Chapter one
Introduction

Thyroid gland is the largest exclusively endocrine gland in the body; it is butterfly shaped and sits, in front of the upper part of the trachea in the anterior neck. It is comprised of two lobes connected in the middle by an isthmus. The thyroid's job is to make thyroid hormones (tetraiodothyronine or T4 and tri-odothyronine or T3), which are secreted into the blood and then carried to every tissue in the body. Thyroid hormone helps the body use energy, stay warm and keep the brain, heart, muscles, and other organs working as they should (Gray H, Lewis WH, 2000).

The term thyroid nodule refers to an abnormal growth of thyroid cells that forms a lump within the thyroid gland. Although the vast majority of thyroid nodules are benign (noncancerous), a small proportion of thyroid nodules contains thyroid cancer. In order to diagnose and treat thyroid cancer at the earliest stage, most thyroid nodules need some type of evaluation (H. J. Baskin and D. S. Duick,2006).

Thyroid ultrasound is a key tool for thyroid nodule evaluation. It uses high-frequency sound waves to obtain a picture of the thyroid. This very accurate test can easily determine if a nodule is solid or fluid filled (cystic), and it can determine the precise size of the nodule. Ultrasound can help identify suspicious nodules since some ultrasound characteristics of thyroid nodules are more frequent in thyroid cancer than in noncancerous nodules (S. Bastin, et al, 2009).

Thyroid ultrasound can identify nodules that are too small to feel during a physical examination. Ultrasound can also be used to accurately guide a needle directly into a nodule when the doctor thinks a fine needle biopsy is needed (J. R. Wienke, et al, 2003).

Once the initial evaluation is completed, thyroid ultrasound can be used to keep an eye on thyroid nodules that do not require surgery to determine if they are growing or shrinking over time. The ultrasound is a painless test which many doctors may be able to perform in their own office (J. D. Iannuccilli, et al, 2004).

A fine needle biopsy (FNA or FNAB) of a thyroid nodule may sound frightening, but the needle used is very small and a local anesthetic may not even be necessary. This simple procedure is often done in the doctor's office. Sometimes, medications like blood thinners may need to be stopped for a few days before to the procedure. Otherwise, the biopsy does not usually require any other special preparation (no fasting). Patients typically return home or to work after the biopsy without even needing a bandaid! For a fine needle biopsy, the doctor uses a very thin needle to withdraw cells from the thyroid nodule (Nguyen GK, et al. 2005).

Ordinarily, several samples will be taken from different parts of the nodule to give your doctor the best chance of finding cancerous cells if they are present. The cells are then examined under a microscope by a pathologist (Frates MC, et al. 2003).

Imaging has long been established as an essential element in the workup of clinically suspected lesions of the thyroid gland. Ultrasonography (US) is the modality of choice for initial characterization of a thyroid nodule (1). Although thyroid nodules may be detected at computed tomography (CT) and magnetic resonance (MR) imaging, these modalities are not useful for characterization of a nodule. Positron emission tomography (PET) may occasionally help identify thyroid nodules, but it is considered by some authors to have limited utility in differentiating benign from malignant lesions.

There are several recently published guidelines for determining whether a nodule should undergo US-guided fine-needle aspiration biopsy (FNAB) on the basis of its US and clinical features (Cesur M, et al. 2006). These guidelines were published by (among others) the Society of Radiologists in Ultrasound (2005), the American Thyroid Association (2009), the American Association of Clinical Endocrinologists/Associazione, Endocrinologi /European Thyroid Association (2010), and the National Comprehensive Cancer Network (updated in 2013). In this study, we discuss the imaging appearance by ultrasound of thyroid nodules, current indications for thyroid FNAB and proper US-guided FNAB technique. The purpose of this study is to compare the cytological results of ultrasound-guided fine-needle aspiration (US-FNA) cytology of thyroid nodules to sonographic findings and determine whether US findings are helpful in the interpretation of cytological l results (Khalid AN, et al. 2006).

1-1 Problem of the study:

Thyroid most of the time encountered problem mostly due to iodine deficiency or stimulus hormones problems. Nodules in thyroid could be malignant therefore assessment of nodules mostly carried out by nuclear medicine imaging, with it is drawback like radiation hazard this is mostly followed by needle biopsy. Ultrasound might solve the problem associated with nuclear medicine as well as needle biopsy where only suspicious cases can be referred to needle biopsy.

1-2 Objectives of the study:

The general objective of this study was to evaluate the thyroid nodules using ultrasound and FNA biopsy result.

Specific Objectives of the study

1. To find the sonographic characteristics of benign and malignant thyroid nodules.
2. To cross-correlate biopsy result with ultrasound imaging findings.
3. To find the accuracy, sensitivity and specificity of ultrasound.

1-3 Significant of the study

This study will provide sonographic characteristics of benign and malignant nodules which help in allocating the potential candidate for needle biopsy; and therefore save patient with benign nodules from unnecessary trauma and other types of examinations; which might have some risk.

1-4 Overview of the study

This study consisted of five chapters with chapter one is an introduction which include overview of the thyroid context, problem of the study, objectives and overview. Chapter two include background and literature review (previous study) while chapter three include material and method used for data collection and analysis. Chapter four presents the result of the study in graphs and tables and finally chapter five includes the discussion, conclusion, recommendation and references.

Chapter two
Background and Literature

2-1 Thyroid gland Anatomy:

2-1-1 Shape and Location:

The thyroid is a butterfly-shaped endocrine gland located within the lower neck and is draped anteriorly around the trachea (Fig 1). The left and right lobes are located immediately to the left and right of the trachea, respectively, and are connected anteriorly by a thin rim of thyroid tissue known as the isthmus. The internal carotid arteries and internal jugular veins are located posterolateral to the thyroid lobes, whereas the strap muscles of the neck are located anteriorly (Kim EK,et al,2002). The thyroid gland is located adjacent to the cranial trachea close to the recurrent laryngeal nerve, carotid sheath and sternohyoid and sternothyroid muscles. The Parathyroid Glands are located dorsally to, or within the thyroid gland itself (Papini E, et al,2004).

2-1-2 Blood Supply:

The thyroid gland is supplied by the cranial thyroid artery which is a branch of the common carotid artery. A subsidiary supply is provided by the caudal thyroid artery. The cranial and caudal thyroid arteries are united by substantial anastamoses along their caudal edge. Venous drainage is provided by the internal jugular vein and lymph drains into the cranial deep cervical nodes. (Papini E, et al,2004)

2-1-3 Ultrastructure and Histology:

The gland consists of varying sized follicles, which are bounded by a single layer of cuboidal epithelial cells (follicular cells} and a basement membrane, urrounding a central lumen filled with a homogenous protein rich colloid (thyrogloblin). The apical surface of the cell membranes is covered with numerous micovilli to increase surface area. The follicular cells are connected by tight junctions, and have a dense capillary network. The colloid is a store of thyroid hormones prior to secretion. The thyroid gland is the only endocrine gland to store its hormone in large quantities. In the active gland colloid is diminished and epithelial cells are tall and columnar. Within the connective tissue close to the follicles are C-cells alternatively known as parafollicular cells. They are found in clusters in the interfollicular space and are also known as clear cells as their cytoplasm doesn't stain with H and E. They secrete calcitonin, a hormone which acts to lower plasma Ca^{2+} levels. (Peccin S, et al. 2005)

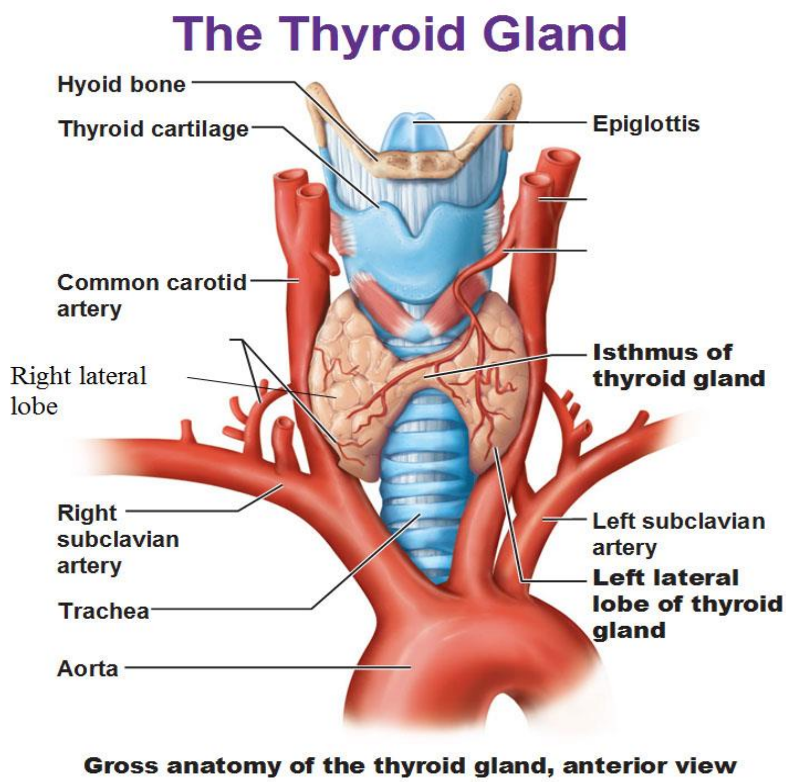

Figure 2-1 : An anterior view showing the gross anatomy of the thyroid gland and adjacent structures.

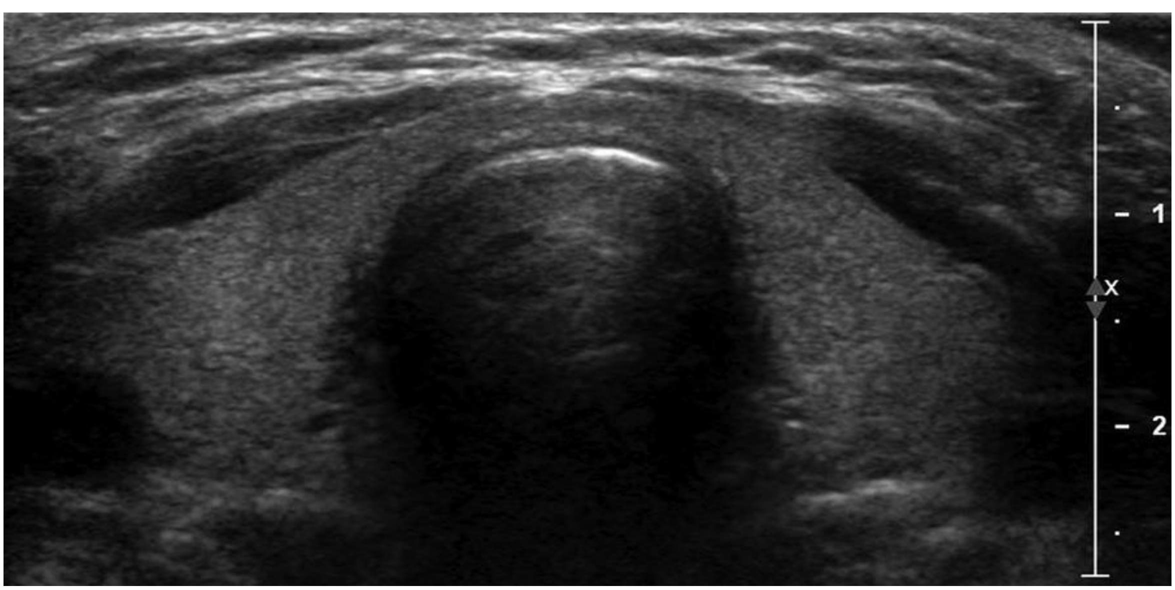

Figure 2-2: Transverse US image shows the homogeneous echogenicity of the normal thyroid tissue and the normal thickness of the isthmus.

