyrotoxicosis patients based on biochemical reports were included in the study. They underwent further evaluation with ultrasonography and 99mTc scintigraphy , A total of 60 patients of thyrotoxicosis, 45 cases were of Grave's disease, 10 cases were of thyroiditis and five cases were of Toxic Multinodular Goiter (MNG). The clinical characteristics were helpful in establishing the diagnosis in only six (10%) patients who presented with classic features of Grave's disease with ophthalmopathy. T3/T4 ratio greater than 20 was seen only in 29 (66%) patients of Grave's disease and also in three (33.33%) of thyroiditis patients. USG had a sensitivity and specificity of 81.82% and 93.75% in diagnosing Graves' disease and 100% and 82.4% in diagnosing thyroiditis respectively, clinical findings do not help in accurately delineating aetiological diagnosis of thyrotoxicosis. Serum T3/T4 ratio when used as a criterion has marked overlap between the various conditions causing thyrotoxicosis. USG has reasonable sensitivity however, misses many cases of early Grave's disease. Follow up scintigraphy helps in a small population with resolving thyroiditis or early Grave's disease where the initial scintiscan is normal or inconclusive.

Liankun zhuo et al (2021), analyzed and compared the diagnostic value of nuclear medicine and ultrasonography in subacute thyroiditis. Methods: Sixty patients with subacute thyroiditis admitted to our hospital were included into the observation group, and 60 healthy controls that underwent physical examination in our hospital during the same period were enrolled into the control group. Examinations of nuclear medicine and ultrasonography were performed in the neck, and the results were compared between the two groups. Results: There were significant differences in the width and thickness of thyroid bilateral lobes between the two groups ($P<0.05$), and for patients in the observation group, the detection rates of nuclear medicine technique and ultrasonography were 98.33% and 95.00%, respectively. Both methods showed no significant difference in the detection rate of subacute thyroiditis ($P>0.05$). Conclusion: Both nuclear medicine imaging and ultrasonography can provide clinical guidance for diagnosis and treatment of subacute thyroiditis.

Lorenzo Scappaticcio et al (2019) compared the diagnostic effectiveness of two TSH receptor antibody immunoassays (IMAs), ultrasonography and thyroid scintigraphy in hyperthyroidism scenario, It is retrospective study analyzed consecutive patients with newly diagnosed and untreated thyrotoxicosis who underwent thyroid functional tests, both TRAb and TSI measurements, thyroid scintigraphy and ultrasonography. TRAb assessment was carried out by Kryptor® compact PLUS, while TSI by Immulite®. Echo pattern 3 corresponded to 'thyroid inferno', and the final diagnosis of GD vs non-Graves' hyperthyroidism was made according to the thyroid scan (qualitative scintigraphy). Receiver operating characteristic (ROC) curves were drawn using the final diagnosis as reference. Clinical sensitivity and specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) were calculated for all the tests , A total of 124 untreated hyperthyroid patients were included in our study (GD, n = 86 vs non-Graves' hyperthyroidism, n = 38). ROC curves showed that the optimal cut-off values associated with the highest diagnostic sensitivity and specificity was 0.7 IU/L for TRAb Kryptor® (93 [85.4-97.4] and 86.8 [71.9-95.5]) and 0.1 IU/L for TSI Immulite® (94.2 [86.9-98.1] and 84.2 [68.7-93.9]), respectively. For the echo pattern 3, we found a good sensitivity (92.1%) and a high PPV

(95.2%) but a quite low specificity value (69.8%) and a relative low NPV (57.5%). For thyroid scintigraphy, the TcTU cut-off value of 1.3% corresponded to the best limit for sensitivity and specificity in our patients (95.3 [88.5-98.7] and 96.4 [81.6-99.4]). The Passing-Bablok regression equation and the Bland-Altman test showed a great degree of correlation and agreement existed between TRAb Kryptor® and Immulite® TSI results.

C O Sahlmann et al (2004) used that iodine clearance of non-TSH regulated tissue TCTUs (global ^{99m}Tc-pertechnetate thyroid uptake under suppression) as an estimate of the. High TCTUs levels are characteristic for Graves' disease (GD). Decreased uptake has been described in autoimmune thyroiditis (AIT). However, systematically investigated data in a larger series of AIT-patients with subclinical or overt hyperthyroidism are not published so far. The purpose of this study is the evaluation of the TCTUs in the differentiation between AIT and GD in patients with hyperthyroidism. Methods: We determined the TCTUs in 59 patients with untreated hyperthyroid GD and in 51 patients with AIT who had subclinical or manifest hyperthyroidism without medication. Patients with GD were characterized by the presence of hyperthyroidism, decreased echogenicity of the thyroid, elevation of TSH-receptor autoantibodies (TRAb). AIT was defined by a decreased echogenicity of the thyroid, absence of elevated TSH-receptor autoantibodies (TRAb), autoantibodies against the thyroid peroxidase (anti-TPO) and spontaneous remission or development of subclinical hypothyroidism within 3 months. Results: Thyroid volumes of patients with AIT were significantly lower than those of patients with GD ($p < 0.05$). TRAb levels were significantly higher in GD-patients (median: 19.5 U/ml; range: 15.3-35 U/ml) than in AIT-patients (median: 1.3 U/ml; range: 0-4.1 U/ml). 73% (38/59) of patients with GD had elevated anti-TPO levels. In these patients anti-TPO levels (median: 768 U/l; range: 83-6397 U/l) were not significantly different from anti-TPO levels of patients with AIT (median: 834 U/l; range: 107-8675 U/l; p = 0.17). TCTUs values of patients with AIT were significantly lower ($p < 0.05$; median: 0.9%; range: 0.1-3.2%) than those of patients with GD (median: 5.7%; range: 1.9-28.3%). Conclusion: In our patients quantitative thyroid scintigraphy with $^{99m}TcO_4$ - offered rapid and reliable differentiation between hyperthyroid GD and AIT.

Ann Bettencourt et al (2016) was analyzed Thyroid-to-salivary ratio and percent dose uptake are the most widely recognized scintigraphic measurements. Recently, the thyroid-to-background ratio has been proposed as an alternate method. However, this method has not been validated. The purpose of this observational, cross-sectional, prospective study was to determine the location of a background region of interest (ROI) that is most reflective of blood pool activity. We also hypothesized that the thyroid-to-background ratio using this background ROI would be a better predictor of thyroid function. Fifty-six cats presented to the Virginia-Maryland College of Veterinary Medicine seeking radioiodine therapy for hyperthyroidism were enrolled in this cross-sectional study to evaluating thyroid-to-background ratio. A blood sample for measuring plasma radioactivity was collected at the time of scintigraphy. The plasma radioactivity was compared to the background ROIs in eight anatomic regions. Scintigraphic measures of thyroid-to-background and thyroid-to-salivary ratios, and percent dose were then compared to serum T_4. The heart ROI was most closely correlated with plasma pertechnetate activity ($r = 0.70$). Percent dose uptake was most closely correlated with serum T_4 ($r = 0.74$), followed by thyroid-to-salivary ratio ($r = 0.66$) and thyroid-to-background ratio using the heart ROI ($r = 0.59$). Thyroid-to-background ratio using the heart background ROI is a good predictor T_4

but percent dose uptake and thyroid-to-salivary ratio proved to be better predictors of T_4 than any of the thyroid-to-background ratios.

Bhairavi Mohit Bhat et al (2018) find out role of Technetium-99m Pertechnetate Thyroid Scintigraphy (TS) to detect functioning thyroid tissue in ectopic locations presenting as midline neck swelling. Methods: A retrospective observational study was done where 26 subjects presenting with midline neck swelling were included. These subjects were injected with 1-5MBq/kg of Technetium-99m Pertechnetate to perform the TS. The uptake of tracer in the midline neck swelling and in other ectopic location was assessed. The comparison with Ultrasound (USG) was also done. Results: 12 (46.15%) subjects presented with infra hyoid swelling and rest 14 (53.85%) presented with supra hyoid and submental swelling. 33.3% subjects presenting with thyroglossal duct cyst showed functioning thyroid tissue. Also 4 subjects showed dual functioning ectopic tissue. USG an TS showed concordant results for detecting thyroid tissue in ectopic location (p=0.68). However, TS performed better to detect ectopically located thyroid tissue (p=0.0086). Conclusions: USG and TS showed similar results to detect thyroid tissue in normal location. However, TS is better to detect topically located thyroid tissue. TS adds information of functioning thyroid tissue during workup of midline neck swelling.

Md. Monirul Haque et al (2018) illustrated the role of uptake and scintigraphy tests in determining the thyroid status of hyperthyroid patients. The present study consists of 68 hyperthyroid samples, among which 67% are female and 33% are male. In total, 184 studies have been performed including uptake measurements and scintigraphy. ^{131}I-sodium-iodide uptakes absorbed at 2 hrs as well as at 24 hrs are presented. The present study provides a good separation of hyperthyroid patients from others, and none of them has uptake lower than or within the normal range. The reports of scintigraphic scan also differentiated successfully the thyroid condition in different states. Present study also shows that the most common cause of hyperthyroidism is Graves' disease (46%) followed by multinodular goiter (24%), toxic adenoma (20%) and thyromegaly (10%). As most of the patients are younger (age ≤ 40 years), they all are at higher risk, especially the women, because the Graves' disease is more common in them. Our observations were also compared with the reported series and found to be excellent agreement in some cases. We, therefore, expect our study will contribute some useful data in literature, and provide a guideline for the diagnosis.

Amel Bushra Abakar et al (2018) was evaluated the thyroid abnormalities using ultrasound and scintigraphy. The study population consisted of 173 patients were seen by surgeons and medical doctors , were diagnosed clinically as having thyroid issues, and referred to Nuclear Medicine and Radiology Department, Fujairah hospital for thyroid scintigraphy and neck ultrasound during the period from Jan 10, 2016 to June 30, 2018. All patients Thyroid function test were done before coming to radiology department. So all results were comparing with the TFT results. The results of this study revealed that 173 patients 86% were female (149) and 14% were male (24), their mean age was 38 years. Thyroid ultrasound scan finding normal in 6% (11 patients) and abnormal in 94 % (162 patients).thyroid nuclear medicine scan were reported as normal in 9% (16 patients) and abnormal in 91% (157 patients),most affected patient's age group (20 - 50) years and commonest disease is Multinodular goiter(48%),Nodules site in both examinations, thyroid scintigraphy and thyroid ultrasound 80 and 114 is Right lobe respectively. Thyroid scintigraphy and ultrasound reached the almost same imaging findings in patients with thyroid abnormality. Ultrasonography compared to nuclear medicine scintigraphy, Ultrasound detected 93.6% (162 patients) more than nuclear medicine 90.3% (157 patients) by 3.3 %. Ultrasonography v was found to be an appropriate study in the detection of thyroid abnormality. Both US and thyroid scintigraphy have diagnosed the thyroid gland abnormality and suggested the diagnosis of others disorders in all other patients. This study concluded that the relationship between the two studies cannot be changed and does not have a significant effect because the level and degree of sensitivity of the examination of the thyroid gland by nuclear medicine is not more sensitive and accurate than the ultrasound examination. Ultrasound has the additional advantages of being non-ionizing radiation and accurately localizes and characterizes the thyroid abnormalities. Ultrasound examination should be obtained routinely for patients with suspected thyroid diseases and scintigraphy is reserved for selected cases (Amel Bushra Abakar et al.,2018).

2:2:9 Tirtha Upadhyaya et al (2018) assessed the prevalence of thyroid disorders from neck ultrasonography in relation to age, gender and disease type was performed retrospectively in Diabetes Thyroid and Endocrinology Care Center, Pokhara Nepal. Methods: Five hundred computer saved datas from the Radiology Department of Diabetes Thyroid & Endocrinology Care Center from April 2017 to April 2018 were collected. Cases were reviewed for age, gender and disease type and statistical analysis was done using SPSS tool.Results: Out of 500 patients 14% were males, 86% were females; age ranged from three days to 86 years. Hasimoto's thyoiditis was commonest problem and very prevalent in women. Conclusions: Thyroid problems are so common in general population, especially in females. Simple diagnostic tool like neck ultrasonography gives clue to make clinical diagnosis.

Anuradha Kapali et L(2017) evaluated the cases referred to our institute with suspected thyroid abnormalities and studied in them the accuracy of USG in diagnosing Hashimoto's thyroiditis and also studied the associated malignancies and their USG characteristics. Settings and Design: The patients referred to our department with suspected thyroid abnormalities were included in the prospective study. The study period was of 1 year; we included 28 patients with Hashimoto's thyroiditis. Materials and Methods: We evaluated the USG features of the cases namely echogenicity, echotexture, micronodules, and increased vascularity and followed them up for final diagnosis by fine needle aspiration cytology, histopathology, or antithyroglobulin and thyroid peroxidase tests, other 60 cases were used as a control. The results were analyzed. Statistical Analysis Used: Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Results: Hashimoto's thyroiditis was present in 28 patients. The most sensitive parameter in diagnosing Hashimoto's thyroiditis was hypoechogenicity and increased vascularity. The most specific parameter was micronodules. Nodules were seen in 13 patients, out of which malignant nodules was present in six patients. Microcalcification, thick halo, and internal vascularity increase the likelihood of nodules being malignant. Conclusions: The most sensitive parameter in diagnosing Hashimoto's thyroiditis was hypoechogenicity and increased vascularity. The most specific parameter was micronodules. Coarsened echo texture had an intermediate sensitivity and specificity. The USG is a specific modality for diagnosing Hashimoto's thyroiditis with a good sensitivity. Microcalcification, thick halo, and internal vascularity also increase the likelihood of nodules being malignant in the background of Hashimoto's thyroiditis. Hence, these nodules must be subject to FNA.