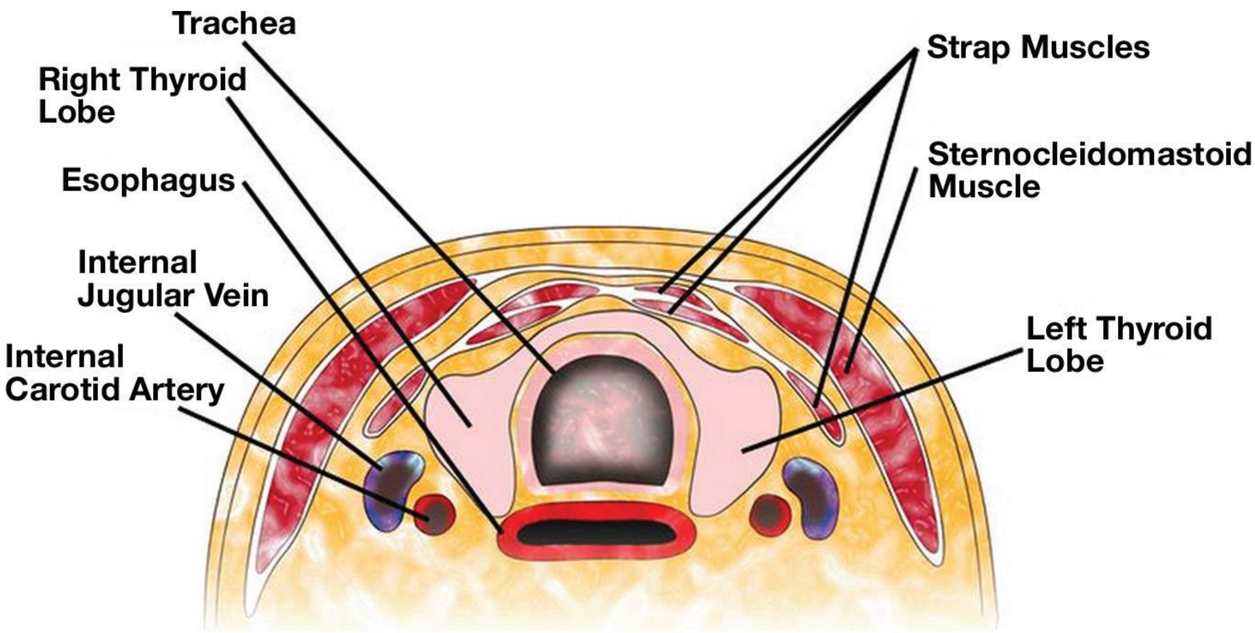

Figure2- 3: Drawing illustrates the cross-sectional anatomy of the thyroid and adjacent soft tissue structures.

2-2 Thyroid gland Physiology:

The thyroid is the largest exclusively endocrine gland in the body. The endocrine system is the body's communication hub, controlling cell, and therefore organ, function. A primary goal of the endocrine system is to maintain homeostasis within the organism, despite external fluctuations of any sort. Hormones, which act as chemical messengers, are the mechanism for this communication. The two types of hormones secreted by the thyroid gland which are the iodine containing hormones; tri-iodothyronine(T3) and thyroxine (T4), are essential in this process, targeting almost every cell in the body (only the adult brain, spleen, testes, and uterus are immune to their effects.) Inside cells, thyroid hormone stimulates enzymes involved with glucose oxidation, thereby controlling cellular temperature and metabolism of proteins, carbohydrates, and lipids. Through these actions, the thyroid regulates the body's metabolic rate and heat production. Thyroid hormone also raises the number of adrenergic receptors in blood vessels, thus playing a major role in the regulation of blood pressure. In addition, it promotes tissue growth, and is particularly vital in skeletal, nervous system, and reproductive development (Frates MC, et al. (2004).

Follicular cells synthesize thyroglobulin in their golgi apparatus. This is a glycoprotein consisting of 70 linked tyrosine molecules, 10% of which are iodinated, and is stored in the colloid (Peccin S, et al. 2005).

The thyroglobulin is then split to form the two amino acid derivative hormones produced in the thyroid gland which are triiodothyronine (T3) and thyroxine (T4). Thyroxine contains 4 iodine atoms, triiodothyronine contains 3. Creation of these two hormones is the only role of iodine in the body ((Peccin S, et al. 2005).

The majority (90%) of hormone produced by the follicular cells is T4. T4 can only be made in the thyroid gland. It can then be converted by other tissues into T3.

2-2-1 Iodine Uptake

Iodine circulates within the blood as iodide (I-). It is actively transported into the follicular cells by an Na+/I- symport in the basal membrane. This pump concentrates iodine in the colloid at a level up to 250x greater than the plasma level. This process is known as iodide trapping. The pump is activated by thyroid stimulating hormone (TSH) a hormone from the pituitary gland (Cesur M, et al. (2006).

2-2-2 Secretion of Thyroid Hormones

Colloid uptake into the follicular cells takes place by endocytosis. The intracellular vesicles containing the colloid then fuse with lysosomes, where enzymes split the thyroglobulin into T3 and T4. The hormones diffuse across the basal plasma membrane into the interstitium (they are lipid soluble hormones) (Cesur M, et al. (2006).

2-2-3 Transport

Thyroid hormones are lipid soluble, thus need a transporting protein in order to travel in the blood. Half-life in the blood is 1 day for T3, 6 days for T4. 99% of thyroid hormones in circulation are bound. The primary transport protein for thyroid hormones is thyroid binding globulin (TBG). Synthesized in the liver, this protein binds 70-80% of the circulating thyroid hormones. The remainder are carried by thyroxine-binding prealbumin or albumin (Frates MC, et al. (2004).

2-2-4 Degradation

Only free T3 and free T4 can enter cells to exert their actions. T4 is deiodinated to T3 in many cells of the body, particularly the liver and kidneys. The thyroid secretes 90% T4, with 50% of this being deiodinated to T3. The remainder is converted to reverse T3 (rT3). This is an inactive form of T3, and so creation of it is a regulatory mechanism. More rT3 is created when the body needs to reduce the action of T3 and T4. The hormones are further deiodinated to diiodothyronine and monoiodothyronine in the liver and kidneys. Iodine is recycled or excreted in the urine (Frates MC, et al. (2004).

2-2-5 Regulation

The hypothalamus releases thyrotropin releasing hormone (TRH) which stimulates the adenohypophysis (anterior pituitary gland) to release thyroid stimulating hormone (TSH). This water soluble hormone travels in the blood to activate the thyroid gland by 5 actions: Increased endocytosis and proteolysis of thyroglobulin from colloid, increased activity of the Na+/I- symport, increased iodination of tyrosine, increased size and secretory activity of thyroid follicular cells and ncreased number of follicular cells (Peccin S, et al. 2005).

2-2-6 Thyroid Hormone Actions

T3 and T4 have effects on all body systems and at all stages of life. These include: Development where thyroid hormones are vital during the fetal period and the first few months after birth. Thyroid hormones also promote growth as they enhance amino acid uptake by tissues and enzymatic systems involved in protein synthesis thus promoting bone growth. They also help with metabolic actions such as carbohydrate metabolism, as thyroid hormones stimulate glucose uptake, glycogenolysis, gluconeogenesis. In fat metabolism they mobilise lipids from adipose stores and accelerate oxidation of lipids to produce energy (occurs within mitochondria), as well as increasing the size and number of mitochondria. Thyroid hormones also increase basal metabolic rate (BMR) in all tissues except brain, spleen and gonads. The results in increased heat production, increased oxygen consumption. This increased metabolic rate also results in increased utilisation of energy substrates causing weight loss. Some of thyroid hormones cardiovascular actions are to increase cardiac output, heart rate and contractility. They affect the respiratory system indirectly through increased BMR causing increased demand for oxygen and increased excretion of carbon dioxide. In the nervous system thyroid hormones are required for myelination of neurons during the development. They also enhance the sympathetic nervous system (by increasing epinephrine receptors). Reproductive system is affected by reduced levels of thyroid hormone causing irregular cycling and decreased libido. Finally, in the alimentary system, thyroid hormone increases appetite and feed intake, increases secretion of pancreatic enzymes and increases motility (Bellantone R, et al.2004).

2-3 Thyroid gland Pathology:

The thyroid gland is prone to several very distinct problems, some of which are extremely common. These problems can be broken down into those concerning the production of hormone (too much, or too little), those due to increased growth of the thyroid, causing compression of important neck structures or simply appearing as a mass in the neck, the formation of nodules or lumps within the thyroid which are worrisome for the presence of thyroid cancer, and those which are cancerous. Each thyroid topic is addressed separately and illustrated with actual patient x-rays and pictures to make them easier to understand. The information on this web site is arranged to give you more detailed and complex information as you read further.

Goiters: thyroid goiter is a dramatic enlargement of the thyroid gland. Goiters are often removed because of cosmetic reasons or, more commonly, because they compress other vital structures of the neck including the trachea and the esophagus making breathing and swallowing difficult. Sometimes goiters will actually grow into the chest where they can cause trouble as well (Cai XJ, et al. (2006).

Hyperthyroidism: hyperthyroidism means too much thyroid hormone. Current methods used for treating a hyperthyroid patient are radioactive iodine, anti-thyroid drugs, or surgery. Each method has advantages and disadvantages and is selected for individual patients. Many times the situation will suggest that all three methods are appropriate, while other circumstances will dictate a single best therapeutic option. Surgery is the least common treatment selected for hyperthyroidism (Cai XJ, et al. (2006).

Hypothyroidism**:** hypothyroidism means too little thyroid hormone and is a common problem. In fact, hypothyroidism is often present for a number of years before it is recognized and treated. Hypothyroidism can even be associated with pregnancy. Treatment for all types of hypothyroidism is usually straightforward.

Thyroiditis: thyroiditis is an inflammatory process ongoing within the thyroid gland. Thyroiditis can present with a number of symptoms such as fever and pain, but it can also present as subtle findings of hypo or hyper-thyroidism (Cai XJ, et al. (2006).

Thyroid nodules**:** thyroid nodules are lumps that commonly arise within an otherwise normal thyroid gland. Often these abnormal growths of thyroid tissue are located at the edge of the thyroid gland, so they can be felt as a lump in the throat. When they are large or when they occur in very thin individuals, they can even sometimes be seen as a lump in the front of the neck. Thyroid nodules increase with age and are present in almost 10% of the adult population. Autopsy studies reveal the presence of thyroid nodules in 50% of the population, so they are fairly common. 95% of solitary thyroid nodules are benign, and therefore, only 5% of thyroid nodules are malignant. The common types of the benign thyroid nodules are adenomas (overgrowths of normal thyroid tissue), thyroid cysts, and Hashimoto's thyroiditis. Uncommon types of benign thyroid nodules are due to subacute thyroiditis, painless thyroiditis, unilateral lobe agenesis, or Riedel's struma (Wu HH, Jones JN, 2006).

The following is a list of facts regarding thyroid nodules:

- One in 12 to 15 young women has a thyroid nodule.
- One in 40 young men has a thyroid nodule.
- More than 95% of all thyroid nodules are benign (non-cancerous).
- Some are actually cysts, which are filled with fluid rather than thyroid tissue.
- Most people will develop a thyroid nodule by the time they are 50 years old.
- The incidence of thyroid nodules increases with age.
- 50% of 50 year olds will have at least one thyroid nodule.
- 60% of 60 year olds will have at least one thyroid nodule.
- 70% of 70 year olds will have at least one thyroid nodule.

The Following Features Favor a Benign Thyroid Nodule:

- Family history of Hashimoto's thyroiditis
- Family history of benign thyroid nodule or goiter
- Symptoms of hyperthyroidism or hypothyroidism
- Pain or tenderness associated with a nodule
- A soft, smooth, mobile nodule
- Multi-nodular goiter without a predominant nodule (lots of nodules, not one main nodule)
- "Warm" nodule on thyroid scan (produces normal amount of hormone)
- Simple cyst on an ultrasound

The Following Features Increase the Suspicion of a Malignant Nodule:

- Age less than 20
- Age greater than 70
- Male gender
- New onset of swallowing difficulties
- New onset of hoarseness
- History of external neck irradiation during childhood
- Firm, irregular, and fixed nodule
- Presence of cervical lymphadenopathy (swollen, hard lymph nodes in the neck)
- Previous history of thyroid cancer
- Nodule that is "cold" on scan (shown in picture above, meaning the nodule does not make hormone)
- Solid or complex on an ultrasound

Usually a fine needle aspiration biopsy (FNA) will tell if the nodule is cancerous or benign. This one test can get right to the bottom of the issue. Often an ultrasound is necessary to determine the characteristics of a thyroid nodule.

Solitary Thyroid Nodule: there are several characteristics of solitary nodules of the thyroid which make them suspicious for malignancy. Although as many as 50% of the population will have a nodule somewhere in their thyroid, the overwhelming majority of these are benign. Occasionally, thyroid nodules can take on characteristics of malignancy and require either a needle biopsy or surgical excision (Wu HH, Jones JN, 2006).

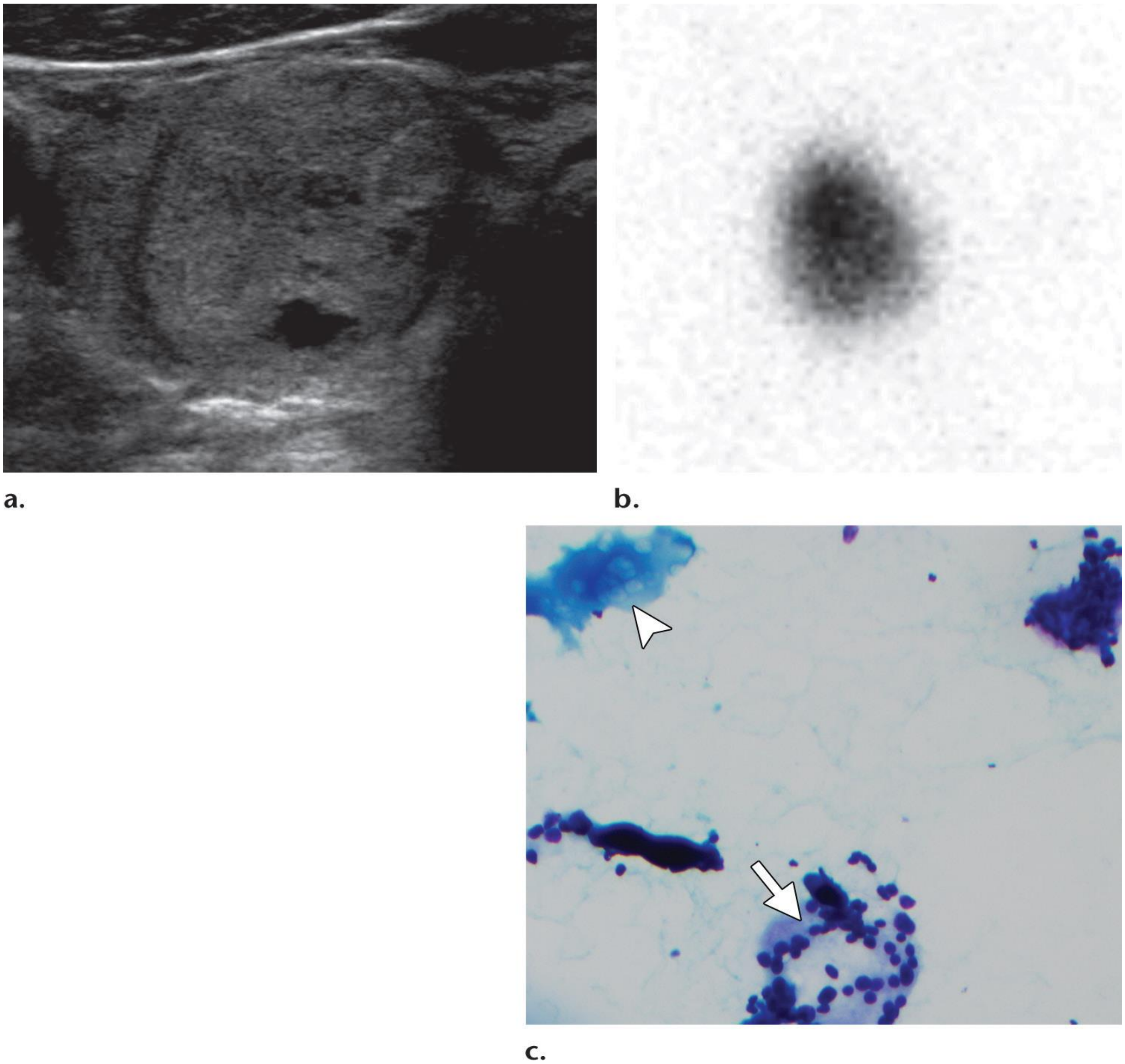

Figure 2-4: Adenomatous nodule in a 66-year-old man (a) Transverse US image shows a predominantly solid 2.4-cm nodule with well-circumscribed margins and a surrounding halo (benign US features). b) Scintigraphic image obtained with 123I shows increased uptake in a hot nodule and relative photopenia of the adjacent normal thyroid tissue. The outline of the neck is not well visualized. (c) Photomicrograph of an FNAB specimen demonstrates an adenomatous nodule. Features include groups and sheets of bland follicular cells without significant crowding (arrow), with colloid in the background (arrowhead).

***Thyroid Cancer*:** thyroid cancer is a fairly common malignancy, however, the vast majority have excellent long term survival. According to the National Cancer Institute, there are about 56,000 new cases of thyroid cancer in the US each year, and the majority of those diagnoses are papillary thyroid cancer—the most common type of thyroid cancer. Females are more likely to have thyroid cancer at a ratio of 3:1. Thyroid cancer can occur in any age group, although it is most common after age 30, and its aggressiveness increases significantly in older patients. Thyroid cancer does not always cause symptoms; often, the first sign of thyroid cancer is a thyroid nodule. (Bellantone R, et al.2004).

Thyroid cancer types and incidences:

There are 4 main types of thyroid cancer, and some are more common than others.

- Papillary and/or mixed papillary/follicular thyroid cancer: ~ 80%
- Follicular and/or Hurthle cell thyroid cancer: ~ 15%
- Medullary thyroid cancer: ~ 3%
- Anaplastic thyroid cancer: ~ 2%

Most thyroid cancers are very curable. In fact, the most common types of thyroid cancer (papillary and follicular thyroid cancer) are the most curable. In younger patients, both papillary and follicular cancers have a more than 97% cure rate if treated appropriately. Both papillary and follicular thyroid cancers are typically treated with complete removal of the lobe of the thyroid that harbors the cancer, in addition to the removal of most or all of the other side. Medullary thyroid cancer is significantly less common but has a worse prognosis. Medullary cancers tend to spread to large numbers of lymph nodes very early on, and therefore require a much more aggressive operation than the more localized thyroid cancers, such as papillary and follicular thyroid cancer. The least common type of thyroid cancer is anaplastic thyroid cancer, which has a very poor prognosis. Anaplastic thyroid cancer tends to be found after it has spread, and it is incurable in most cases. (Bellantone R, et al.2004).

2-4 Ultrasound

2-4-1 Basic physics Instrumentation of ultrasound:

Diagnostic ultrasound employs pulsed, high frequency sound waves that are reflected back from body tissues and processed by ultrasound machine to create characteristic images. Ultrasound is a form of mechanical energy which passes in wave form like sound waves and having a frequency wavesthe same type of wave as detected by the human ear, except the frequency is higher. Ultrasonic imaging uses frequencies in the range from 1 to 20 Mhz at powers from 0.01 to 200 mW/cm2. (Oak Brook, IL, et.al, 2000)

The ultrasound is generated and received by piezoelectric transducers. Ultrasound can be aimed in a specific direction and obeys the laws of geometric optics with regard to reflection, transmission and refraction. When an ultrasound wave meets an interface of differing echogenicity, the wave is reflected, refracted and absorbed. Only reflected sound waves (echoes) can be sensed by the transducer and processed to generate an Image. The transducer acts as a receiver over 99% of the time. (Oak Brook, IL, et.al, 2000)

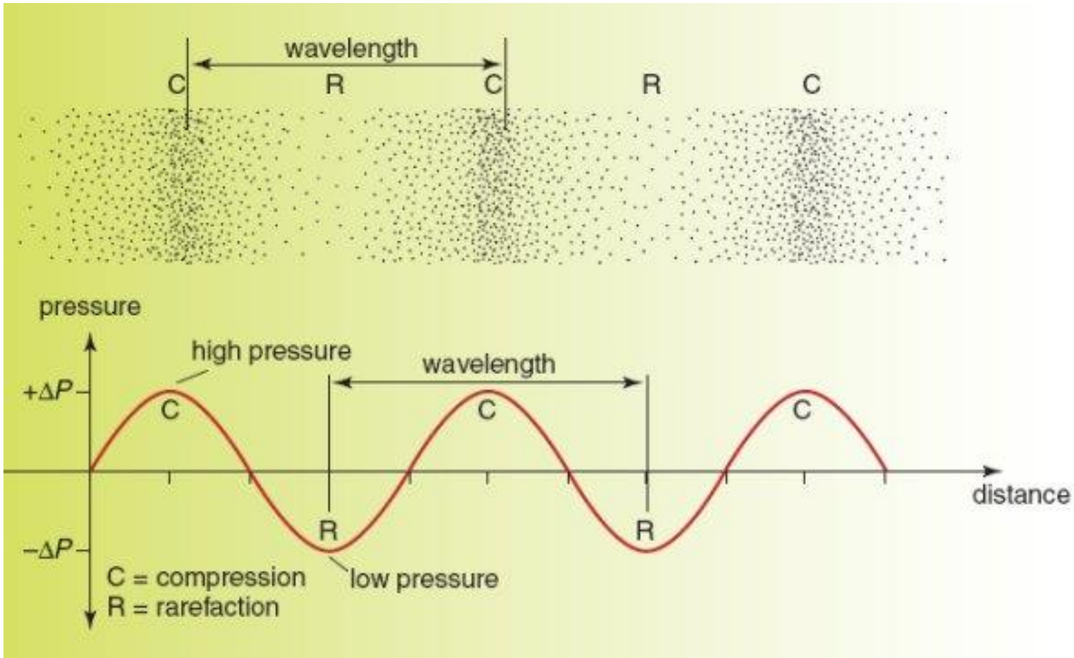

Figure 2-5: Ultrasound waves.

2-4-2 Transducer:

Transducers convert electrical energy into mechanical energy toproduce ultrasound and vice versa. The part of the transducer which does this work is a piezo electric crystal. It can be synthetic or natural. They have an inherent property of vibrating when anelectric current is applied and thus produce ultrasonic waves and conversely produce electric impulse when vibrated thus helping the acquisition of data for the formation of image. This effect is called "Piezoelectric effect". (TX, D. Armstrong 1996).

Quartz is a naturally occurring piezoelectric crystal. Synthetic ones are prepared from ceramics like lead zirconate and lead titanate. (Oak Brook, IL, et.al, 2000).

The range of the velocities of ultrasound in body tissues is fortunately limited,so that time of return of an echo is a reliable indication of depth. Small variations giverise to geometrical distortions (Oak Brook, IL, et.al, 2000).

Different tissues have different attenuation coefficients and this determines the quantum of reflection. This property has helped in imaging, tissue characterization and appropriate diagnosis. The greater the mismatch in acoustic impedance between two adjacent tissuesthe more reflective will be their boundary. (TX, D. Armstrong 1996).

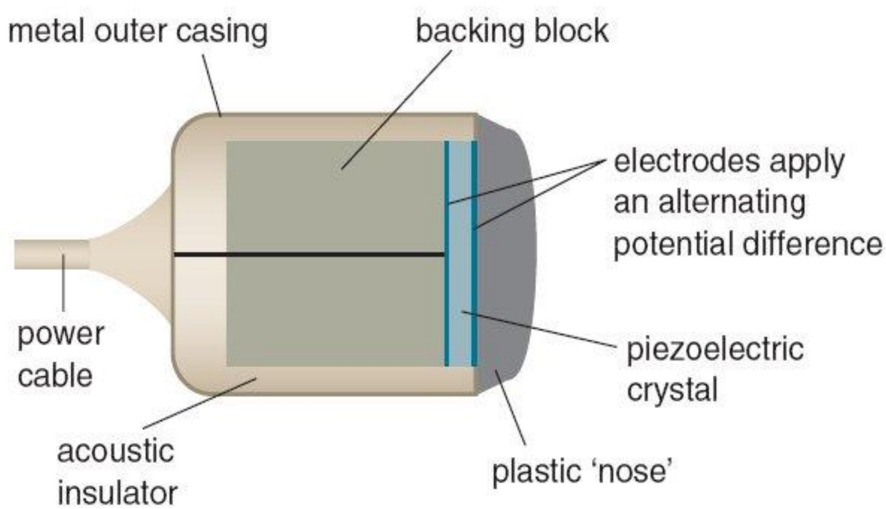

Figure2- 6: Ultrasound transducer.

2-4-3 Modes of display in ultrasonography

Static imaging modes:

1-A mode. (Amplitude modulation)

2-B mode. (Brightness Modulation)

Dynamic imaging modes:

3-M mode. (Motion M-mode)

4-Real time B mode

2-4-3 Real time ultrasound:

B-Scan produces a single image frame. A real time ultrasound transducer produces multiple images in a very short time i.e., at least 16 or more images (frames) per second, which gives us a impression as though we are seeing the moving structures in real. This quick presentation of images is possible by oscillating the piezoelectric crystals (TX, D. Armstrong 1996).

2-4-4 Doppler Basics

Doppler imaging can determine the presence and the direction of blood flow. The movement of the blood cells toward the transducer compresses the sound waves and creates shorter wavelengths and higher frequencies than those emitted by the transducer and called a positive shift or red shift (W, Popper A, 2000).

The movement of the blood cells away from the transducer expands the sound waves and creates a longer wavelengths and lower frequencies than those emitted by the transducer which is called a negative shift or Blue shift (W, Popper A, 2000).

2-4-4 Ultrasound Artifacts:

Artifacts are echoes that appear on the image that do not correspond in location or intensity to actual interfaces in the patient.