Fausto Bogazzi et al (2021) evaluated Thyroid blood flow is greatly enhanced in untreated Graves' disease, but it is not known whether it is due to thyroid hormone excess or to thyroid hyperstimulation by TSH-receptor antibody. To address this issue in vivo patients with different thyroid disorders were submitted to color flow doppler sonography (CFDS). Subjects and methods: We investigated 24 normal subjects, and 78 patients with untreated hyperthy- roidism (49 with Graves' hyperthyroidism, 24 with toxic adenoma, and 5 patients with TSH-secreting pituitary adenoma (TSHoma)), 19 patients with thyrotoxicosis (7 with thyrotoxicosis factitia, and 12 with subacute thyroiditis), 37 euthyroid patients with goitrous Hashimoto's thyroiditis, and 21 untreated hypothyroid patients with Hashimoto's thyroiditis. Results: Normal subjects had CFDS pattern 0 (absent or minimal intraparenchimal spots) and mean intraparenchimal peak systolic velocity (PSV) of 4.8 61.2 cm/s. Patients with spontaneous hyperthy- roidism due to Graves' disease, TSHoma, and toxic adenoma had significantly increased PSV ($P < 0.0001$, $P = 0.0004$, $P < 0.0001$ respectively vs controls) and CFDS pattern. Patients with Graves' disease had CFDS pattern II (mild increase of color flow doppler signal) in 10 (20%) and pattern III (marked increase) in 39 cases (80%). Mean PSV was 15 63 cm/s.

Patients with toxic adenoma had CFDS pattern I (presence of parenchymal blood flow with patchy uneven distribution) in 2 (8%), pattern II in 16 (70%) and pattern III in 5 (22%). Mean PSV was 11 62.4 cm/s. Patients with TSHoma showed CFDS pattern I in one case (20%) and pattern II in 4 (80%). Mean PSV was 14.8 64.2 cm/s. Patients with thyrotoxicosis had normal PSV (4.2 61.1 cm/s in subacute thyroiditis, 4 60.8 cm/s in thyrotoxicosis factitia, P= not significant vs controls) and CFDS pattern 0. Untreated euthyroid patients with goitrous Hashimoto's thyroiditis had CFDS pattern 0, and mean PSV (4.3 60.9 cm/s; P = not significant vs controls). Untreated hypothyroid patients with goitrous Hashimoto's thyroiditis had CFDS pattern I in 14 cases (67%), pattern II in 4 (19%) and pattern 0 in 3 (14%) and mean PSV (5.6 61.4 cm/s) was higher than that of controls ($P = 0.026$). Conclusions: An increase in both intrathyroidal vascularity and blood velocity was observed in patients with spontaneous hyperthyroidism but not in thyrotoxicosis due to either ingestion of thyroid hormones or to a thyroidal destructive process. The slightly increased vascularity and blood velocity observed in patients with hypothyroid Hashimoto's thyroiditis suggests that thyroid stimulation by either TSH-receptor antibody or TSH is responsible for the increased thyroid blood flow.

Susanne L. Schulz et al (2003) evaluated the value of color Doppler sonography in patients with hypothyroidism. Methods*:* 89 patients with hypothyroidism have been evaluated. They were examined clinically; laboratory tests on thyroid function and color Doppler sonography have been performed. The color flow distribution and intensity were estimated and the fastest flow velocity (PSV) detectable with a pw-doppler was registered. The color pattern was graded from 0 to III as has been described by others and the color Doppler findings were then correlated to both the clinical picture and the laboratory results. *Results:* 56 of the 89 hypothyroid patients showed pattern 0 with a PSV of 22 cm/s. In 33 patients different degrees of increased parenchymal color could be found with a concordant PSV: 16 patients showed pattern I with a PSV of 39 cm/s; 11 showed pattern II with PSV 58 cm/s, and 6 showed pattern III with PSV 63 cm/s. Regarding the corresponding clinical and laboratory variables, there was a very close correlation between color intensity and anti-Tg/anti-TPO antibody levels: pattern 0: anti-Tg 474 IU/ml, anti-TPO-Ab 810 IU/ml; pattern I: 1053/1733; pattern II: 1774/2432; pattern III: 1951/2633. Some correlation could also be found for the TSH values and the calculated volume of the thyroid gland, whereas the duration of hypothyroidism showed an inverse correlation to color intensity. (Pattern 0: TSH 3.1 mE/ml, volume 9.2 ml, duration 43 months; pattern I: 4.2 mE/l, 15.7 ml, 24 mos.; pattern II: 11.5 mE/l, 22.3 ml, 16 mos.; pattern

III: 38.2 mE/l, 34.3 ml, 10 mos, respectively). *Conclusions:* The color Doppler pattern of intense hypervascularization of the thyroid gland formerly attributed only to the hyperthyroid state of active Graves' Disease can also be seen in hypothyroidism. Our data support the concept that the color flow appearance is not the result of stimulated thyroid hormone production, but a measure of the activity of an autoimmune process.

Ali Pooria et l (2021) evaluated underlying pathology in the patients presenting hyperthyroidism using RAIU test results. Methods: This is a cross-sectional retrospective study conducted on the patients with hyperthyroidism referred to Shahid Madani Hospital in Khorramabad. Data regarding the biochemical analysis and RAIU test was collected from the records and a questionnaire based on demographic and clinical information was completed for each patient. Results: Of 137 patients presenting hyperthyroidism, 62.04% were presented with Graves' disease, 24.08% with toxic multinodular goiter and 13.86% with toxic adenoma. 24-hour RAIU test showed that the percent of radioiodine uptake was most in toxic adenoma 67.7%, Graves' disease 53.5% and multinodular goiter 39%, respectively. From the age-based analysis, we found that Graves' was most common in 20-30 years old individuals 34%, multinodular goiter in 50+ aged individuals 36.3% and toxic adenoma was most prevalent in 30-40 and 50+ aged patients, 26.3% each. In our population of interest, 81.8% toxic multinodular goiter patients were females. Conclusions: Our study presents the outcome of RAIU tests in hyperthyroidism based on the underlying pathologies. We also conclude, in light of other findings, Graves' disease is the most common cause of hyperthyroidism in our population.

Parvin Layegh, et al (2020) compared thyroid volume, thyroid stimulating hormone (TSH), free t4 and the prevalence of thyroid nodules between obese and non-obese subjects. Also, the association between BMI and insulin resistance status with various parameters of thyroid gland was evaluated .Fifty–two patients with obesity and 38 volunteers aged 20-50 years with normal body mass index (BMI), were enrolled in this cross-sectional study. Patients with diabetes, history of thyroid disorders, and patients, who were taking medications that influence their blood glucose or insulin levels or modified thyroid function tests, were excluded. TSH, free t4, insulin and glucose and thyroid sonography were carried out and the results compared between two groups. $P<0.05$ was considered as significant .The result showed that thyroid volume was higher ($p<0.001$) and free t4 was lower ($p<0.001$) in patients with obesity but there was no difference in TSH between groups. Prevalence of thyroid nodules was 15.7% and 10.8% in obese and non-obese groups, respectively ($p=0.51$). Frequency of nodules was significantly higher in insulin resistant than non- insulin resistant subjects (22% vs.2%, $p=0.01$). BMI was associated with thyroid volume ($r=0.44$, $p<0.001$) and free t4 ($r=-0.35$, $p=0.001$). HOMA-IR (homeostatic model assessment for insulin resistance) had no correlation with thyroid volume ($p=0.38$), but associated with free t4 ($r=-0.25$, $p=0.01$).Free T4 was lower and volume of thyroid was higher in obese subjects, but TSH and frequency of thyroid nodules had no significant difference between obese and non-obese counterparts. Insulin resistant individuals had more nodules but thyroid volume was mainly associated with BMI.

Maimoona Rasool et al (2020) correlated the sonographic findings of maternal thyroid gland with thyroid function tests during pregnancy. 135 pregnant women were recruited in this study , data of TSH, T3 and T4 was obtained and correlated it with the sonographic findings of maternal thyroid gland in each trimester of pregnancy. In the 135 sampled pregnant women, mean thyroid gland volume was 4.08 ± 1.19 cm^3. The mean levels of T3, T4 and TSH were v3.37±.44 pmol/L, 14.96±2.49 pmol/L and 1.21±.92 mIU/L respectively. A remarkable correlation between thyroid hormones and thyroid volume was observed,: It is concluded that the ultra-sonographic findings is correlated with the thyroid function tests during pregnancy.

Yuksekkaya et al (2020) correlated the increased levels of thyroid hormones with increased thyroid blood flow in patients with Graves' Disease by color Doppler Ultrasonography and a newly developed software Color. Forty-one consecutive subjects with GD and 41 healthy controls were enrolled. Color Doppler ultrasonography parameters of the thyroid arteries and Color Quantification values of the gland were measured. The correlations between thyroid blood flow parameters, levels of ^{99m} Technetium pertechnetate uptake, thyrotropin, and free thyroxin were evaluated. The diagnostic performances of these parameters were investigated. The result showed that The peak systolic-end diastolic velocities of thyroid arteries and Color Quantification values were increased in the study group ($p < 0.05$ for all). We observed negative correlations between thyrotropin levels and peak-systolic and end-diastolic velocities of superior thyroid arteries and Color Quantification values. There were positive correlations between ^{99m} Technetium uptake levels and thyroid blood flow parameters ($p < 0.05$ for all). In the diagnostic performance of thyroid blood flow parameters, we observed utilities significantly in peak-systolic and end-diastolic velocities of thyroid arteries and Color Quantification values. ($P< 0.05$ for all).It concluded that the increased peak-systolic and end-diastolic velocities of thyroid arteries, and increased Color Quantification values might be helpful in the diagnosis of Graves' disease.

Anjuman Ara Akhter et al (2017) evaluated the utility of CFD in differentiation of hyperthyroid Graves' disease from subacute thyroiditis as well as comparing its sensitivity and specificity in light of RAIU test .This study analyzed thyroid blood flow, peak systolic velocity (PSV) by CFD and thyroid volume by Gray scale sonography in thyrotoxicosis. Methods and materials: Thyrotoxic cases (N=78; Graves: M/F=21/27, age: 35.73±1.38; subacute thyroiditis: M/F=09/21, age: 35.37±1.61 (M±SEM, years)) were recruited and divided into Graves' and subacute thyroiditis holding RAIU as gold standard. CFD and Gray scale sonography were done for all. Results: Goiter was tender in 33% of subacute thyroiditis. Neither free thyroxin (FT4: 3.38±0.22 vs. 2.78±0.23, P=0.549) nor thyroid stimulating hormone (TSH: 0.05±0.01 vs. 0.06±0.02, P=0.084) were statistically different between the two groups. Echo pattern was predominantly homogeneous in Graves and heterogeneous in subacute thyroiditis (60.4% vs. 43.3%, P=0.007). Gray scale sonography revealed increased thyroid volume in 73%, normal in 20.8% and decreased in 6.3% of Graves which were 33.3%, 56.7% and 10.3% respectively in subacute thyroiditis (p=0.002). All Graves' had increased flow while 76.7% of the subacute thyroiditis had decreased flow by CFD.

M. Faruk Hossain1et al (2017) was correlated the serum T4, T3 and TSH Levels with Radioiodine Thyroid Uptakes. A total of 48 adult patients including 25 female and 23 male, referred to the Institute of Nuclear Medicine and Allied Sciences (INMAS), Dhaka for thyroid function tests were evaluated to study the correlation of serum T4, T3, TSH levels with 24 and 2 hours thyroid RAIU values. The present results revealed a positive and statistically significant correlation of serum T4 and T3 levels with RAIU values. Serum TSH levels, on the other hand, showed an expected negative correlation with uptake values. The results obtained in this study were also found to be in fairly good agreement with the reported data. However, the positive correlation of serum T4 and T3 RIA values with 24 and 2 hours RAIU, in this study, is not a perfect one because correlation coefficient (r) though greater than zero ($r > 0$) is less than one ($r < 1$). The present study, therefore, suggests that thyroid RAIU cannot be recommended as the sole diagnostic investigation for thyroid function tests.

Almohammed HI et al (2020) evaluate thyroid scintigraphy for identifying hyperthyroidism in comparison with thyroid stimulating hormone (TSH) and ultrasound. This is cross sectional study including convenient patients sample (n = 50, 15 males and 35 females) aged (20-50 years) with primary hyperthyroidism and were attending endocrine clinics at King Faisal Specialist Hospital and Research Centre. All patients performed clinical investigations (TSH, ultrasound and thyroid scintigraphy). Among these patients, 96%, 48/50, had positive findings for hyperthyroidism with thyroid SC (95% CI; 96.0-99.5%); 84%, 42/50, had positive findings for hyperthyroidism by US (95% CI; 70.9-92.8%); and 56%, 28/50, had positive findings for hyperthyroidism by TSH measurement (95% CI; 41.3.0-70.0%). There was very good agreement between scintigraphy diagnosis and ultrasonography (kappa score = 0.812 ($P < 0.0001$), 95% CI (0.77-0.85). In many cases, scintigraphy provides considerably more functioning and anatomic details than ultrasound. In conclusion, these findings bring forth practical aspects of thyroid scintigraphy utilization for hyperthyroidism. By combining functional and anatomical information in one step, scintigraphy provides non-invasive, simple, fast and cost effective hyperthyroidism diagnostic method and has the potential to replace TSH and ultrasonography in hyperthyroidism investigation.

Chapter Three
Materials and methods

3.1 Study design:

This is retrospective, controlled study

3.2 Duration of the study:

This study was conducted from 2017-2021.