They can be of two types:

1. Good Artifacts - which are helpful

2. Bad Artifacts - which are disturbing

Good Artifacts

- Acoustic shadowing
- Acoustic enhancement
- Comet tail

Bad Artifacts

- Refraction
- Reverberation
- Mirror Image artifacts
- Beam width artifacts
- Movement artifacts
- Operator pressure artifacts

2-5 Previous studies:

Between January 2000 and March 30, 2005, records of 11,618 thyroid ultrasound exams performed for any reason in 8806 patients (some had multiple nodules) were reviewed. Different ultrasound features such as nodule size, microcalcification, solid feature (vs cystic), coarse calcifications, texture of the gland, blood flow within the nodule, the edges of the nodule and shape (more tall than wide) were evaluated and recorded in all cases. A total of 96 patients diagnosed with cancer were matched for age, sex and year of ultrasonography with 369 controls with benign thyroid nodules. On average, 1 case of thyroid cancer was found for every 111 ultrasound exams performed. Thyroid nodules were found in 97% of patients with thyroid cancer and in 56% of without thyroid cancer. Microcalcifications were found in 38% of cancerous nodules and only in 5% of benign, non-cancerous nodules. The risk of cancer increased with the size of nodule. Data analysis of this study showed that only 3 ultrasound features were related with the risk of cancer: microcalcification, nodule size greater than 2 cm, and solid form (Smith-Bindman et al. 2013)

The objective of this study was to determine the likelihood of malignancy in thyroid nodules and the risk of a nondiagnostic fine-needle aspiration biopsy (FNAB) on the basis of the demographic characteristics of the patients and sonographic features of the nodules. ultrasound-guided thyroid, thyroid bed, and cervical lymph node FNABs were performed at a tertiary referral center. Entry criteria for our retrospective study were adult patients who underwent thyroid nodule FNAB and had previously undergone diagnostic sonography. From previous reports for 944 thyroid nodules (739 nodules in women and 205 nodules in men), four sonographic features were recorded: longest dimension, morphology, presence of microcalcifications, and presence of lymphadenopathy. The final diagnosis of each nodule was classified as benign, malignant, or nondiagnostic on the basis of surgical pathology when available and cytology otherwise and was analyzed for correlation with individual sonographic features and combinations of features. The prevalence of malignancy and of nondiagnostic FNAB in this study was 11.0% and 11.8%, respectively. Statistically significant ($p < 0.05$) findings in malignant nodules were younger patient age (≤ 45 years; odds ratio [OR], 1.54) and solid nodule morphology (OR, 2.38). The significant predictors of a nondiagnostic-quality FNAB were older patient age (> 75 years; OR, 1.95) and a nodule ≥ 10 mm (OR, 1.45). Adding information about the other evaluated ultrasound features did not lead to a significant result. In the conclusion, Malignant thyroid nodules tend to be solid (86.5%). Patients older than 75 years showed a clearly increased risk of nondiagnostic FNAB, but to predict a higher risk of malignancy or of nondiagnostic FNAB using ultrasound remains difficult (Baier et al. 2009).

The purpose of this study is to compare the cytological results of ultrasound-guided fine-needle aspiration (US-FNA) cytology of thyroid nodules to sonographic findings and determine whether US findings are helpful in the interpretation of cytological results. Materials and Methods: Among the thyroid nodules that underwent US-FNA cytology, we included the 819 nodules which had a conclusive diagnosis. Final diagnosis was based on pathology from surgery, repeated FNA cytology or follow-up of more than one year. Cytological results were divided into five groups: benign, indeterminate (follicular or Hurthle cell neoplasm), suspicious for malignancy, malignant, and inadequate. US findings were categorized as benign or suspicious. Cytological results and US categories were analyzed. Results: Final diagnosis was concluded upon in 819 nodules based on pathology (n=311), repeated FNA cytology (n=204) and follow-up (n=304), of which 634 were benign and 185 were malignant. There were 560 benign nodules, 141 malignant nodules, 49 nodules with inadequate results, 21 with indeterminate results, and 48 that were suspicious for malignancy. The positive and negative predictive values of the US categories were 59.1% and 97.0%, and those of the cytological results were 93.7% and 98.9%. The US categories were significantly correlated with final diagnosis in the benign (p=0.014) and suspicious for malignancy (p<0.001) cytological result groups, but not in the inadequate and indeterminate cytological results groups. The false positive and negative rates of cytological results were 1.9% and 3.2%. Conclusion: Sonographic findings can be useful when used alongside cytological results, especially in nodules with cytological results that are benign or suspicious for malignancy (Mi-Jung et al. 2010)

The purpose of this study is to evaluate the diagnostic accuracy of sonography and Fine Needle Aspiration Cytology (FNAC). This follow-up study was approved by review board and conducted at Endocrine Clinic and Radiology Department of Imam Reza, Kermanshah. The patients were diagnosed to have thyroid nodule examined by FNA and Sonography suspicious malignant cases underwent surgery. Results were entered in SPSS 11.5 chi-Square and Fisher exact test applied to compare malignant and benign nodule characters. In this study 144 patients were examined and 14 cases (9.7%) had malignant nodule. Most of malignant nodules were single (p=0.001), solid (p < 0.001), hypo-echo (p=0.001), with irregular margins (p < 0.001) and with calcification (p=0.041). There was no significant relationship between malignancy and nodule size of larger than 15 mm (p=0.395).

Compared with surgery, FNA sensitivity and specificity were calculated as 92.8% and 100% respectively. Based on the result of this study, thyroid nodule size must not be considered as a criterion for malignancy and thyroid nodules of any size must be suspected as malignant. Important criteria for malignancy include irregular edges, being solid, hypoechogenicity and being a single nodule respectively. Compared with Surgery, FNA Sensitivity and specificity were calculated as 92.8% and 100% respectively (Mehrali, et al. 2013)

Chapter three

Materials and methods

3.1 Study design

This is a descriptive, cross-sectional study type where the data were collected prospectively

3.2 Study population

The patients included in this study they had thyroid nodular diseases (benign and malignant nodules) underwent both fine needle aspiration (FNA) and ultrasonography. The patients had different nationality and gender their age ranged from 23 to 70 years.

3.3 Sample size and type

The data of this study collected from 100 patients underwent ultrasound scan and FNA selected conveniently.

3.4 Place and duration of the study:

This study carried out in UAE –Abu Dhabi –Al Mafraq hospital –Radiology department in ultrasound section in the period from Jan 2015 to Aug 2015.

3.5 Materials

For ultrasound a high-frequency (6–15 MHz) linear transducer is used. The highest frequency is used while still allowing adequate sonographic penetration. Start by placing the transducer over the neck, then angle the beam as necessary and adjust the time gain compensation (TGC) with adequate sensitivity setting to allow uniform acoustic pattern, thus obtaining the best image of thyroid gland. All patients underwent standard ultrasound scan using **(GE logic E 9)** ultrasound machine and the documented images had been printed.

Figure 3.1 G.E machine logic E 9

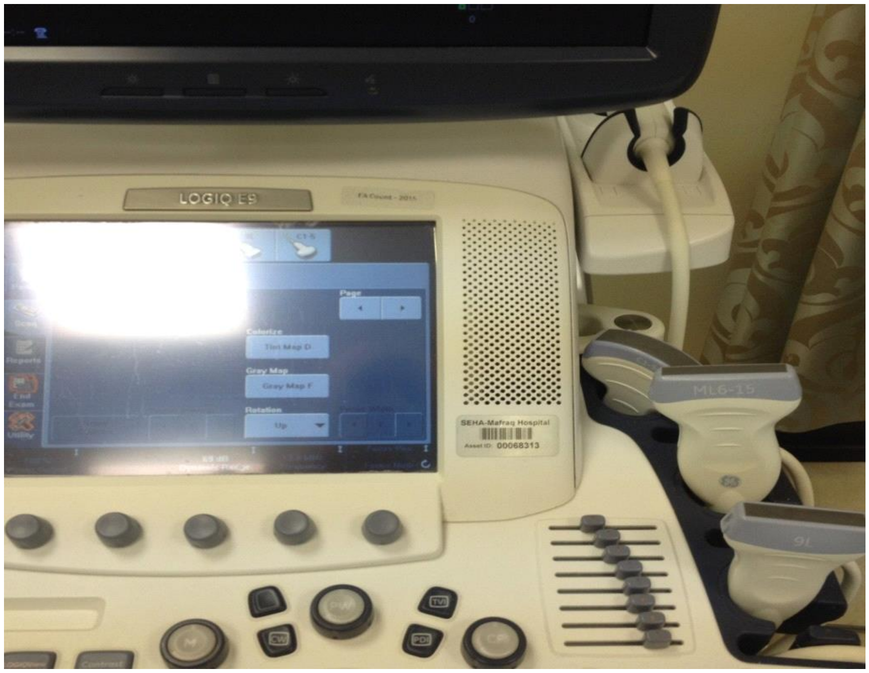

Figure 3.2: GE machine logic E 9.

3.6 Methods of data collection

3.6.1 Patient Preparation:

There is no preparation for this procedure.

3.6.2 Patient's position:

To visualize the thyroid gland optimally, the patient is placed in the supine position with a pillow underneath the shoulders to extend the neck slightly, allowing the head to rest on the examination table.

3.6.3 Technique:

All patients are examined in supine position with hyperextended neck, using a high frequency linear-array transducer (6-15 MHz) that provides adequate penetration and high resolution image. Scanning is done both in transverse and longitudinal planes. Real time imaging of thyroid lesions is performed using both gray-scale and color Doppler techniques. The imaging characteristics of a mass (viz. location, size, shape, margins, echogenicity, contents and vascular pattern) should be identified.

3.6.4 Examination criteria

An acronym has shown to be didactically helpful ["SSOTM"]:

- S = size
- S = shape
- O = outline
- T = texture
- M = measurement

3.6.5 Image analysis

Both ultrasound and FNAB were retrospectively analyzed by a radiologist.

3.6.6 Data analysis method:

By using computer program, Statistical Package for Social Sciences (SPSS), Statistical significance will be determined using chi-square test.

3.7 FNA Procedure

Patient will be helped to lie on his back on the treatment room table. A towel or small blanket will be placed under your shoulders so that the head and neck of the patient will be tilted back. This position gives the doctor the best access to the patient neck, the doctor will look closely at patient neck, and will also feel the neck with his or her fingers and hands. Then the skin on the neck will be cleansed with a liquid containing iodine and alcohol. A thin needle attached to a syringe will be inserted through the skin of the neck and into the thyroid gland. The doctor will "aspirate" (pull back) thyroid cells into the syringe. The syringe will then be passed to a technician who will prepare the cells to be seen under a microscope. It usually takes between four and eight needle passes to obtain enough thyroid cells. The procedure is usually completed in less than 30 minutes.

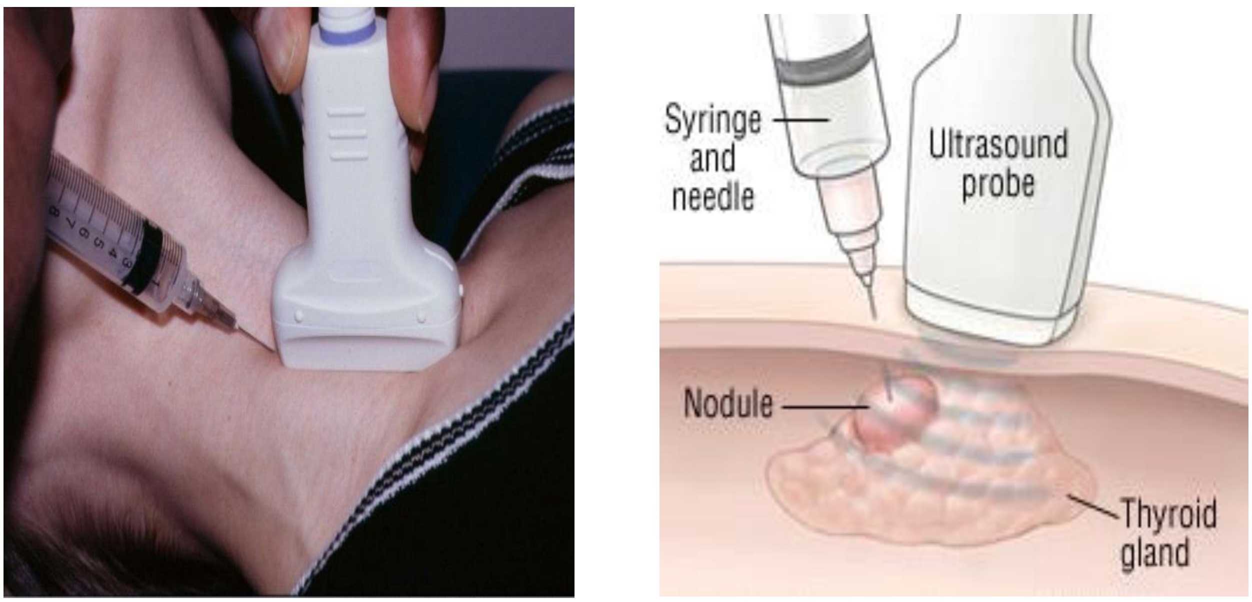

Figure 3.3 Ultrasound guided FNA procedure.