3.3 Area of the study:

The study was conducted in Saudi Arabia at King Saud Medial Center (KSMC).

3.4Study population:

The data was collected from Picture and Communication System (PACS) of nuclear medicine department with different age, gender and thyroid abnormalities.

3.5 Sample size:

The sample size of the study is hundred forty four subjects.

3.5.1 Inclusion criteria:

Age: All ages.

Sex: Male and female.

Types of disease: Any thyroid disorder.

Diagnosis: Subjects was diagnosed with Doppler ultrasound and thyroid scintigraphy.

3.5.2 Exclusion criteria:

Subjects who run only one diagnostic tool.

3.6 Sampling technique:

Randomly sampling technique.

3.7 Data collection technique:

Data was collected using data collection sheet

3.8 Machine:

Procedure was done by GE introduces Discovery NM-CT 670 pro and Q.Merix at nuclear medicine department and GE Logiq E9 equipment at ultrasound department.

3.9 techniques:

A thyroid sonogram was performed with a high-frequency linear array transducer having a short focal zone (1 to 4 cm). The patient was examined in supine position, with the neck extended and pillow under shoulder. Images are obtained in both the sagittal and transverse planes of each lobe and of the isthmus. Normal thyroid tissue is homogeneously fine textured with medium to high levels of echogenicity. The echogenicity is usually greater than the normal neck muscles. Each adult pear-shaped lobe measures approximately 4 to 6 cm in length, 2 to 3 cm in width, and 1 to 2 cm in thickness, with the right lobe typically being the largest. Then the thyroid volume can be calculated using the following formula: length × width × thickness × 0.529. Moreover each thyroid lobe should be evaluated using color Doppler because the amount of vascularity may be evident of disease.

Then the patient was referred for thyroid uptake and scan, it was performed by preparing patient well as certain foods and medications interfere with radiotracer uptake in the thyroid gland. Firstly the radiotracer (Technitium 99mTC) which emits gamma radiation was prepared and pulls it into the syringe , the scan was done for full syringe and the counts were collected, then the patient was injected intravenously by radiotracer and the empty syringe was scan again, 20-30 min after radiotracer administration the patient lied down on the movable examination table, and the gamma camera took serial images of the thyroid gland from different angles. The images were analyzed and the counts were collected to calculate the percentage of thyroid uptake using below equation:

$$\text{uptake\%} = \frac{Neck\ Counts - \text{Thigh Counts}}{(Admin.\ counts\ X\ decay\ factor) - \text{Background Counts}} \text{X100}$$

The normal values of thyroid uptake of radiotracer was (0.5 – 2)% The thyroid gland can uptake more or less than normal. More than normal uptake of radioactive iodine by the thyroid gland indicates hyperactive thyroid and less than normal uptake infers hypoactive thyroid gland, or interference with the uptake.

3.10 Method of data analysis:

Data entry and statistical analysis were performed using personnel computer software, the statistical package for social science (SPSS) version21.suitable descriptive statistics were used such as: frequency, percentage ,median , range, mean and standard deviation .Chi-square test was used to detect the relation between variables in addition correlation coefficient (r) test was used to estimate the closeness association between variables. Paired (t) test was used to compare mean score between both studied variables. The p-value is the degree of significant and using the correlation (r) test. The p-value is the probability of that an observed difference is due to chance and not a true differences .A significant level value was considered when p- value ≤0.05 and a highly significant level value was considered when p-value ≤0.001 ,while p-value >0.05 indicates non- significant results.

3.11 Ethical consideration:

All procedures and techniques used in this study will be in accordance with the National Guidelines for Ethical Conduct of Research Involving Human Subjects. The protocols for the study were approved by Institutional review board (IRB) of King Saud Medical City (KSMC).

Chapter Four

Results

4.1 Results:

Table (4.1): Frequency distribution for all patients

Gender	Number	Percent
Female	111	77.1
Male	33	22.9
Total	144	100.0

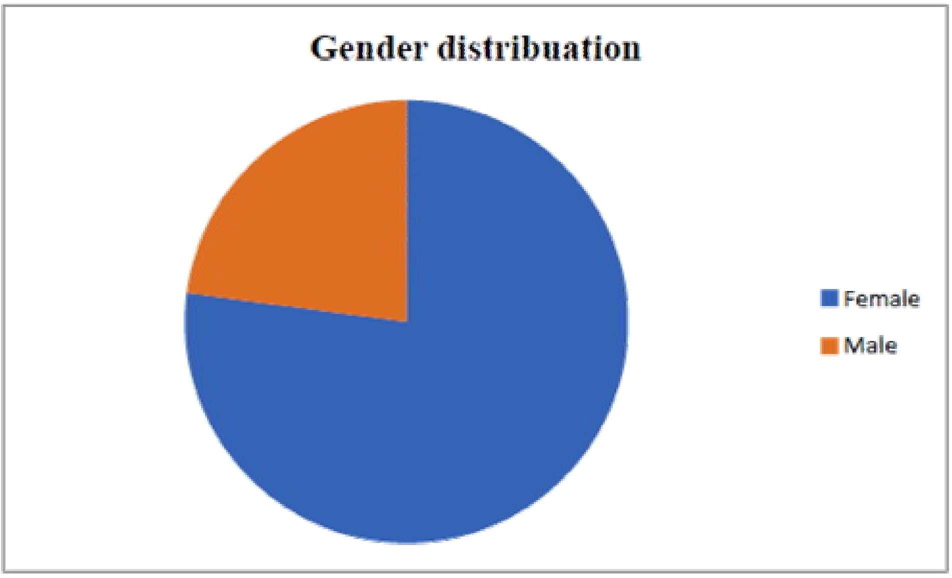


Figure 4.1: Frequency distribution for all patients

Table 4.2: Descriptive statistics for all patients

Variables	Mean	Std. Dev.	Minimum	Maximum
TSH	.99	2.5	.00	18.00
T4	32.2	29.2	2.27	228.04
Rt lobe Length (cm)	5.2	1.8	.0	8.8
Rt lobe width (cm)	3.0	1.5	.0	8.9
Rt lobe size (cm)	15.3	7.80	.00	45.65
RT lobe volume	15.9	14.3	.0	87.0
LT lobe length(cm)	4.8	1.9	.0	9.5
LT lobe width (cm)	2.8	1.5	.00	8.00
LT lobe size(cm)	14.1	8.9	.00	47.88
lt lobe volume	12.8	11.9	.0	66.4
thyroid uptake	7.7	9.4	.0	39.8

Table 4.3: Group statistics for patients according to their gender

Variables	Gender	Mean	Std. Dev	Std. Error Mean
TSH	Female	.8812	1.89253	.17963
	Male	1.3771	3.82381	.66564
T4	Female	32.4676	31.50799	2.99061
	Male	31.3988	19.76986	3.44149
Rt lobe Length (cm)	Female	4.996	1.7876	.1697
	Male	5.767	1.7537	.3053
Rt lobe width (cm)	Female	2.990	1.4780	.1403
	Male	3.094	1.5199	.2646
Rt lobe size (cm)	Female	14.5337	7.37442	.69995
	Male	17.8388	8.75026	1.52323
RT lobe volume	Female	14.955	12.9958	1.2335
	Male	19.410	17.7676	3.0929
LT lobe length (cm)	Female	4.553	1.8661	.1771
	Male	5.645	2.1452	.3734
LT lobe width (cm)	Female	2.7405	1.44794	.13743
	Male	3.1667	1.52800	.26599
LT lobe size (cm)	Female	12.7135	7.65221	.72632
	Male	18.9212	10.83173	1.88556
Lt lobe volume	Female	11.356	9.9740	.9467
	Male	17.555	16.1052	2.8035
thyroid uptake	male	7.432	9.2197	.8751
	Male	8.742	9.8931	1.7222

Table 4.4: Frequency distribution of nuclear medicine finding

NM finding	Frequency	Percent
Normal	11	7.6
multinodular goiter	24	16.7
graves' disease	60	41.7
autonomous toxic nodule	8	5.6
Hyperthyroidism	3	2.1
Hypothyroidism	5	3.5
Nodule	14	9.7
Thyroiditis	5	3.5
Goiter	12	8.3
thyroglossal cyst	2	1.4
Total	144	100.0

Table 4.5: Frequency distribution of Ultra-sound finding

US finding	Frequency	Percent
Normal	32	22.2
Cyst	4	2.8
Thyroiditis	9	6.3
thyrotoxic goiter	5	3.5
Enlargement	14	9.7
nodule with mixed echogenicity	45	31.3
hypoechoic nodule	14	9.7
hyperechoic nodule	7	4.9
graves' disease	2	1.4
diffuse heterogenicity	12	8.3
Total	144	100.0

Table 4.6: Frequency distribution of vascularity

Vascularity	Frequency	Percent
Normal	51	35.4
Increased	92	63.9
Low	1	.7
Total	144	100.0

Table 4.7: Frequency distribution for background

Background	Frequency	Percent
Normal	42	29.2
Increase	13	9.0
moderately low	6	4.2
mildly low	12	8.3
Low	71	49.3
Total	144	100.0

Table 4.8: Correlation between the nuclear medicine findings with background

NM finding * background Cross tabulation						
NM finding	Background					Total
	Normal	Increase	moderately low	mildly low	Low	
Normal	10	1	0	0	0	11
multinodular goiter	10	3	1	2	8	24
graves' disease	2	1	3	8	46	60
autonomous toxic nodule	2	0	1	0	5	8
Hyperthyroidism	1	0	0	0	2	3
Hypothyroidism	0	3	0	0	2	5
Nodule	6	3	1	1	3	14
Thyroiditis	2	2	0	0	1	5
Goiter	7	0	0	1	4	12
thyroglossal cyst	2	0	0	0	0	2
Total	42	13	6	12	71	144

Table 4.9: Analysis of variance grouped as nuclear medicine results

		Sum of Squares	Df	Mean Square	F	p. value
TSH	Between Groups	212.124	9	23.569	4.814	.000
	Within Groups	656.004	134	4.896		
	Total	868.128	143			
T4	Between Groups	22440.2	9	2493.36	3.365	.001
	Within Groups	99298.7	134	741.035		
	Total	121739	143			
Rt_lobe_ Length	Between Groups	84.324	9	9.369	3.298	.001
	Within Groups	380.711	134	2.841		
	Total	465.035	143			
Rt_lobe_width	Between Groups	65.795	9	7.311	3.939	.000
	Within Groups	248.690	134	1.856		
	Total	314.485	143			
Rt_lobe_ Size	Between Groups	2413.28	9	268.143	5.706	.000
	Within Groups	6296.75	134	46.991		
	Total	8710.04	143			
Lt_lobe_ Length	Between Groups	67.666	9	7.518	2.043	.039
	Within Groups	493.022	134	3.679		
	Total	560.688	143			
Lt_lobe_width	Between Groups	53.501	9	5.945	3.106	.002
	Within Groups	256.452	134	1.914		
	Total	309.953	143			
Lt_lobe_ Size	Between Groups	1767.35	9	196.372	2.797	.005
	Within Groups	9408.51	134	70.213		
	Total	11175.8	143			
hyroid_ uptake	Between Groups	3607.25	9	400.806	6.022	.000
	Within Groups	8918.71	134	66.558		
	Total	12525.9	143			
Rt_lobe_ Volume	Between Groups	5049.49	9	561.055	3.115	.002
	Within Groups	24135.3	134	180.114		
	Total	29184.8	143			
lt_lobe_ volume	Between Groups	2402.01	9	266.890	2.007	.043
	Within Groups	17818.4	134	132.974		
	Total	20220.5	143			

Table 4.10: Analysis of variance grouped as ultrasound results

		Sum of Squares	Df	Mean Square	F	p. value
TSH	Between Groups	39.535	9	4.393	.710	.699
	Within Groups	828.593	134	6.184		
	Total	868.128	143			
T4	Between Groups	8857.261	9	984.14	1.168	.320
	Within Groups	112881.76	134	842.40		
	Total	121739.02	143			
Rt_lobe_ Length	Between Groups	64.316	9	7.146	2.390	.015
	Within Groups	400.719	134	2.990		
	Total	465.035	143			
Rt_lobe_ width	Between Groups	13.689	9	1.521	.678	.728
	Within Groups	300.796	134	2.245		
	Total	314.485	143			
Rt_lobe_ Size	Between Groups	631.720	9	70.191	1.164	.323
	Within Groups	8078.322	134	60.286		
	Total	8710.041	143			
Lt_lobe_ Length	Between Groups	69.679	9	7.742	2.113	.033
	Within Groups	491.009	134	3.664		
	Total	560.688	143			
Lt_lobe_ width	Between Groups	19.119	9	2.124	.979	.461
	Within Groups	290.834	134	2.170		
	Total	309.953	143			
Lt_lobe_ Size	Between Groups	1447.336	9	160.81	2.215	.025
	Within Groups	9728.533	134	72.601		
	Total	11175.869	143			
hyroid_ uptake	Between Groups	2450.213	9	272.24	3.621	.000
	Within Groups	10075.751	134	75.192		
	Total	12525.964	143			
Rt_lobe_ Volume	Between Groups	4489.568	9	498.84	2.707	.006
	Within Groups	24695.244	134	184.29		
	Total	29184.812	143			
lt_lobe_ volume	Between Groups	1773.902	9	197.10	1.432	.181
	Within Groups	18446.605	134	137.66		
	Total	20220.507	143			