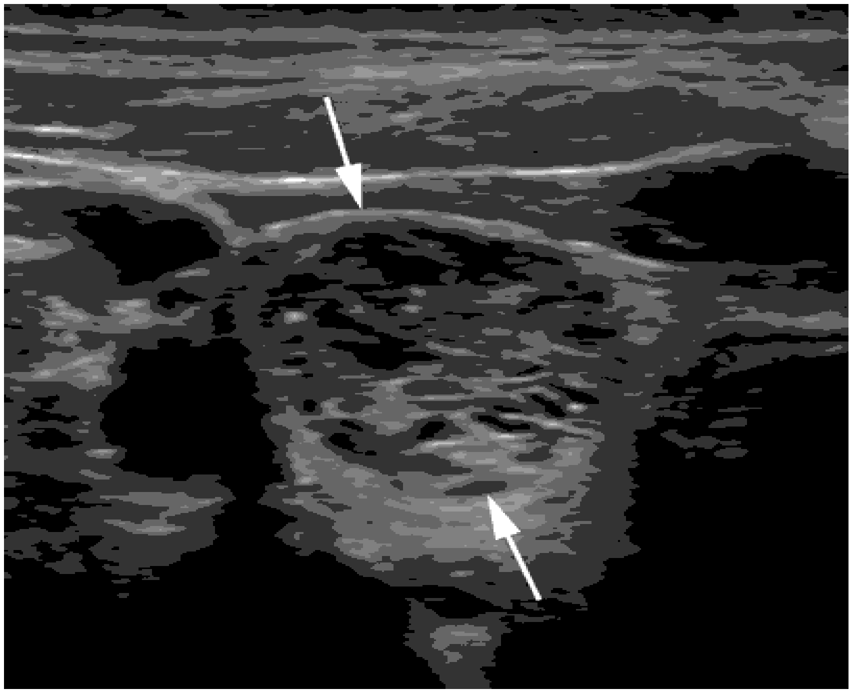

Figure 3.4: Dominant mixed cystic-solid right lobe nodule (arrows) 59-year-old woman, for FNA.

- US guidance
- 25 gauge needle
- 3-4 passes

Figure 3.5: ultrasound guided FNA procedure.

Chapter four
Results

Table 4-1 Frequency distribution table of patients' gender

Gender	Frequency
Male	12
Female	88
Total	100

Table 4-2 frequency distribution table of patients- age group

Age group	Frequency
20-30	9
31-40	28
41-50	30
51-60	13
61-70	20
Total	100

Table 4-3 Frequency distribution of patients- biopsy result

Biopsy result	Frequency
Benign	81
Malignant	19
Total	100

Table 4-4 frequency distribution of thyroid nodule types

Nodule type	Frequency
Solitary	34
Multiple	66
Total	100

Table 4.5 cross-tabulation table demonstrating the relationship between the age group and biopsy result

Age groups	Biopsy results		
	Benign	Malignant	Total
20-30	8	2	10
31-40	23	2	25
41-50	24	11	35
51-60	12	2	14
61-70	14	2	16
Total	81	19	100

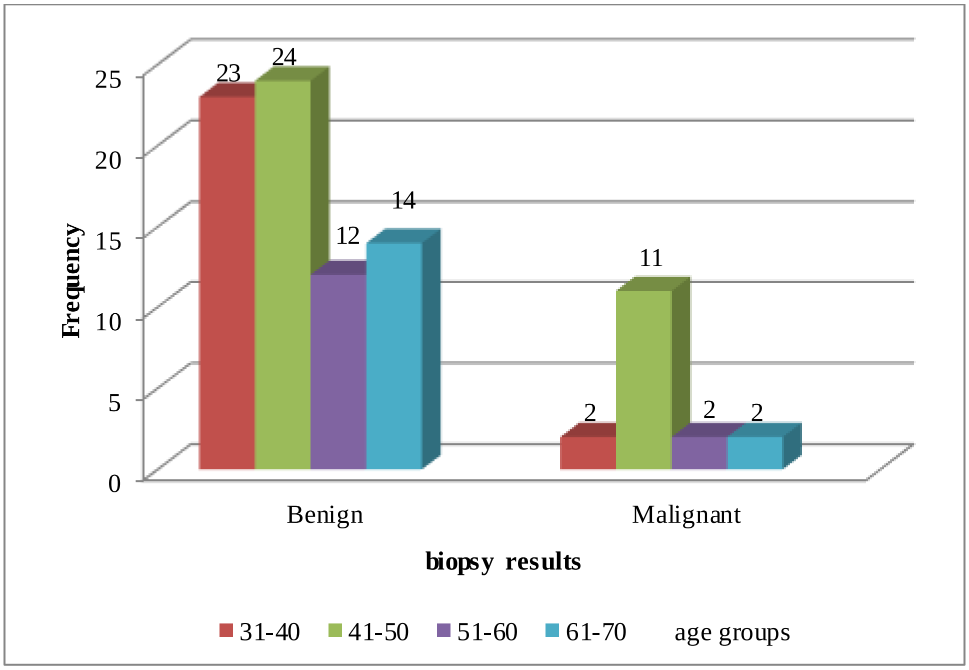

Figure 4-1 a bar plot shows the distribution of biopsy result in relation to age groups

Table 4-6 cross-tabulation table demonstrating the relationship between the age group and nodule types

Age group	Nodule types		
	Solitary	Multiple	Total
20-30	8	2	10
31-40	23	2	25
41-50	24	11	35
51-60	12	2	14
61-70	14	2	16
Total	81	19	100

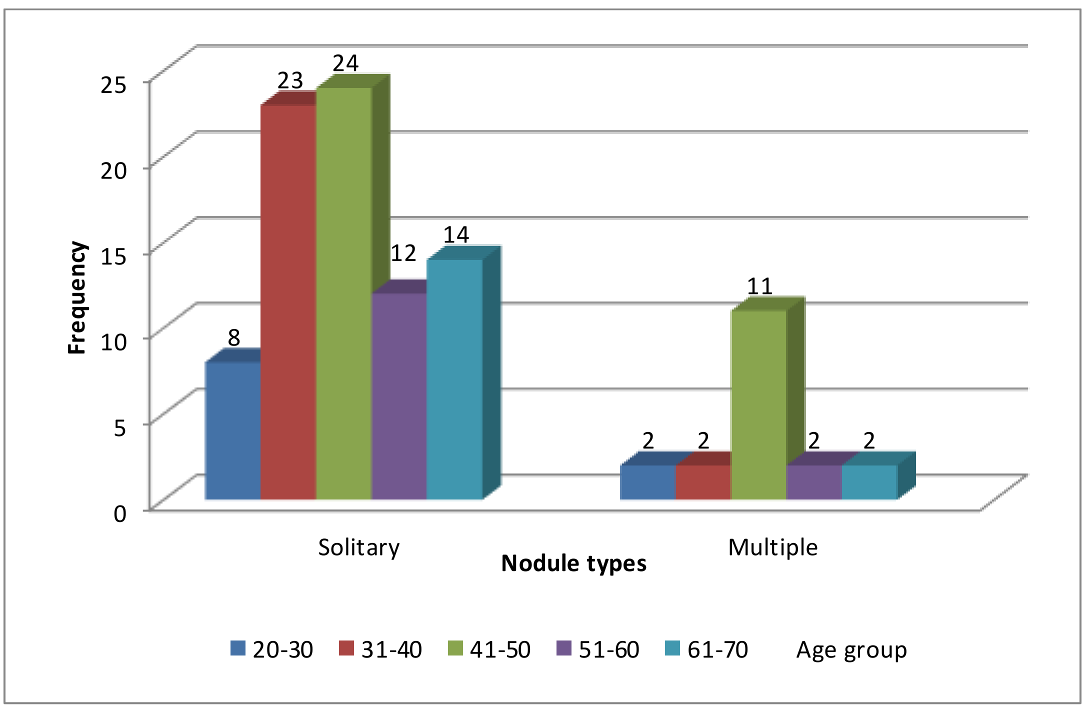

Figure 4-2 a bar plot shows the distribution of nodule types in relation to age groups

Table 4-7 cross-tabulation table demonstrating the relationship between the nodule size and type of nodule.

Size	Nodule types		Total
	Solitary	Multiple	
0 - 2 cm	17	37	54
> 2 cm	18	28	46
Total	35	65	100

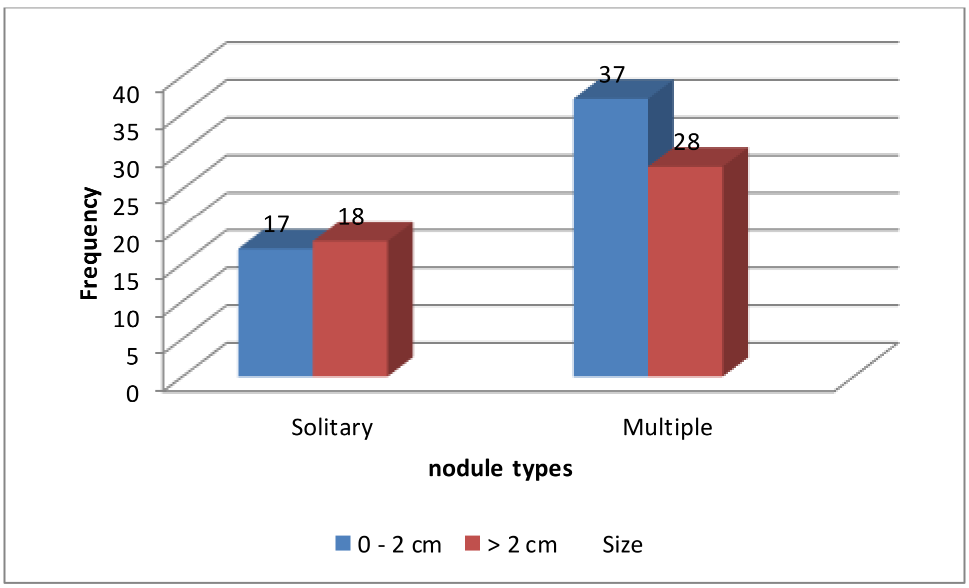

Figure 4-3 a bar plot shows the distribution of nodule types in relation to its size

Table 4-8 cross-tabulation table demonstrating the relationship between the nodule site and type of nodule.

Site	Nodule site			Total
	Rt lope	Lt lope	Isthmus	
Solitary	21	12	2	35
Multiple	26	32	7	65
Total	47	44	9	100

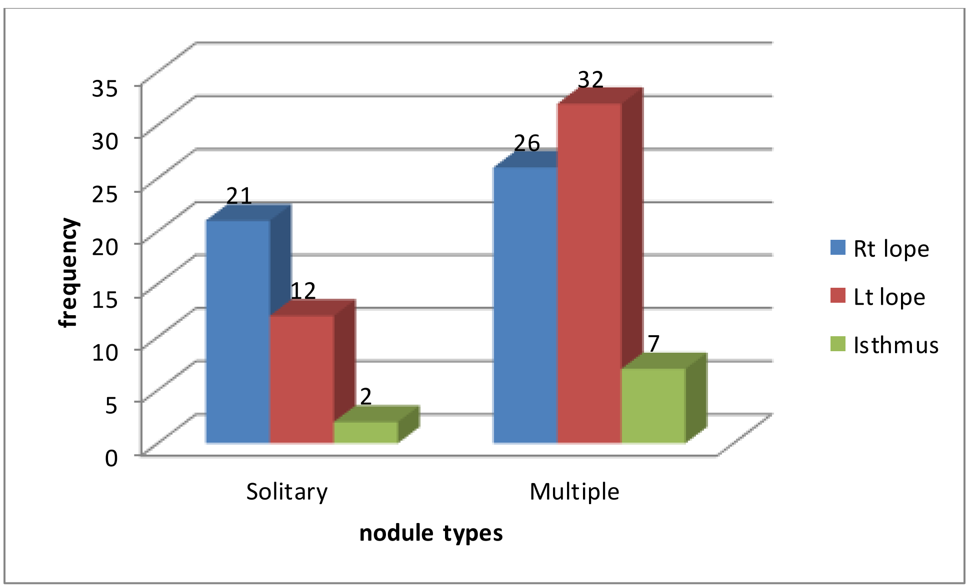

Figure 4-4 a bar plot shows the distribution of nodule types in relation to its site

Table 4-9 cross-tabulation table demonstrating the relationship between vascularity site and biopsy result

Tumour types	Vascular			
	A vascular	Central	peripheral	Total
Benign	13	13	55	81
Malignant	2	9	8	19
Total	15	22	63	100

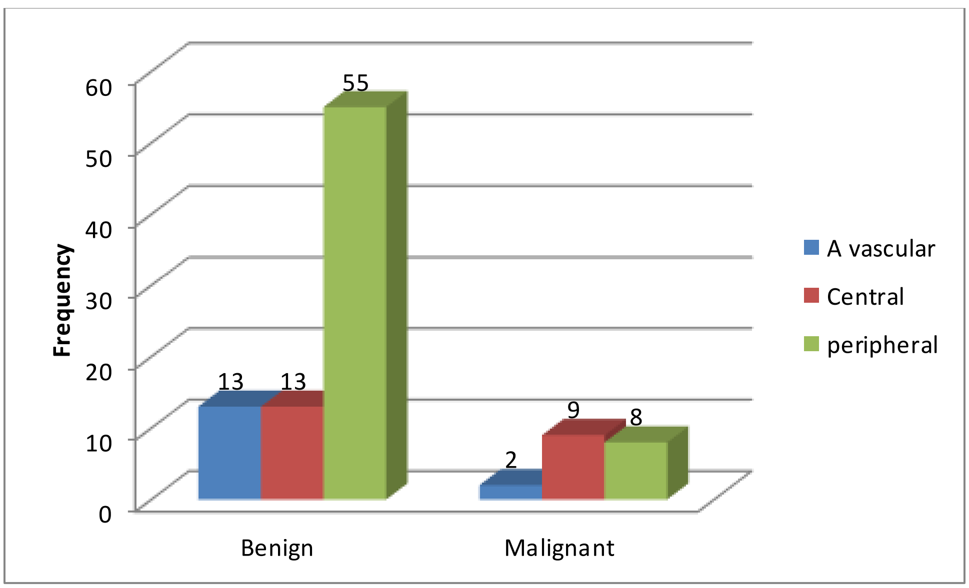

Figure 4-5 a bar plot shows the distribution of vascularity in relation to tumour types