Table 4.11: Analysis of variance for thyroid uptake with other variables

		Sum of Squares	Df	Mean Square	F	p. value
Rt lobe Length (cm)	Between Groups	316.265	98	3.227	.976	.550
	Within Groups	148.770	45	3.306		
	Total	465.035	143			
Rt lobe width (cm)	Between Groups	236.772	98	2.416	1.399	.105
	Within Groups	77.713	45	1.727		
	Total	314.485	143			
Rt lobe size (cm)	Between Groups	4771.827	98	48.692	.556	.992
	Within Groups	3938.214	45	87.516		
	Total	8710.041	143			
RT lobe volume	Between Groups	17006.013	98	173.531	.641	.965
	Within Groups	12178.792	45	270.640		
	Total	29184.805	143			
LT lobe length (cm)	Between Groups	433.719	98	4.426	1.569	.047
	Within Groups	126.969	45	**2.8**22		
	Total	560.688	143			
LT lobe width (cm)	Between Groups	275.693	98	2.813	3.695	.000
	Within Groups	34.260	45	.761		
	Total	309.953	143			
LT lobe size(cm)	Between Groups	9139.407	98	93.259	2.061	.004
	Within Groups	2036.462	45	45.255		
	Total	11175.869	143			
lt lobe volume	Between Groups	12112.884	98	123.601	.686	.938
	Within Groups	8107.621	45	180.169		
	Total	20220.504	143			

Table 4.12 Correlation between the nuclear medicine findings with ultrasound finding

	Finding US										Total
Finding NM	Normal	Cyst	Thyro iditis	Thyrotox ic goiter	Enlarge ment	Nodule with mixed echogenicity	Hypoecho ic nodule	Hyperech oic nodule	Graves disease	Diffuse heterogenicity	
Normal	6	1	1	0	0	2	0	1	0	0	11
Multinodular goiter	3	1	0	1	0	14	3	2	0	0	24
Graves disease	16	0	2	4	12	10	4	2	2	8	60
Autonomos toxic nodule	0	0	0	0	0	5	3	0	0	0	8
Hyperthyroidism	0	0	2	0	0	0	0	0	0	1	3
Hypothyrodism	2	0	1	0	0	1	0	0	0	1	5
Nodule	1	0	0	0	0	8	3	2	0	0	14
Thyroditis	2	0	1	0	0	2	0	0	0	0	5
Goiter	2	0	2	0	2	3	1	0	0	2	12
Thyroglossal cyst	0	2	0	0	0	0	0	0	0	0	2
Total	32	4	9	5	14	45	14	7	2	12	144

Figure 4.2: Correlation between the right and left lobe width with nuclear medicine finding

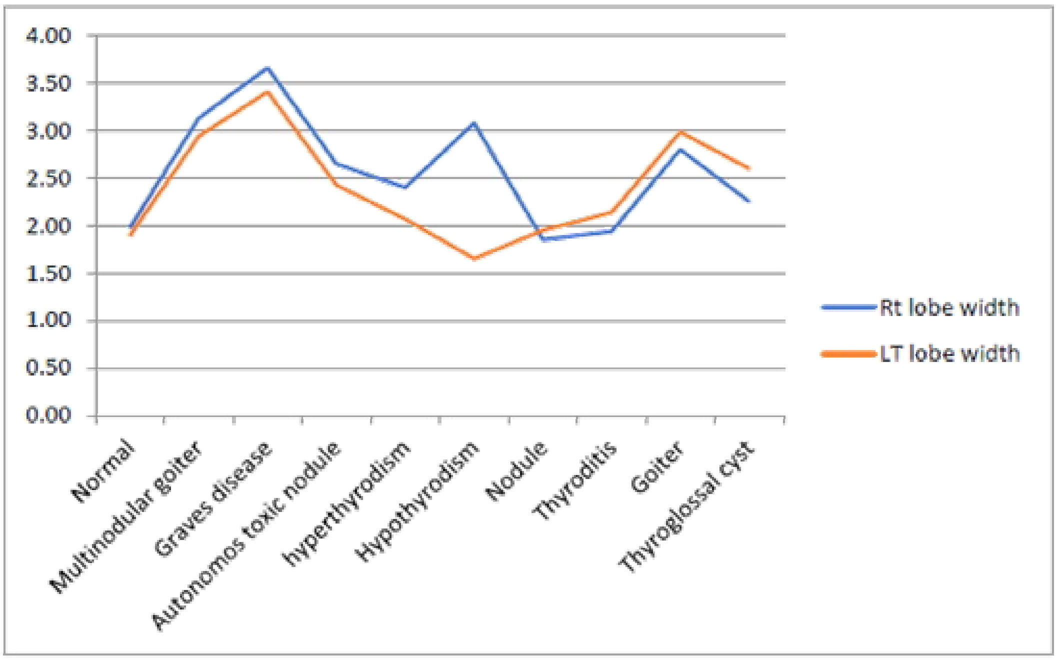


Figure 4.3: Correlation between the right and left lobe size with nuclear medicine finding

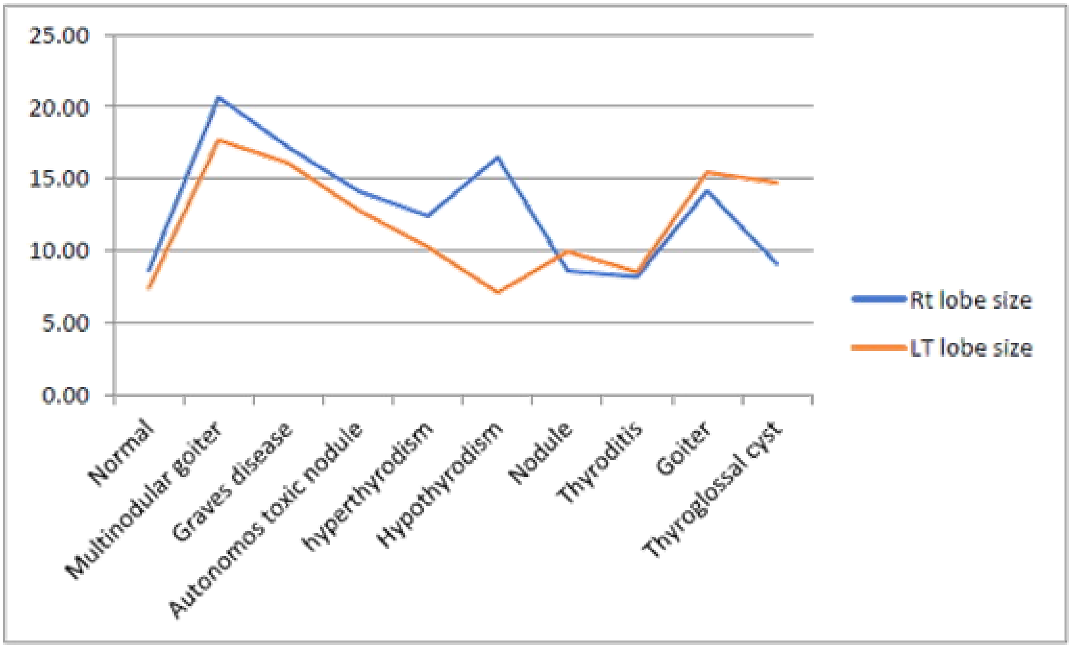


Figure 4.4 Correlation between the right and left lobe length with nuclear medicine finding

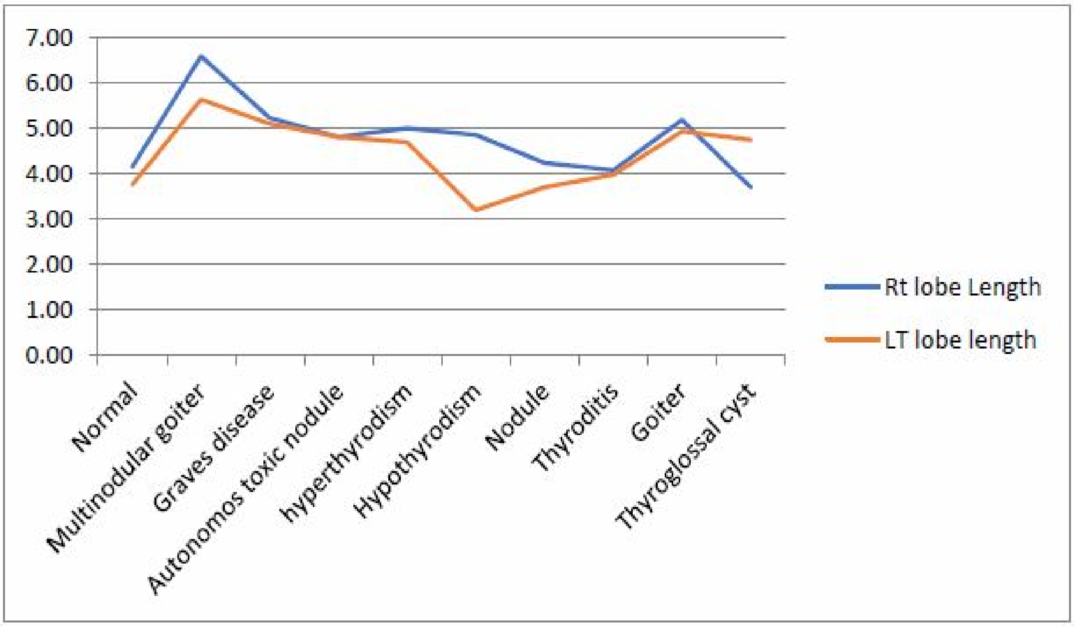


Figure 4.5 Correlation between the right and left lobe volume with nuclear medicine finding

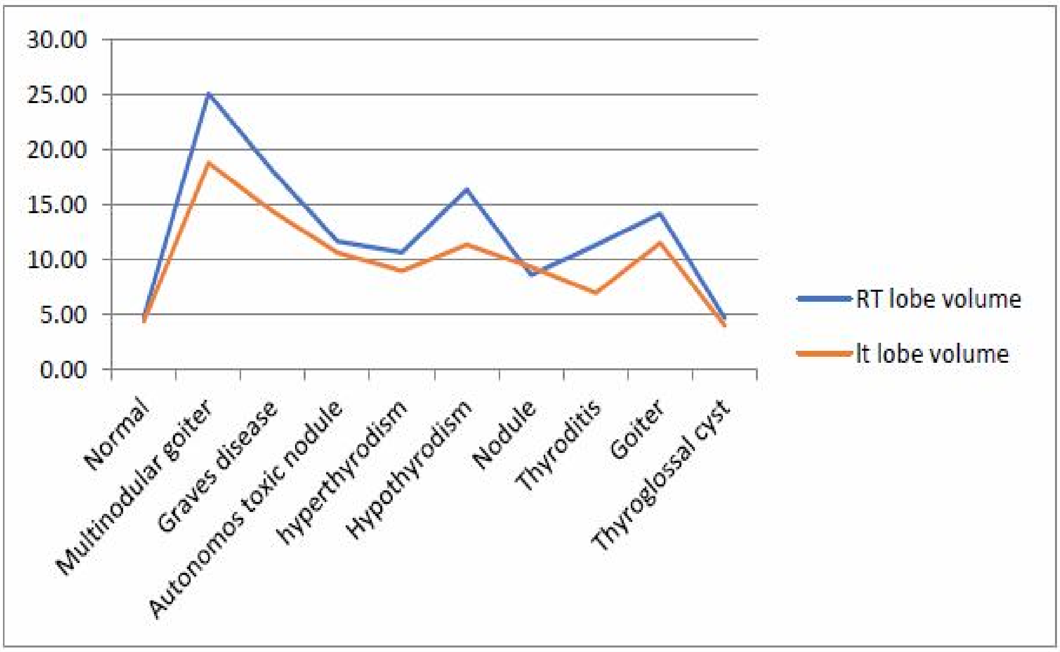


Figure 4.6 Correlation between thyroid uptake with nuclear medicine finding

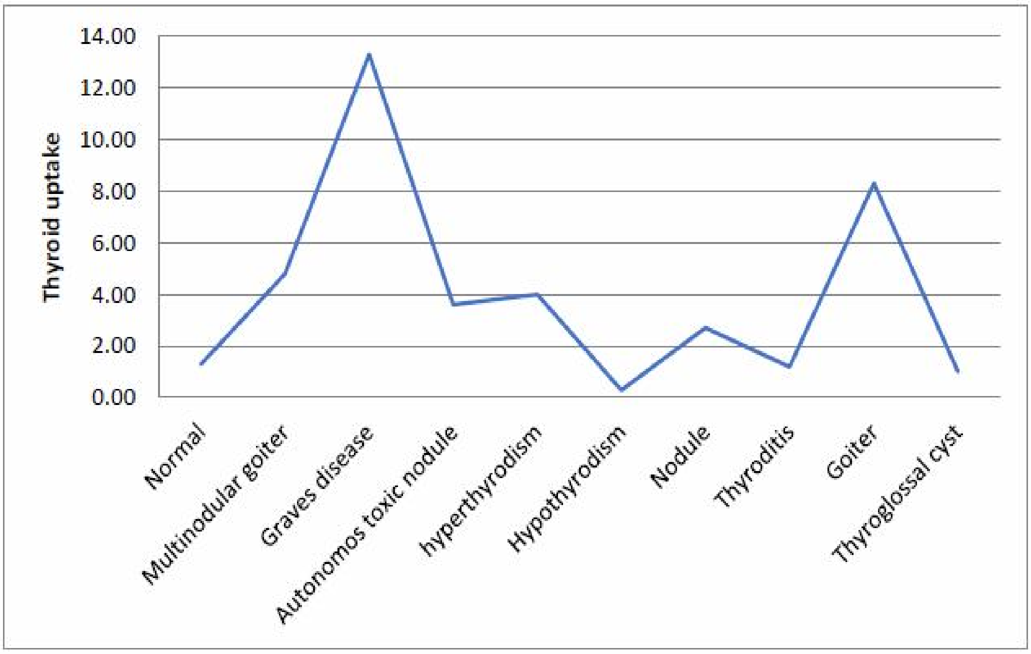


Figure 4.7 Correlation between TSH hormone with nuclear medicine finding

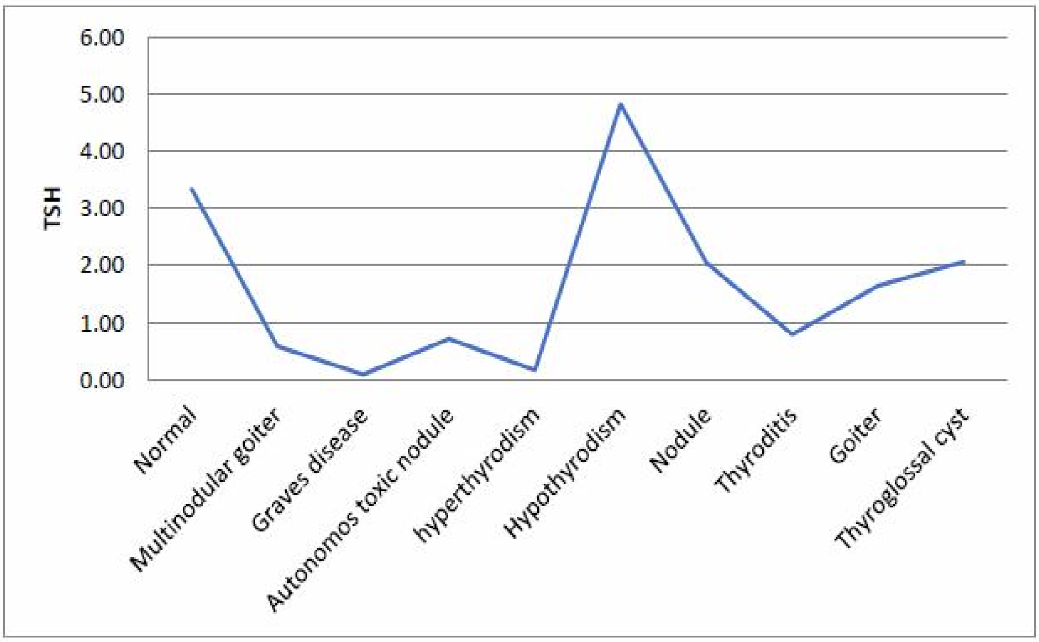


Figure 4.8 Correlation between T4 hormone with nuclear medicine finding

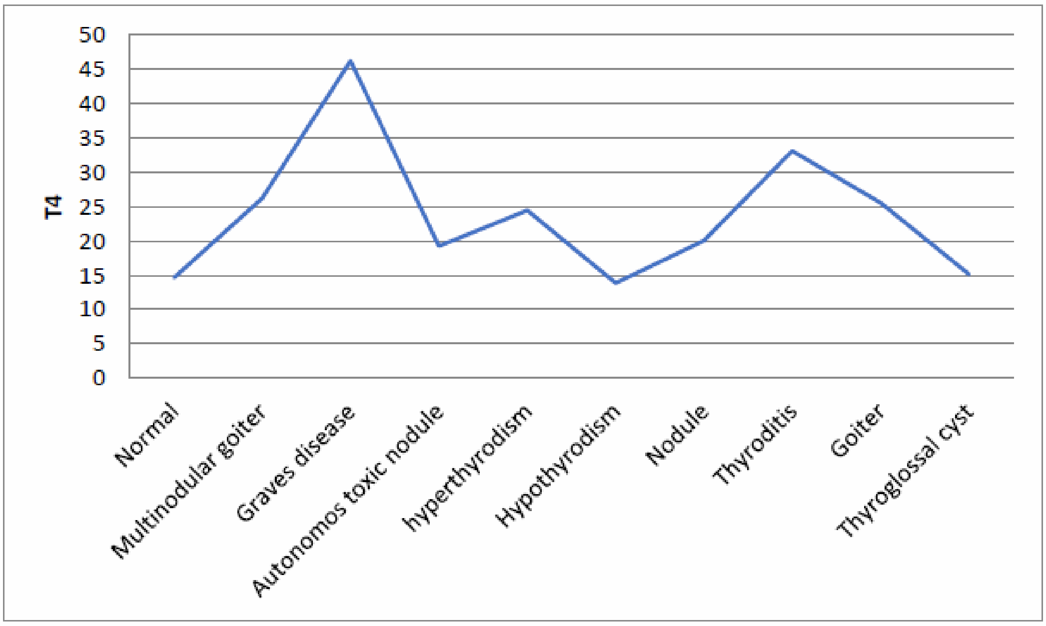


Figure 4.9 Scatter plot between the thyroid uptakes with T4 level

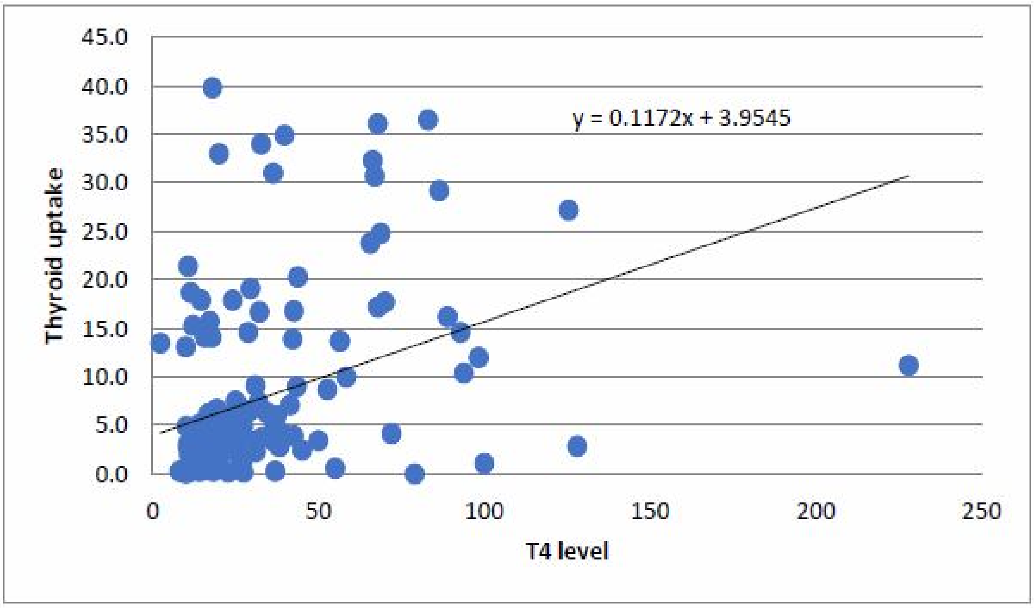
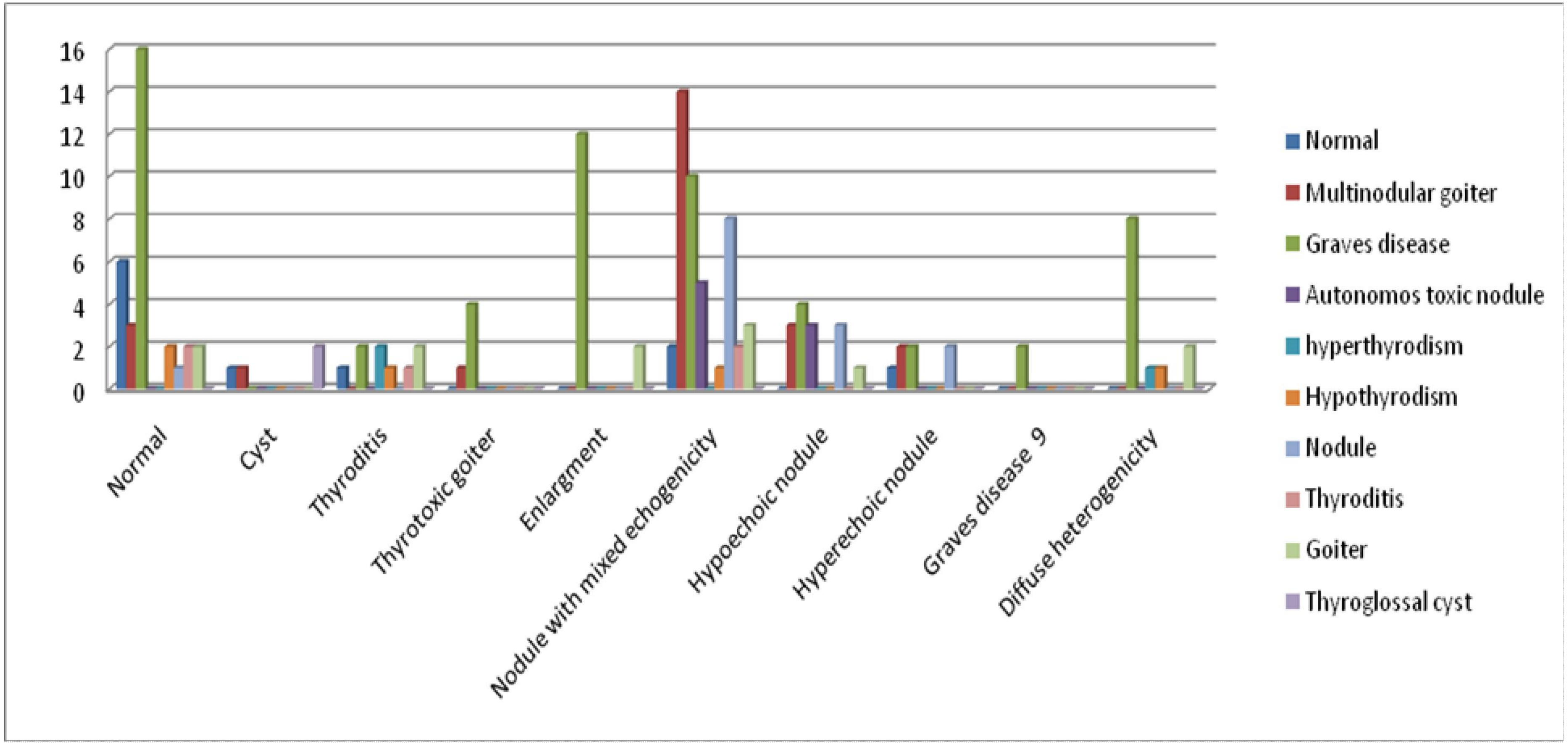


Figure 4.10 Correlation between the nuclear medicine findings with ultrasound findings



Chapter Five

Discussion, Conclusion & Recommendations

5.1 Discussion:

This study carried out to characterize the thyroid abnormalities using Doppler ultrasonography and radionuclide thyroid scintigraphy, the study sample consisted of one hundred forty four subjects referred to Nuclear Medicine and Radiology Department at King Saud hospital for thyroid scintigraphy and neck ultrasound during the period from 2016 to 2021. Doppler thyroid ultrasonography , radionuclide thyroid scintigraphy and demographic data are represented in tables and figures for this study revealed that, Regarding to table (4-1) and figure (4-1) distribution of gender for 144 patients were {111 female (77.1%), 33 male (22.9 %)}, that mean female was higher than male in this study in accordance to study done by (Tirtha Upadhyaya et al (2018)was assessed the prevalence of thyroid disorders from neck ultrasonography in relation to age, gender and disease type was performed retrospectively in Diabetes Thyroid and Endocrinology Care Center, Pokhara Nepal. Methods: Five hundred computer saved data from the Radiology Department of Diabetes Thyroid & Endocrinology Care Center from April 2017 to April 2018 were collected. Cases were reviewed for age, gender and disease type and statistical analysis was done using SPSS tool. Results: Out of 500 patients 14% were males, 86% were females).

Table (4-2) descriptive statistics for all patients were the data presented to show mean, standard deviation minimum and maximum for TSH, T4, right lobe length, right lobe width, right lobe size, right lobe volume, left lobe length, left lobe width, left lobe size ,left lobe volume and thyroid uptake. For TSH the mean ± standard deviation was 0.99 ± 2.46, for T4 was 32.22 ± 29.18, for right lobe length, right lobe width, right lobe size, right lobe volume was 5.17 ± 1.80, 3.01 ± 1.48, 15.29 ± 7.80 and 15.97 ± 14.29 respectively. For left lobe length,

left lobe width, left lobe size, left lobe volume was 4.80 ± 1.98, 2.84 ± 1.47, 14.14 ± 8.84 and 12.77 ± 11.89 respectively, for thyroid uptake was 7.73 ± 9.36.

Table (4-3) showed the group statistics for patients according to their gender. For TSH the mean ± standard deviation for female was 0.88 ± 1.89 and for male was 1.377 ± 3.82, for T4 female was 32.47 ± 31.51 and for male was 31.39 ± 19.77, for right lobe length female was 4.99 ± 1.79 and for male was 5.77 ± 1.75, right lobe width for female was 2.99 ± 1.47 and for male was 3.09 ± 1.52, right lobe size female was 14.53 ± 7.37 and for male was 17.83 ± 8.75, right lobe volume for female was 14.95 ± 12.999 and for male was 19.41 ± 17.77. For left lobe length for female was 4.55± 1.87 and for male was 5.64 ± 2.14 , left lobe width for female was 2.74 ± 1.44 and for male was 3.17 ± 153, left lobe size for female 12.71 ± 7.65 and for male was 18.92 ± 10.83, left lobe volume for female was 11.35 ± 9.97 and for male was 17.55 ± 16.10, for thyroid uptake for female was 7.43 ± 9.21 and for male was 8.74 ± 9.89.