Table 4-10 cross-tabulation table demonstrating the relationship between the nodule echotexture and biopsy result

Tumour Types	Echotexture				
	Solid	Cystic	Mixed	Calcified	Total
Benign	24	19	28	10	81
Malignant	8	1	2	8	19
Total	32	20	30	18	100

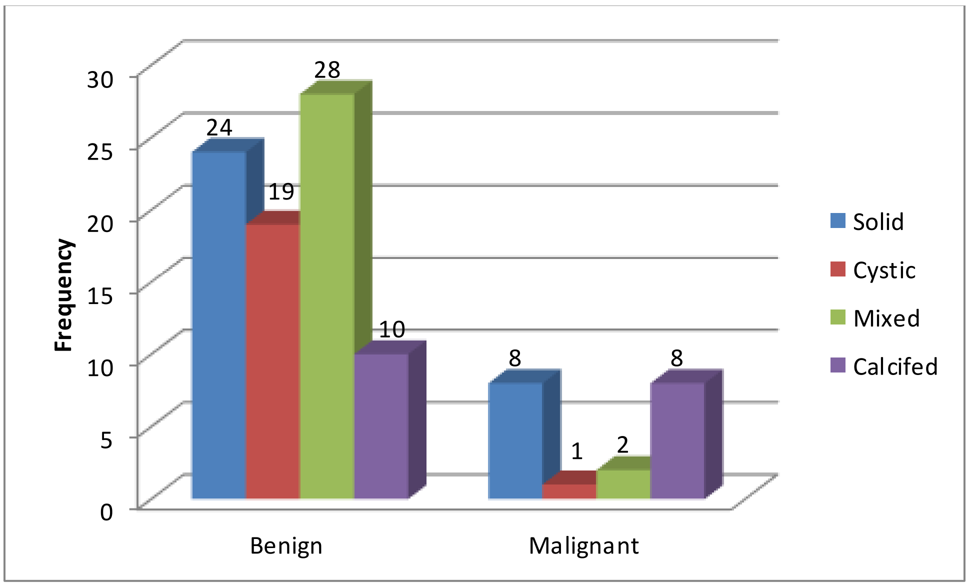

Figure 4-6 a bar plot shows the distribution of echotexture in relation to tumour types

Table (4-11) cross-tabulation table demonstrating the relationship between the nodule echogenicity and biopsy result

Tumour types	Echogenicity			
	Hyperechoic	Hypoechoic	Isoechoic	Total
Benign	15	56	10	81
Malignant	4	13	2	19
Total	19	69	12	100

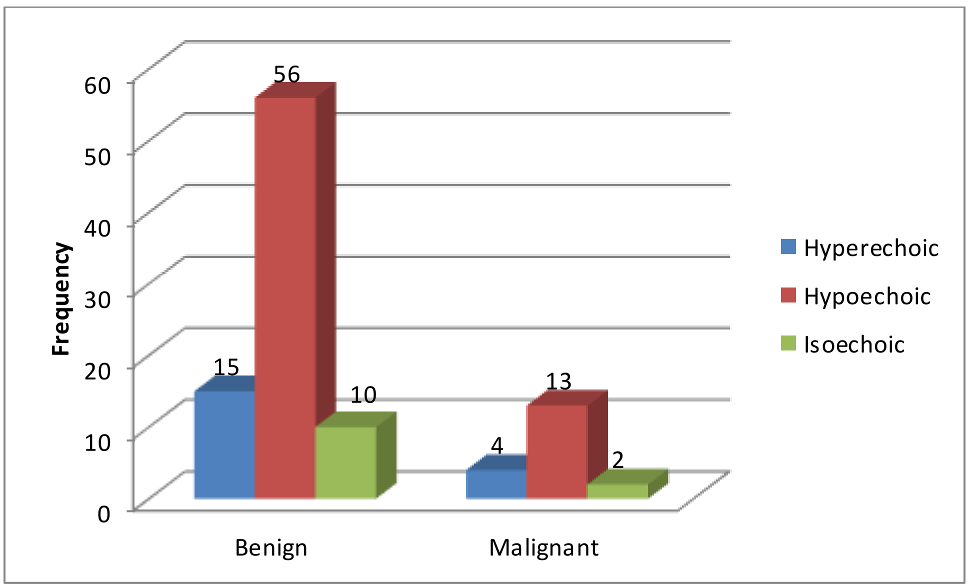

Figure 4-7 a bar plot shows the distribution of echogenicity in relation to tumour types

Table 4-12 crosstabulation table demonstrating the relationship between the lymph nodes involvement and biopsy result.

Tumour types	Total	lymph nodes involvement
Benign	81	11
Malignant	19	9
Total number of patients	100	20

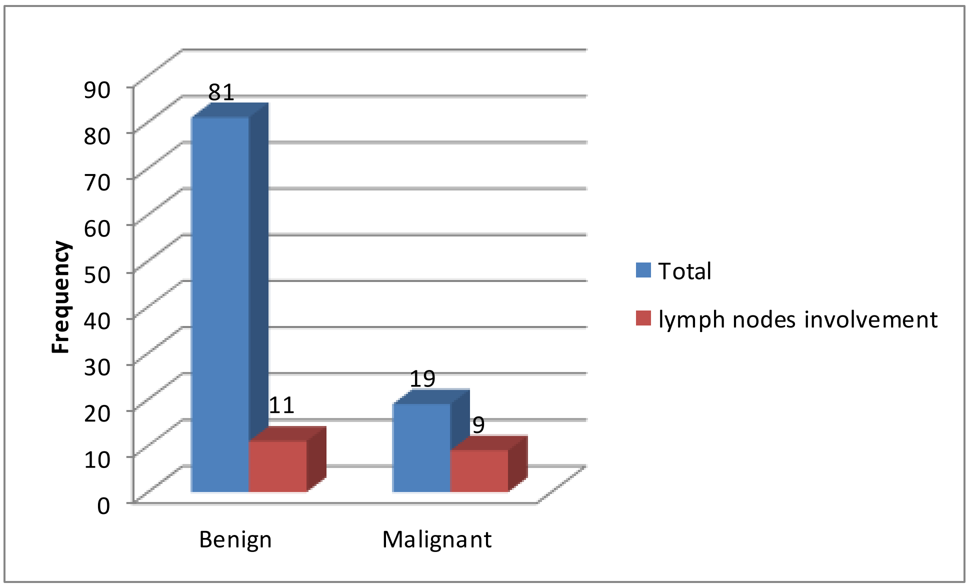

Figure 4-8 a bar plot shows the distribution of lymph node involvement in relation to tumour types

Table 4-13 crosstabulation table demonstrating benign and malignant nodules, detected by cytology and ultrasound.

Tumour types	Ultrasound	Biopsy result	Total
Benign	73	81	81
Malignant	27	19	19
Total			100

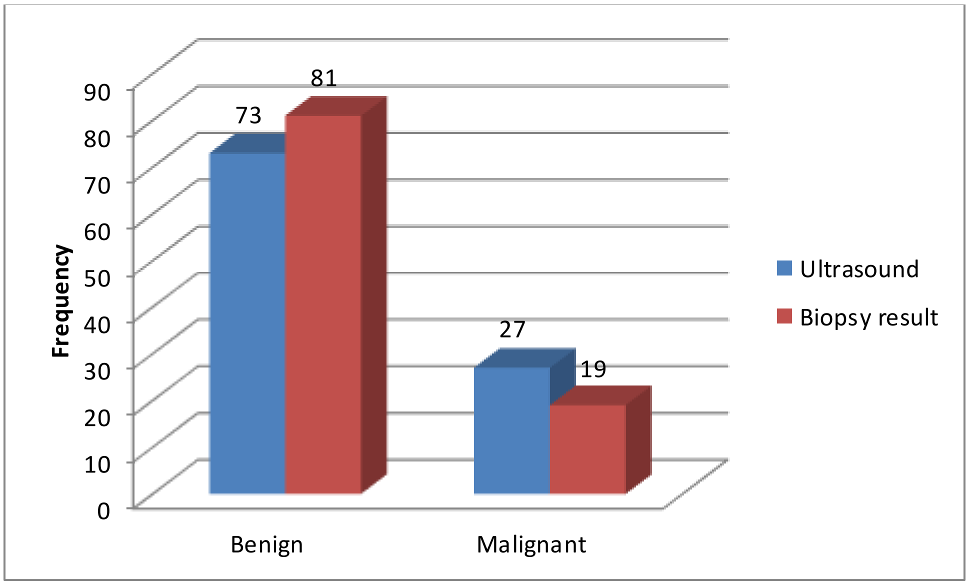

Figure 4-9 a bar plot shows the relation of tumour types using ultrasound to the result

Table 4 -14 frequency distribution table of malignant nodules as reported by cytology

Cytology	***N*o of patients**
Papillary	11
Papillary (follicular variant)	1
Follicular	3
Follicular-Hurtelcellular	1
Hurtelcellular	1
Undifferentiated	1
Atypical parafollicular	1
Total	19

Table 4-15: Comparing malignant and benign nodules based on personal and sonographic features.

Individual or group features	**Benign (Total 81)**	**Malignant (Total 19)**
Gender		
Female	73	15
Male	8	4
Number of nodules		
Single nodule	22	12
Multi nodule	59	7
Nodule type		
Solid	20	13
Cystic and Soft (Mixed)	61	6
Echogenicity Status		
Hypoechoechogenicity	56	13
Hyperechoic/isoechoic	25	6
Nodule edge status		
irregular	0	13
Regular	81	6
Halo		
Without halo	80	11
With halo	1	8
Nodule size		
Larger than 2 cm	36	10
Smaller than 2 cm	45	9
Calcification		
With calcification	18	12
Without calcification	82	7

Chapter five

Discussion, Conclusion and Recommendations

5-1 Discussion

Thyroid ultrasound scan was performed by GE – logic E 9 scanner with a 6 to 15 MHz bandwidth transducer. Compound imaging was performed with Color Doppler in all cases. Sonographic classification based on sonographic features was performed before FNA cytology by one experienced sonographer. Size was measured as the longest diameter. Sonographic features included echogenicity, margin, calcifications, and shape, based on our previous publication. Color Doppler imaging was routinely obtained. Echogenicity was classified as hyperechogenicity, isoechogenicity, hypoechogenicity, and marked hypoechogenicity (cystic). When the echogenicity was similar to thyroid parenchyma, the nodule was classified as isoechogenic. Marked hypoechogenicity indicated lower echogenicity than the surrounding strap muscle. The margin was characterized as well or not well-circumscribed (microlobulated/irregular). Calcifications were categorized as microcalcifications, macrocalcifications, mixed calcifications, or none. Microcalcifications were defined as tiny (less than 2 mm in size), punctuate, and hyperechoic foci, either with or without acoustic shadows. Macrocalcifications were defined as larger than 2 mm. Mixed calcifications were defined as a combination of micro- and macrocalcifications. Shape was assessed by the ratio of anteroposterior (A) and transverse (T) diameter. Mixed nodules, composed of both cystic and solid portions, were classified according to the solid portion. Malignant sonographic features were defined as showing marked hypoechogenicity, not well-circumscribed margin, microcalcifications or mixed calcifications. If any single feature suggestive of malignancy was present, the nodule was classified as suspicious. If a nodule had no suspicious features, it was classified as benign.

The result of this study showed that 88% of patients were females and the 12 % were males. Fig. (4-1).Their mean age was 46.6 years old Fig. (4-2) none of the patients had a history of neck irradiation in childhood, and 80.5% nodules were found among female patients Fig. 7 from all nodules, 34% were single and 66% were multiple nodules. Nodules were solid in 67% of the patient and cystic (Mixed) and 33% were solid nodules. Concerning echogenicity, 82% of nodules were Hypo-echo, 91% of nodules had a regular edge. 91 nodules (91%) had no Halo. 46 nodules (46%) were larger than 2cm. and 64 (64%) nodules were 0-2cm in size. Fig. 8 on page 17, Concerning calcification, 82 nodules (82%) were calcified and 18 (18%) were not calcified. Concerning vascularity , 15 (15%) nodules were a vascular , 22 (22%) show central vascularity and 63 (63%) show peripheral vascularity.

After biopsy result 19 cases (19%) were reported malignant while 81 cases (81%) were confirmed malignant in FNA. Most of the malignant nodules (11) = (57.8%) were papillary thyroid carcinoma.

Thyroid nodules have been examined with ultrasound and based on US scan FNA biopsy has been done. 73 % of the nodules examined by US shown to be benign on benign ultrasound criteria and when biopsy was done 3 % of these nodules were found malignant so the US specificity was high 95.9 %.

From all nodules 27 % shown to be malignant by ultrasound, the biopsy revealed 19 % were malignant and 8 % were benign and sensitivity was which is considered as remarkable result 70 %, the overall accuracy of ultrasound in detecting nodules as benign or malignant in this study was 82.95%.