Regard to table (4-4) showed the frequency distribution of nuclear medicine finding were the patients with graves' disease was the most frequently with 60 patients (41.7%), then the patients with multinodular goiter was 24 patients (16.7%), while the patients with Hyperthyroidism was lower frequency with 3 patients (2.1%) and the patient with thyroglossal cyst was 2 patients (1.4%).

Regard to table (4-5) showed the frequency distribution of ultrasound finding were the patients with nodule with mixed echogenicity was 45 patients (31.3%), then the patients were normal 32 cases (22.2%), while the patients with graves' disease was just 2 cases (1.4%) . Regard to table (4-6) show frequency distribution of vascularity were the patients with normal vascularity was 51 patients (35.4%),and the patients with increase vascularity were 92 (63.1%),while patients with low vascularity was just 1 patient(0.7%).

Regard to table (4-7) show the frequency distribution for background ,the patient with low background were 71 patients (49.3%), while the patients with normal was 42 patients (29.2%), and the low frequency was the patients with moderately low background were 6 patients (4.2%).

Regard to table (4-8) showed the correlation between the nuclear medicine findings with background, where the patients with graves' disease was 60 patients when correlate with background found that: 2 normal patients, one patient increase, 3 patients moderately low, 8 patients mildly low and 46 patients with low. While multinodular goiter found with 24 patients divided to: 10 normal patients, 3 increase, one patient moderately low, 2 patients mildly low, and 8 patients low

Regard to table (4-9) showed the analysis of variance grouped as nuclear medicine results were the P-value show there were significant difference between nuclear medicine results with all variables TSH, T4, Rt_lobe Length, Rt_lobe width. Rt_lobe_size, Lt_lobe Length, Lt_lobe width. Lt_lobe_size, thyroid uptake , Rt_lobe_volume and Lt _lobe_volume, were the P-value were .000, .001, .001, .000, .000, .039, .002 , .005 , .000 , .002 , .043 respectively.

Regard to table (4-10) showed the analysis of variance grouped as ultrasound results were the P- value show there was no significant difference between the ultrasound results with TSH hormone ,T4 hormone, Rt lobe width, Rt lobe size ,Lt lobe width and Lt lobe volume were the P-value with .699, .320 , .728, .323, .461 and .181 respectively, while the P-value show there was significant difference between ultrasound results with Rt lobe length , Lt lobe length , Lt lobe size , thyroid uptake and Rt lobe volume were the P- value with . 015, .033, .025 , .000 and .006 respectively.

Regard to table (4-11) show the analysis of variance for thyroid uptake with right and left lobe volume, were the p, value showed there is no significant difference between the right and left lobe with thyroid uptake were the p. value was 0.965 and 0.938 respectively as shown in table 7.

Regard to table (4-12) show that the Correlation between the nuclear medicine findings with ultrasound findings, were the sixty patients have graves' disease in nuclear medicine whereas forty five patients have Nodule with mixed echogenicity

Figure (4-2) showed the correlation between the right and left lobe width with nuclear medicine finding were the Rt lobe width were approximately larger than left lobe width in most finding except nodule , thyroiditis , goiter and thyroglossal cyst .

Figure (4-3) showed the correlation between the right and left lobe size with nuclear medicine finding were the Rt lobe size were approximately larger than left lobe size in most finding except nodule , thyroiditis , goiter and thyroglossal cyst .

Figure (4-4) showed the correlation between the right and left lobe length with nuclear medicine finding were the Rt lobe length were approximately longer than left lobe length in most finding except in nodule the left lobe was longer. Figure (4-5) showed the correlation between the right and left lobe volume with nuclear medicine finding were the Rt lobe volume were approximately larger than left lobe size in most finding.

Figure (4-6) showed the correlation between thyroid uptake with nuclear medicine finding, the figure show the patients with graves' disease had highest uptake then the patients with goiter, while the patients with hypothyroidism had lowest uptake.

Figure (4-7) showed the correlation between TSH with nuclear medicine finding, the figure show the patients with graves' disease and hyperthyroidism had lowest level of TSH, while the patients with hypothyroidism had highest level of hormones.

Figure (4-8) showed the correlation between T4 hormone with nuclear medicine finding, the figure show the patients with graves' disease had highest level of hormones then the patients with thyroditis, while the patients with hypothyroidism had lowest level.

Figure (4-9) show scatter plot between the thyroid uptake with T4 level, the figure show that there was positive correlation between thyroid uptake and thyroxin hormone level (T4) the thyroid uptake increase by 0.11count-nmol of T4 starting at 3.95 counts.

Figure (4-10) show the correlation between the nuclear medicine findings with ultrasound findings, the figure show that the highest percentage of patients have graves' disease in nuclear medicine whereas highest percentage of patients have Nodule with mixed echogenicity

5.2 Conclusion

Characterize the thyroid gland using Doppler Ultrasonography and Thyroid Scintigraphy at ultrasound department at King Saud Medial Center (KSMC) in Saudi Arabia. The total number of patients was 144 where the males was 33 with percent 22.9 and the number of females was 111 with percent 77.1. The group statistics for patients according to their gender.

Analysis of variance for thyroid uptake with other variables, where the p.value show no significant difference between the thyroid uptake with right lobe length, right lobe width, right lobe size, right lobe volume and left lobe volume were the p.value was 0.550, 0.105, 0.992, 0.965 and 0.938 respectively. While show significant difference between the thyroid uptake with left lobe length, left lobe width and left lobe size were the p.value was 0.047, 0.000 and 0.004 respectively. Correlation between the thyroid uptake with t4 hormone were the rate of change for thyroid uptake increase by 0.1172 with each value for T4 hormone.

And between the thyroid uptake with right and left lobe volume, were the p,value showed there is no significant difference between the right and left lobe with thyroid uptake were the p.value was 0.965 and 0.938 respectively.

5.3 Recommendation:

- Radionuclide imaging is not wide available, expensive and poses limitations due to ionizing radiation, so it is recommended that ultrasound to be used as the primary image modality in initial evaluation of thyroid disorders.
- Another study can be done with large sample size for precise and accurate result.
- Correlate between the thyroid hormones with other nuclear medicine procedures will be better.
- The researcher can study the relation between the hormones level with for thyroid with the descriptive treatment and measure the hormone level many times.

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Appendix (1)

Data collection sheet

Sudan University of Science and Technology

Collage of Graduate studies

Ph.D. of Nuclear Medicine Technology

Characterization of thyroid disorders Using Doppler Ultrasonography and Thyroid uptake scan

Patient Name: ……………………………………………………

Gender:

- Male
- Female

Clinical status :

- Normal
- Hyperthyroidism
- Hypothyroidism
- Others (Specify)……………………………………………...

Copy of thyroid function test (TFT) results

- TSH………………………………
- T4…………………………………

Copy of Doppler Ultrasound report ……………………………………

Copy of Thyroid Scintigraphy report…………………………………..

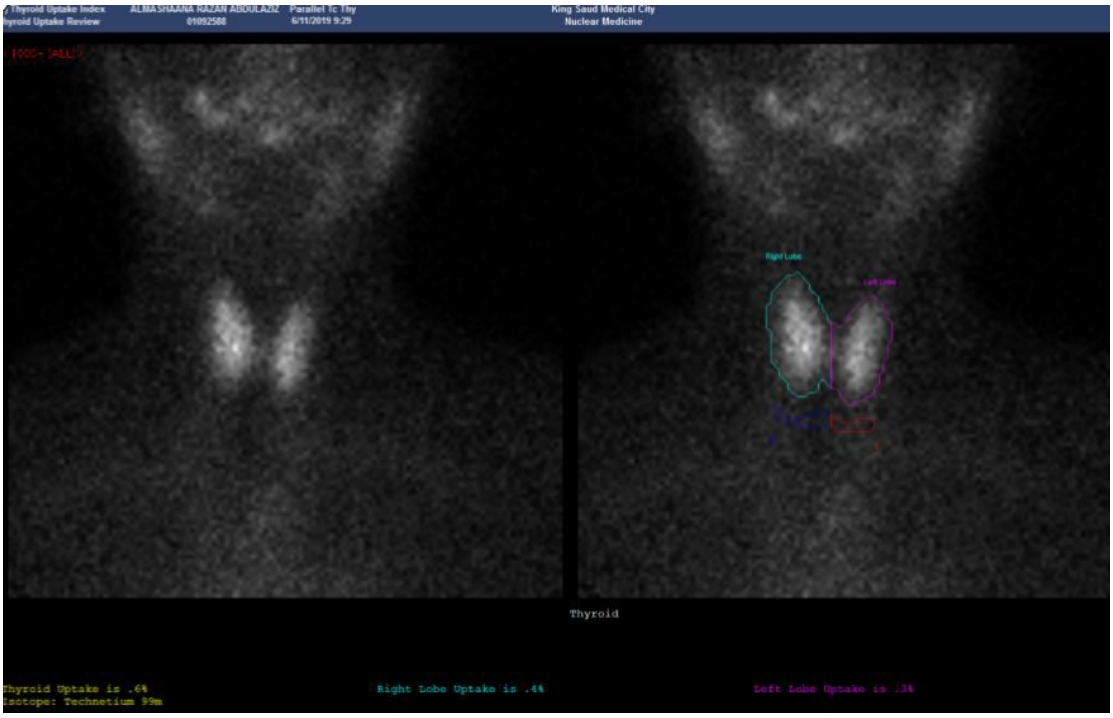
Copy of Doppler Ultrasound scan ……………………………………..

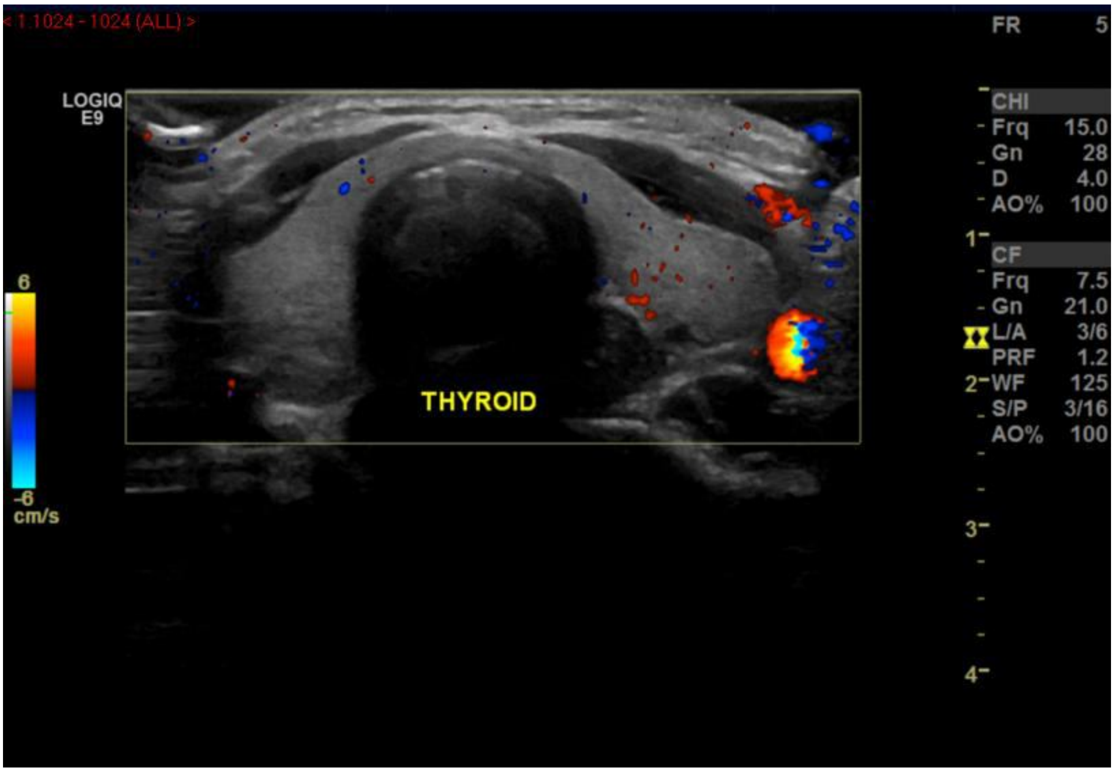
Copy of Thyroid Scintigraphy scan ……………………………………

Copy of thyroid function test (TFT) result ……………………………..

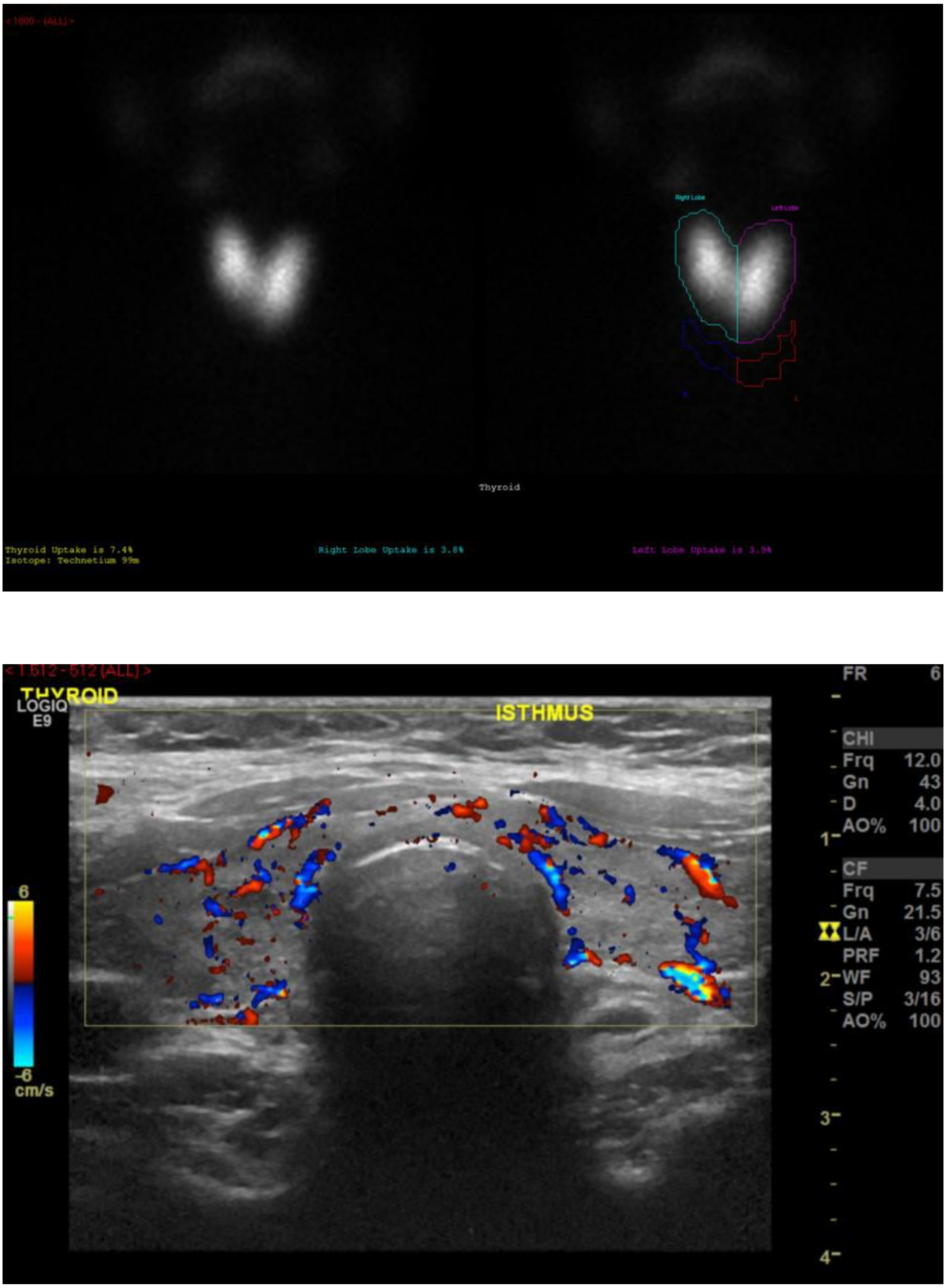
Comment……………………………………..…………………

Appendix(2)

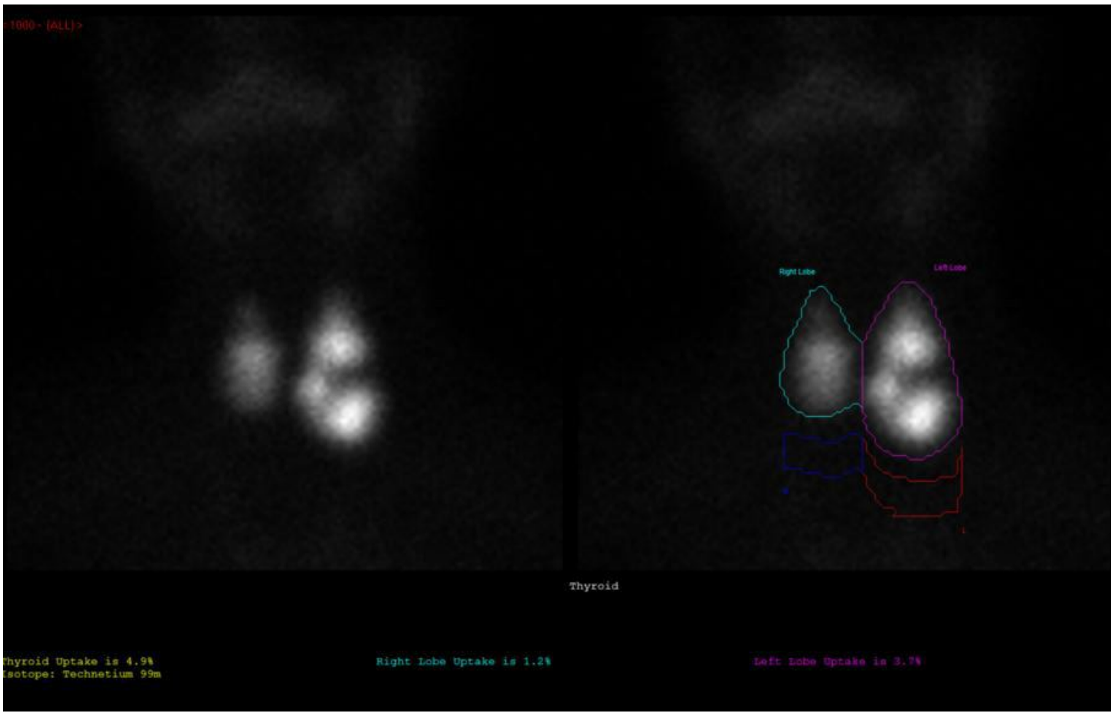


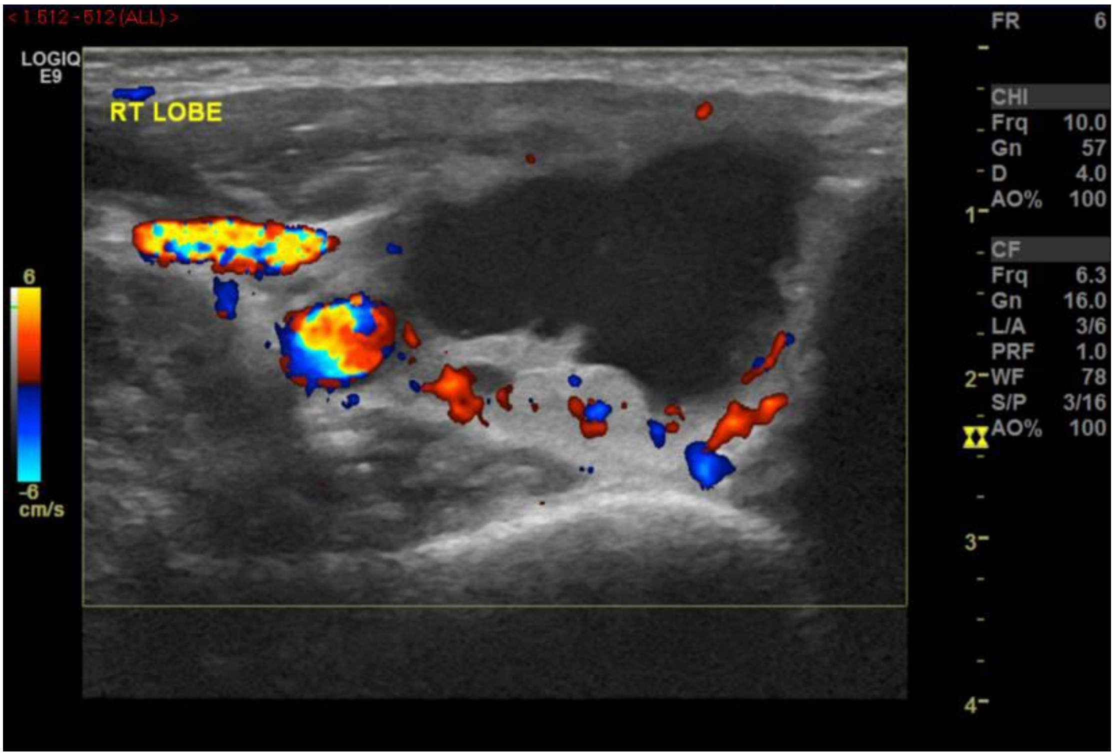


Normal patient in scintigraphy with cyst in ultrasound scan

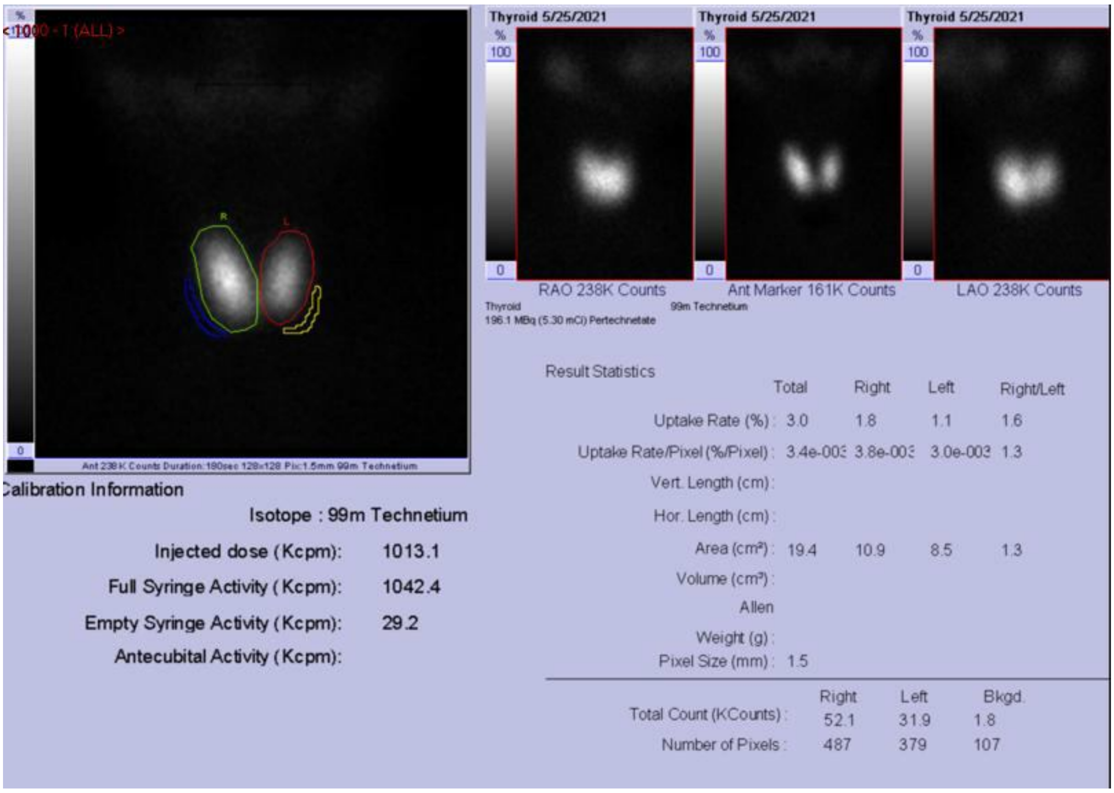


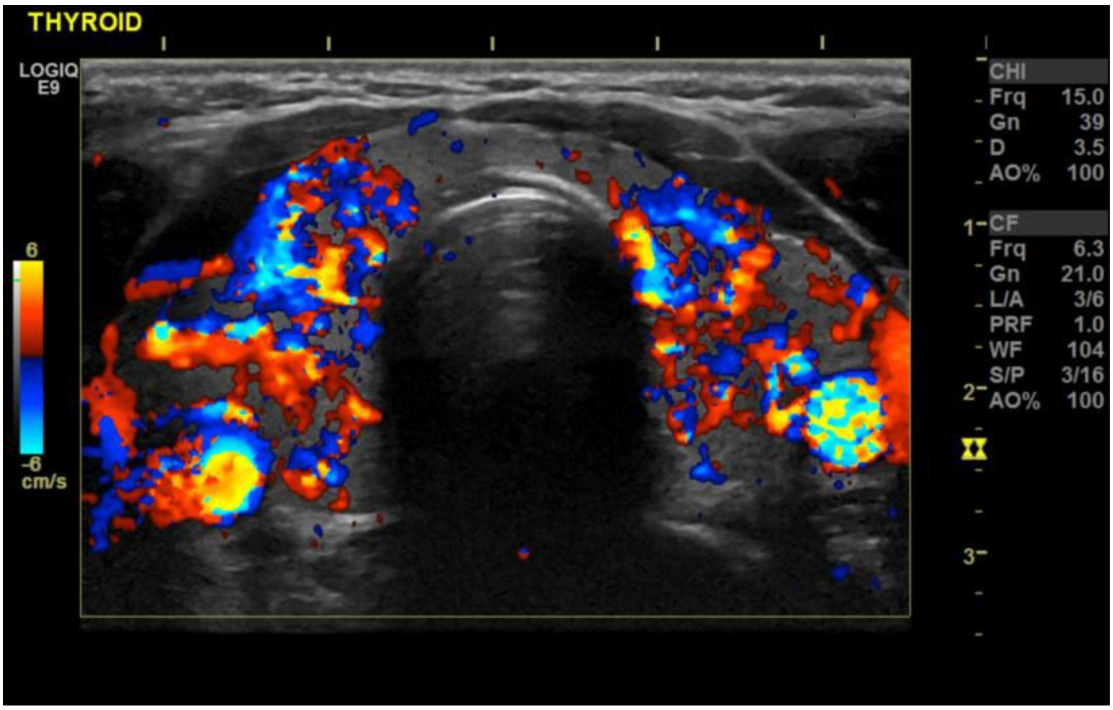
Graves disease patient in scintigraphy with diffuse heterogenicity in ultrasound scan