The appearance of a single nodule, being solid, being hypo-echo, having irregular edges or calcification were the appropriate characteristics for differentiating malignant from benign nodules while the nodule size did not have appropriate differential value.

Previous studies have been conducted to assess sonography parameters in differentiating malignant from benign thyroid nodules; the results have been inconsistent, and it is still controversial. In a study in ultrasound, sonographic features failed to differentiate benign and malignant thyroid nodules and fine-needle aspiration was recommended for all cases. In some studies sonography had been unable to differentiate malignant and benign cases and FNA is recommended for all thyroid nodules regardless palpability. In a study, none of sonography characteristics, except calcification, was able to differentiate benign from malignant thyroid nodes.

However, there are studies in favor of the usefulness of sonography markers in differentiating malignant from benign nodules. In a study, having a single nodule, irregular edges, and micro-calcification increased the chance of malignancy 3.6, 5.4 and 39 times, respectively. In Baier et al. 2009 study 23, having multi nodules was associated with malignancy, while in Mi-Jung Lee et al. 2010 study6 having a single nodule or two nodules increased the chance of malignancy and in Mehrali Rahimi, et al. 2013 study16 being solid and hypo-echo were associated with malignancy. However in another study hypoechoechogenicity was not associated with malignancy.6 Unclear edges, irregular shape, being solid and hypoechoechogenicity can increase the chance of malignancy. In another study, a greater percentage of malignant nodules had irregular edges and hypoechoechogenicity. In Smith-Bindman R. et al. 2013 study25 irregular shape was not associated with malignancy but there was higher percentage of hypoechoechogenicity in malignant nodes. Some studies were in favor of sonography markers for differentiating malignant and benign cases, however none of them can prove the malignancy decisively.

This study showed that the smallness of nodule cannot eliminate the chance of malignancy and it is required for all nodules of any size to be investigated further. Other studies have also questioned using exact sizes for suspecting malignant nodules. Also some study recommended FNA even for 5mm nodules. In another study, nodes larger than 10 mm did not increase the chance of malignancy. Therefore, it seems that the thyroid nodule size is not a good indicator for future actions, such as FNA or surgery, and malignancy must be suspected in nodules of any size.

5-2 Conclusion

Based on the result of this study, thyroid nodule size must not be considered as a criterion for malignancy and thyroid nodules of any size must be suspected as malignant. Important criteria for malignancy include irregular edges, being Solid hypoechogenicity and being a single nodule respectively. Compared with FNA, Sensitivity and specificity and accuracy were calculated as 70%, 95.9% and 83% respectively.

In conclusion, sonographic findings can be useful when used alongside cytology in the overall assessment of thyroid nodules and their likelihood of malignancy. If the nodule is suspicious for malignancy and has positive results on cytology, also it will have suspicious findings on US, it is highly likely that it is malignant. In addition, if a cytologically benign nodule shows suspicious sonographic findings, repeated FNA cytology is recommended. Ultrasound FNAB is a safe and reliable diagnostic approach for thyroid nodules. It is the method of choice for hypo- and isoechoic not purely cystic nodules, regardless of the nodule size.

5-3 Recommendations

- Other study with a large sample size could be done where logistic regression analysis can be used to predict the malignant from benign.
- Also it is recommended to conduct a similar study with larger sample size including other characteristics features in order to identify the malignancy markers more accurately.
- Application of computer analysis program to classify the malignant and benign nodules using texture analysis.
- All thyroid nodules scanned by ultrasound must be examined by Doppler

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Appendices

Examples of benign and malignant thyroid nodules

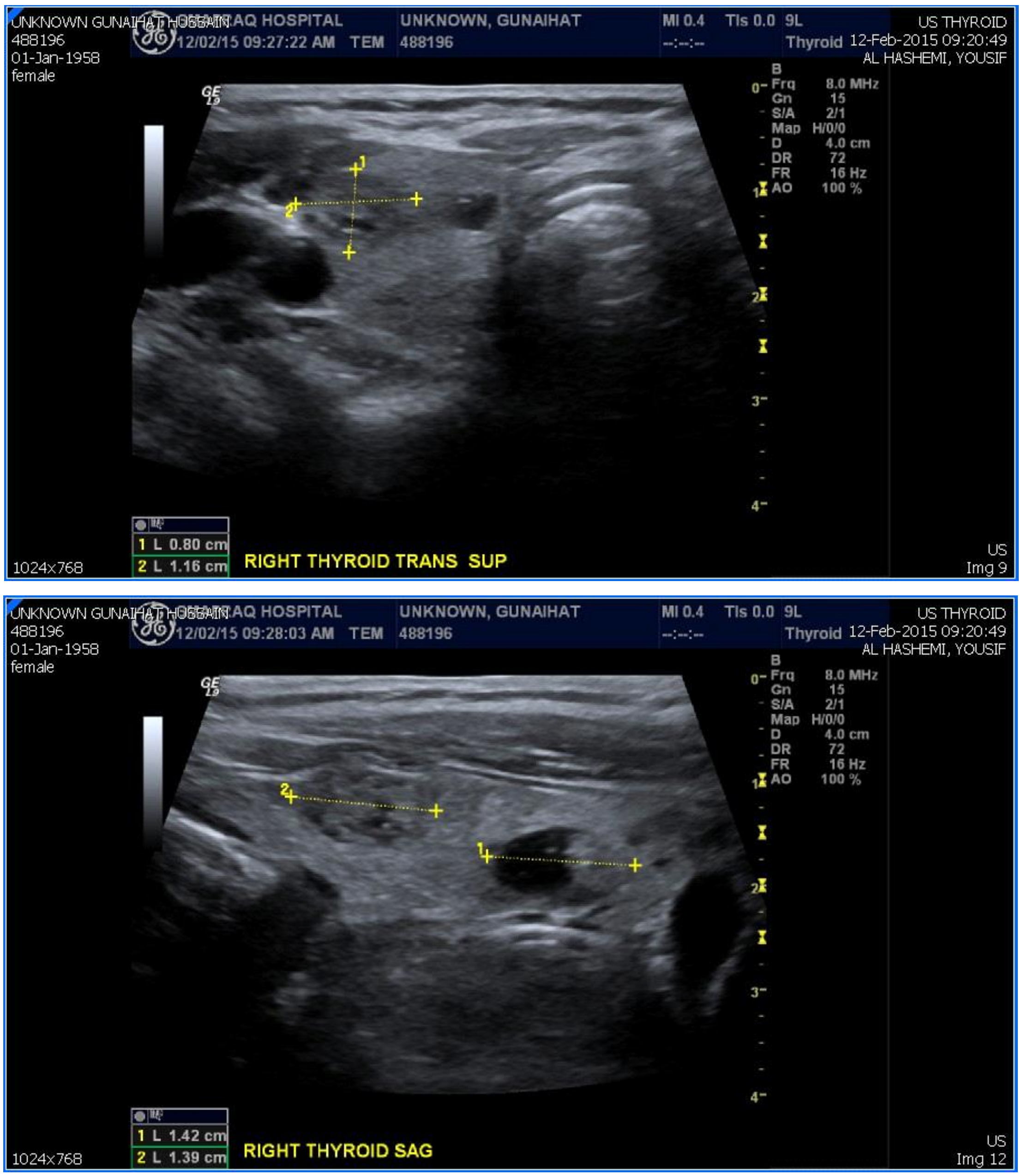


Figure 1 : A 57 , F , patient with multiple nodules , the result of FNAB was negative for malignancy.


SALEM SAFIYA
5699
01-Jan-1962
female
MAFRAQ HOSPITAL
12/02/15 12:03:54
MAG
SALEM, SAFIYA
5699, Age 53
MI 0.8
TIs 0.2
ML6-15
Thyroid
US THYROID
12-Feb-2015 11:59:37
AL HASHEMI, YOUSIF
FR 17
CHI
Frq 9.0
Gn 35
S/A 2/1
Map F/0
D 4.0
DR 66
AO% 100
LOGIQ E9
1 L 1.63 cm
2 L 1.09 cm
Lt Thyroid Long
960x720
W/L: 256/127
US
Img 4096

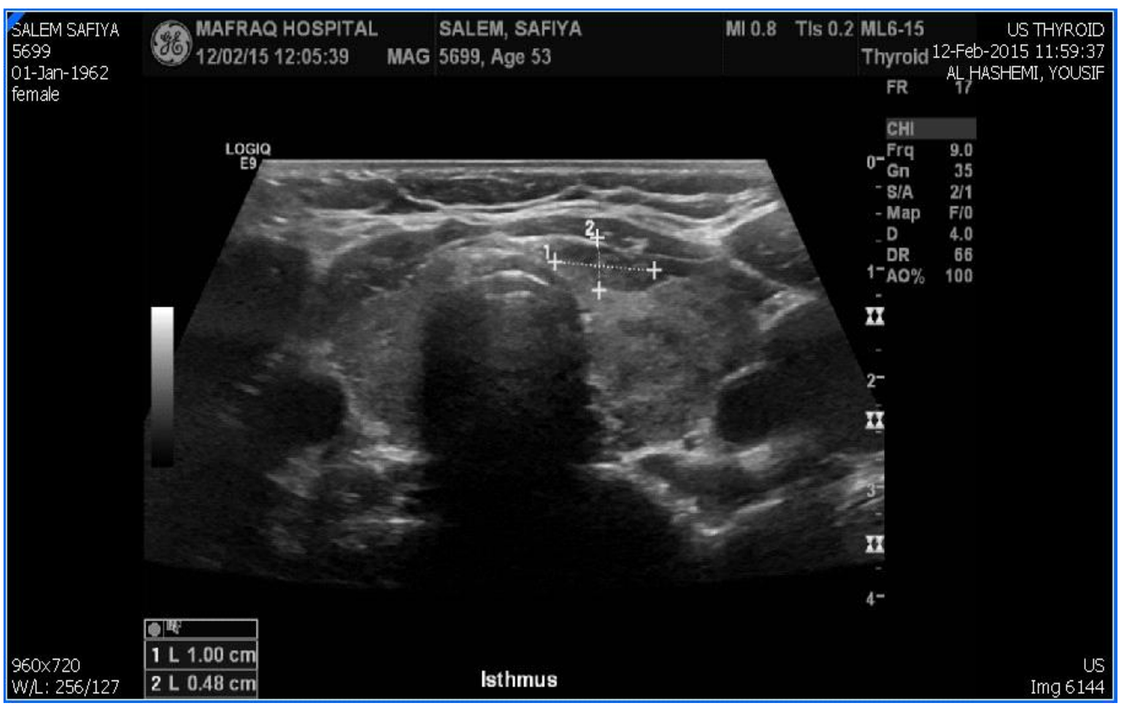

SALEM SAFIYA
5699
01-Jan-1962
female
MAFRAQ HOSPITAL
12/02/15 12:05:39
MAG
SALEM, SAFIYA
5699, Age 53
MI 0.8
TIs 0.2
ML6-15
Thyroid
US THYROID
12-Feb-2015 11:59:37
AL HASHEMI, YOUSIF
FR 17
CHI
Frq 9.0
Gn 35
S/A 2/1
Map F/0
D 4.0
DR 66
AO% 100
LOGIQ E9
1 L 1.00 cm
2 L 0.48 cm
Isthmus
960x720
W/L: 256/127
US
Img 6144

Figure 2 : A 53 , F , patient with multiple nodules , the result of FNAB was negative for malignancy.