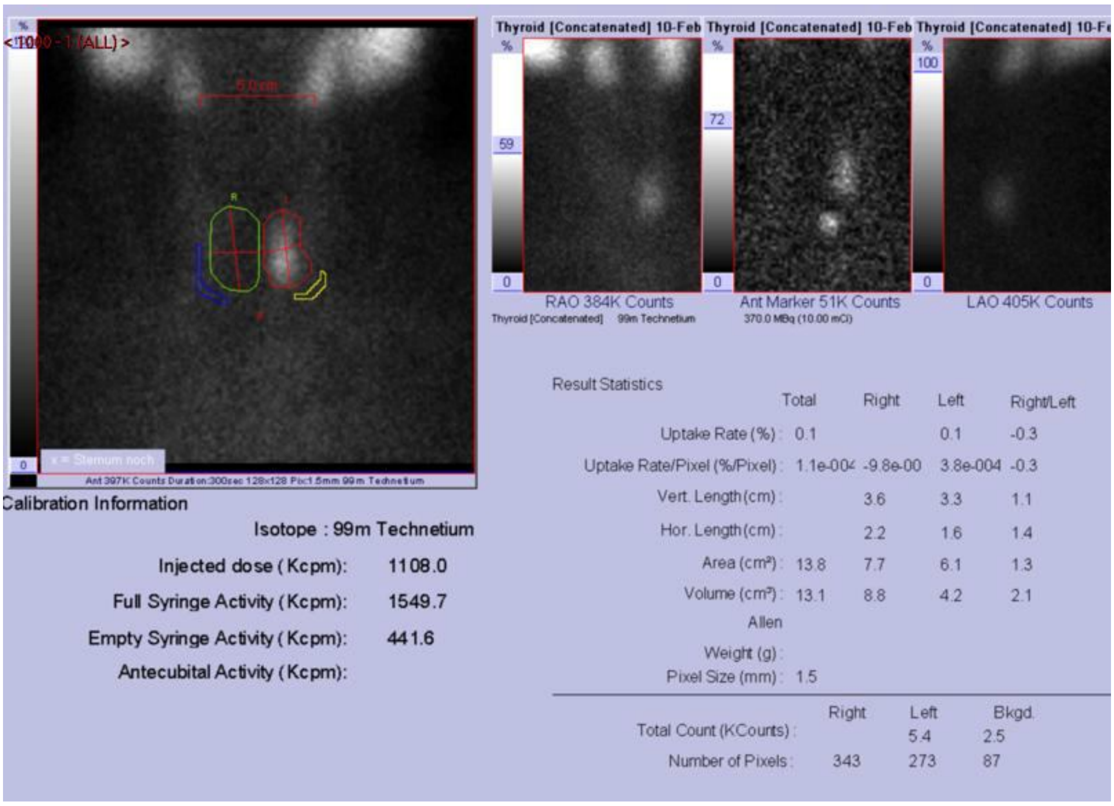


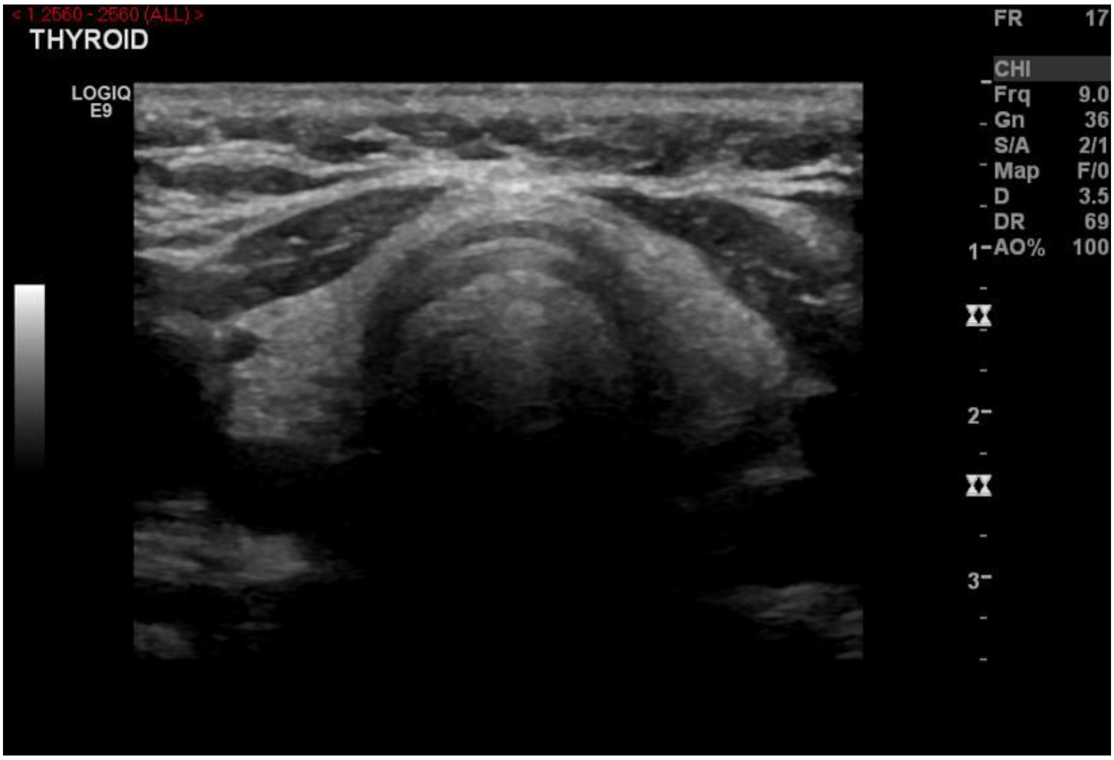
Multinodular goitre in scintigraphy with nodule with mixed echogenicity in ultrasound scan



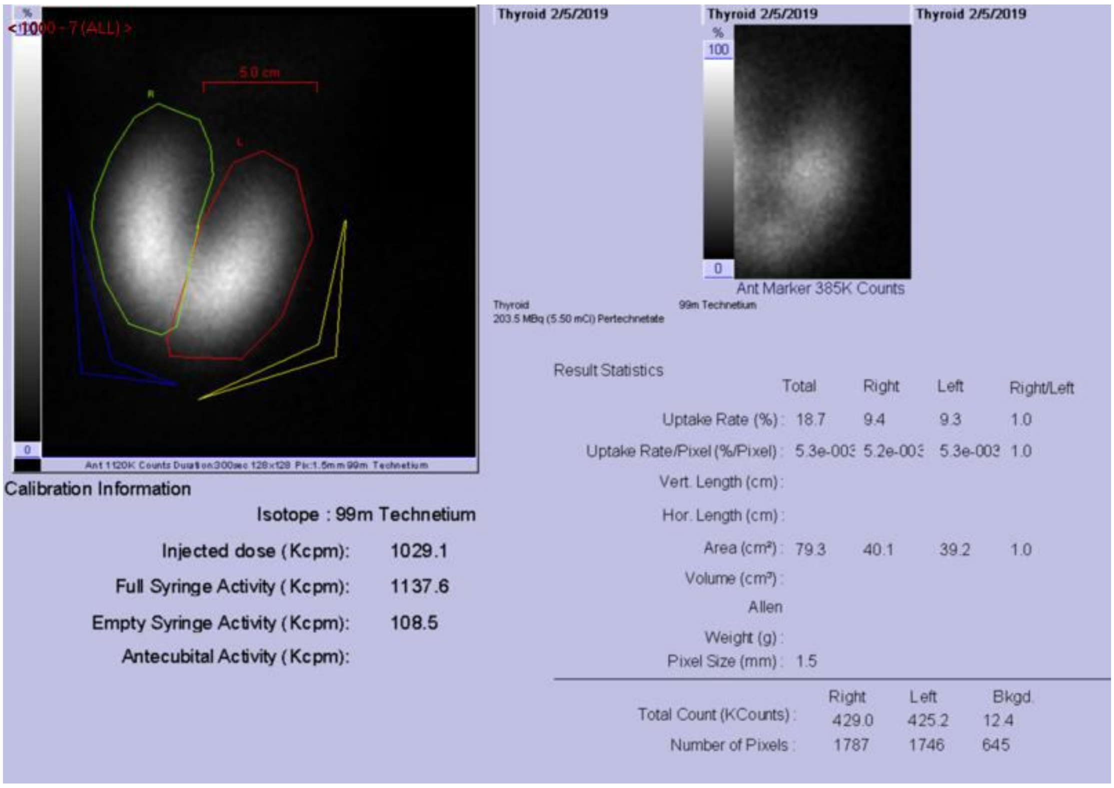


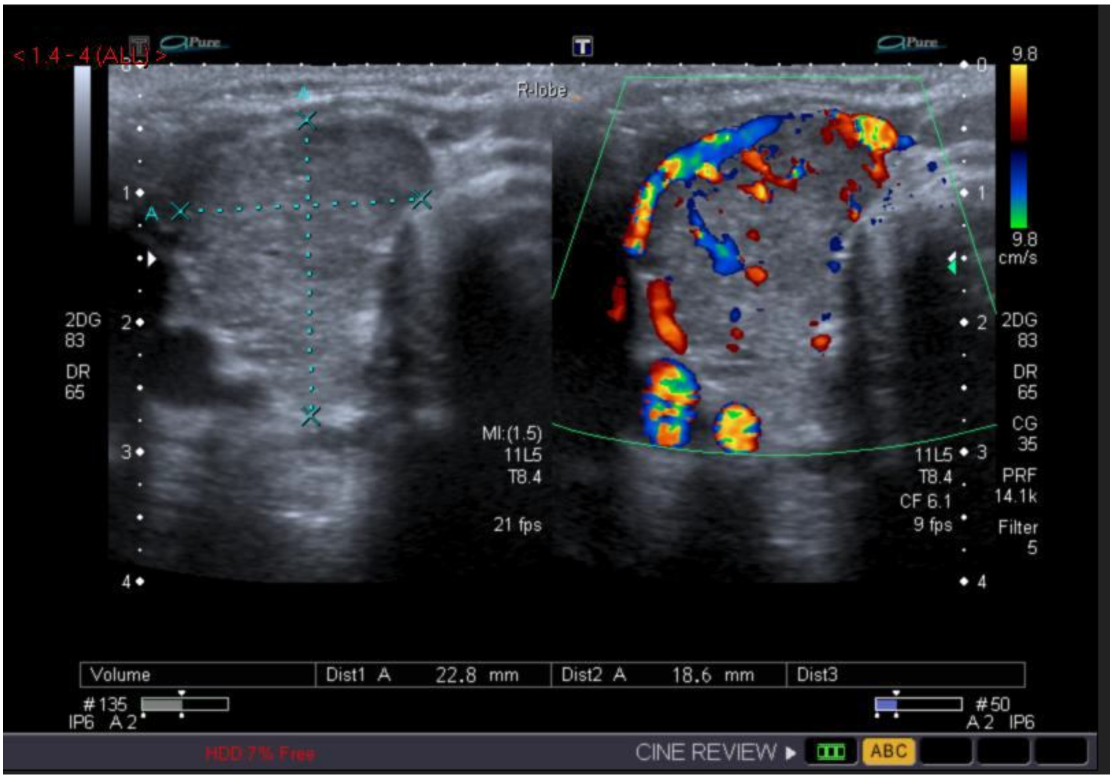
Hyperthyroidism patient in scintigraphy with thyroiditis in ultrasound scan





Hypothyroidism patient in scintigraphy with diffuse heterogenicity in ultrasound scan





Graves' disease patient in scintigraphy with graves' disease in ultra sound scan

Appendix (3)

Kingdom of Saudi Arabia
Ministry of Health
King Saud Medical City

مدينة الملك سعود الطبية
KING SAUD MEDICAL CITY

المملكة العربية السعودية
وزارة الصحة
مدينة الملك سعود الطبية

IRB Registration Number with KACST, KSA: ***H-01-R-053***
IRB Registration Number U.S. Department of HHS IORG #: ***IORG0010374***

- Memorandum -

Date: April 22, 2021

Proposal Reference No.	: **H1RE-11-Apr21-03**
Proposal Title	: "Characterization of thyroid disorders using Doppler Color Ultrasonography & thyroid Scintigraphy"
PI	: Ms. Reham Mohamed Taha
Co-Investigators	: Ali Aamry; Mohamed Elfadel Gar Elnabi
Type of Review	: Modification
Category of Approval	: Exempt
Date of IRB Approval-Expiration (Validity)	: 22/04/2021 21/04/2022 (12 months)

Dear Ms. Reham Mohamed Taha:

We are pleased to inform you that the above-referenced research proposal has been reviewed and was approval. The Institutional Review Board (IRB) committee found that the research met the applicability criteria and was eligible for exempt review. However, to commence the collection of data a permission letter must be issued from the Director of the Research Center first.

This approval is valid for **12 months** from the date of IRB review when approval is granted. The approval will no longer be in effect on the date listed above as the IRB expiration date. Please note that you are obligated to submit the following to IRB committee:

1. progress/final report on the **12 months (21-Apr-2022)** (or earlier in the case the study has completed)
2. any manuscript resulting from this research for approval by IRB before submission to journals for publication.

The approval of the conduct of this proposal will be automatically suspended after 12 months, in the case the Progress Report (or Final Report, if relevant) is pending acceptance. You also need to notify the Research Centre as soon as possible in case of:

1. any amendments to the proposal;
2. termination of the study;
3. any serious or unexpected adverse events;
4. any event or new information that may affect the benefit/risk ratio of the proposal.

All records relating to the research including consent form must be retained and available for audit for at least 3 years after the research has ended.

We wish you every success in your research endeavors.

Dr. Faisal Almutairi
Chairman, Institutional Review Board (IRB)
King Saud Medical City Riyadh, KSA

وزارة الصحة المملكة العربية السعودية
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