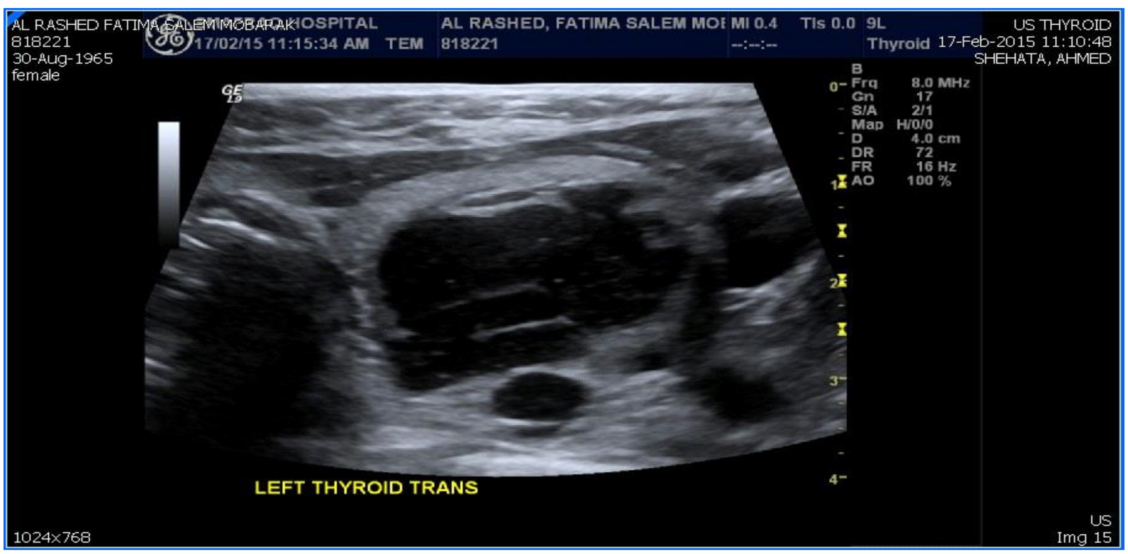
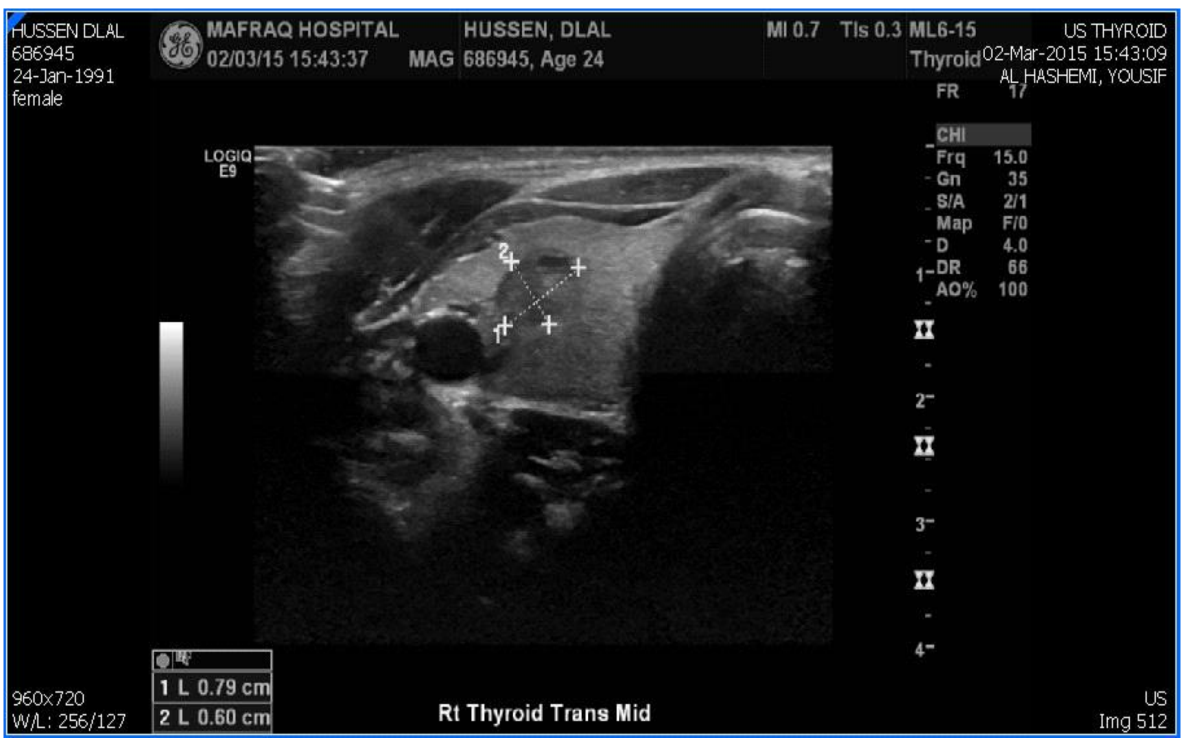
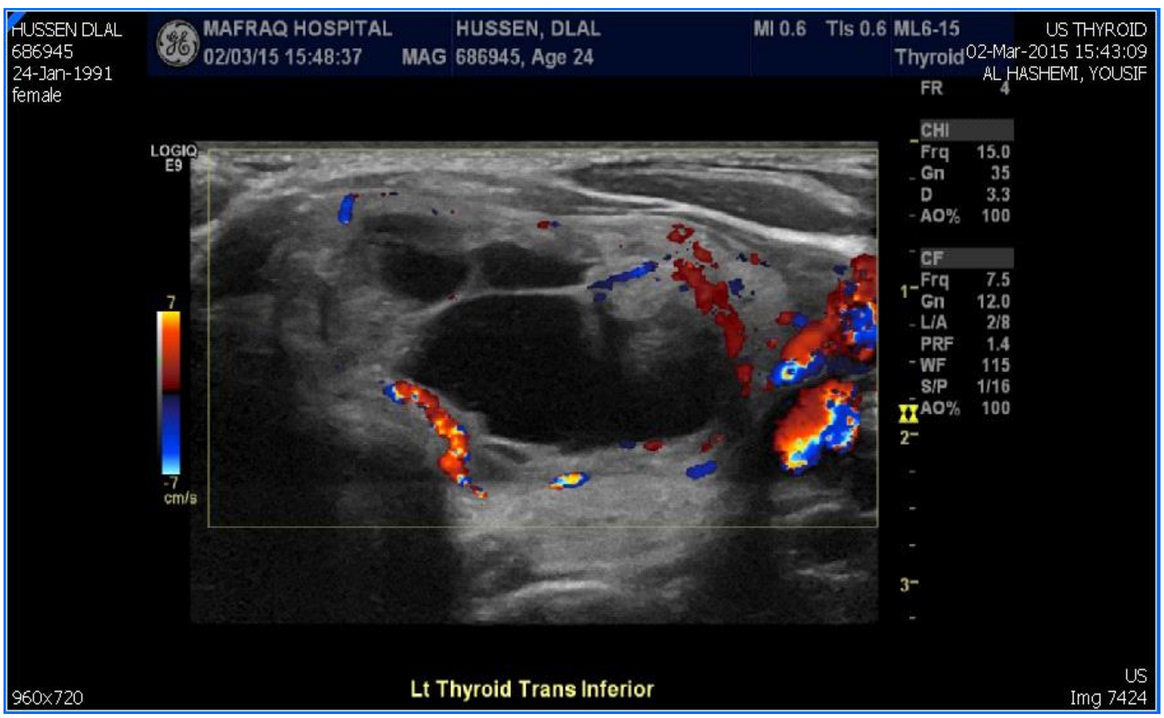


Figure 3 : A 50 , F , patient with multiple nodules , the result of FNAB was negative for malignancy.




HUSSEN DLAL
686945
24-Jan-1991
female
MAFRAQ HOSPITAL
02/03/15 15:44:20
MAG
HUSSEN, DLAL
686945, Age 24
MI 0.7
TIs 0.3
ML6-15
Thyroid
US THYROID
02-Mar-2015 15:43:09
AL HASHEMI, YOUSIF
FR 17
LOGIQ E9
CHI
Frq 15.0
Gn 35
S/A 2/1
Map F/0
D 4.0
DR 66
AO% 100
1 Rt Thyroid L 1.65 cm
Rt Thyroid Vol 2.77 ml
2 L 0.96 cm
Rt Thyroid Trans Inferior
960x720
W/L: 256/127
US
Img 1536


HUSSEN DLAL
686945
24-Jan-1991
female
MAFRAQ HOSPITAL
02/03/15 15:48:37
MAG
HUSSEN, DLAL
686945, Age 24
MI 0.6
TIs 0.6
ML6-15
Thyroid
US THYROID
02-Mar-2015 15:43:09
AL HASHEMI, YOUSIF
FR 4
LOGIQ E9
CHI
Frq 15.0
Gn 35
D 3.3
AO% 100
CF
Frq 7.5
Gn 12.0
L/A 2/8
PRF 1.4
WF 115
S/P 1/16
AO% 100
7
-7
cm/s
Lt Thyroid Trans Inferior
960x720
US
Img 7424

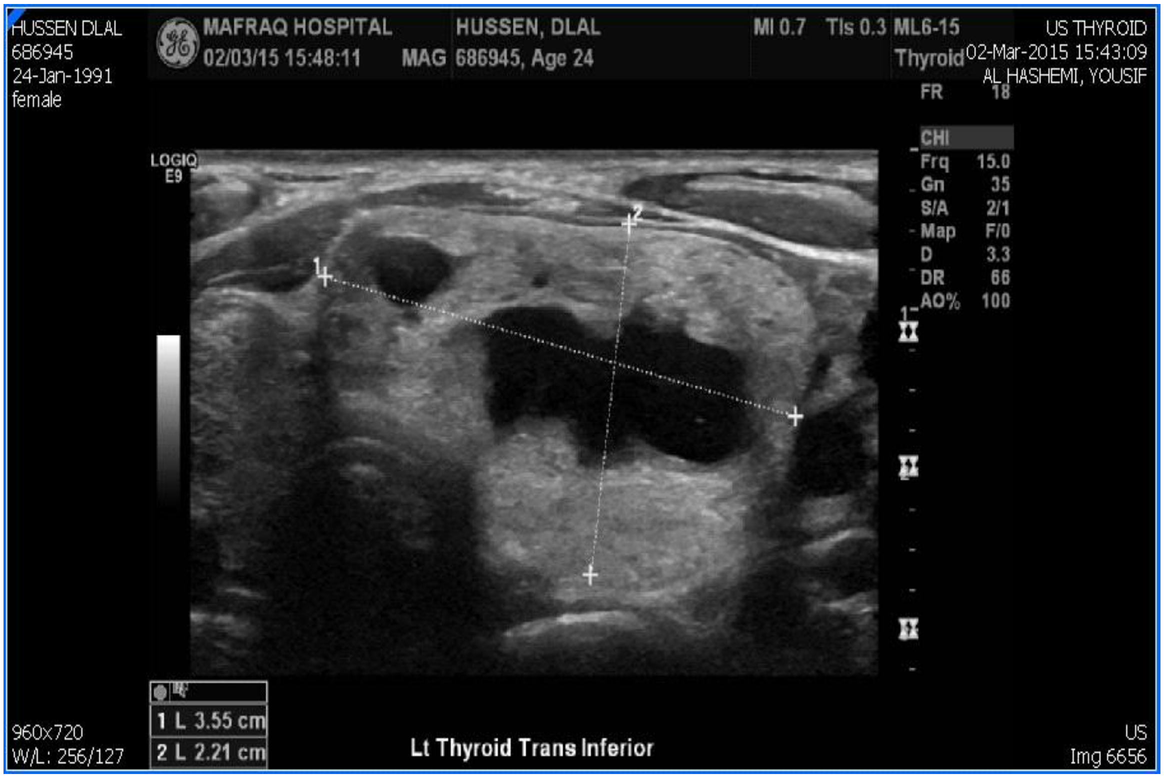
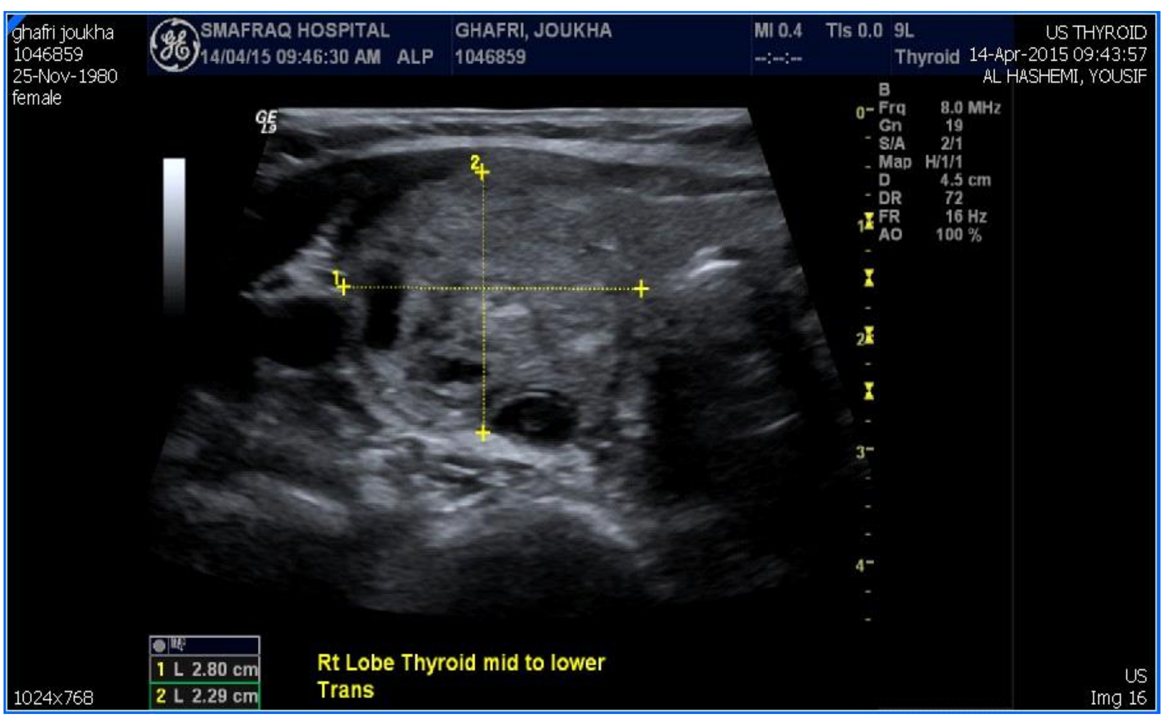


Figure 4 : A 50 , F , patient with multiple nodules , the result of FNAB was negative for malignancy.



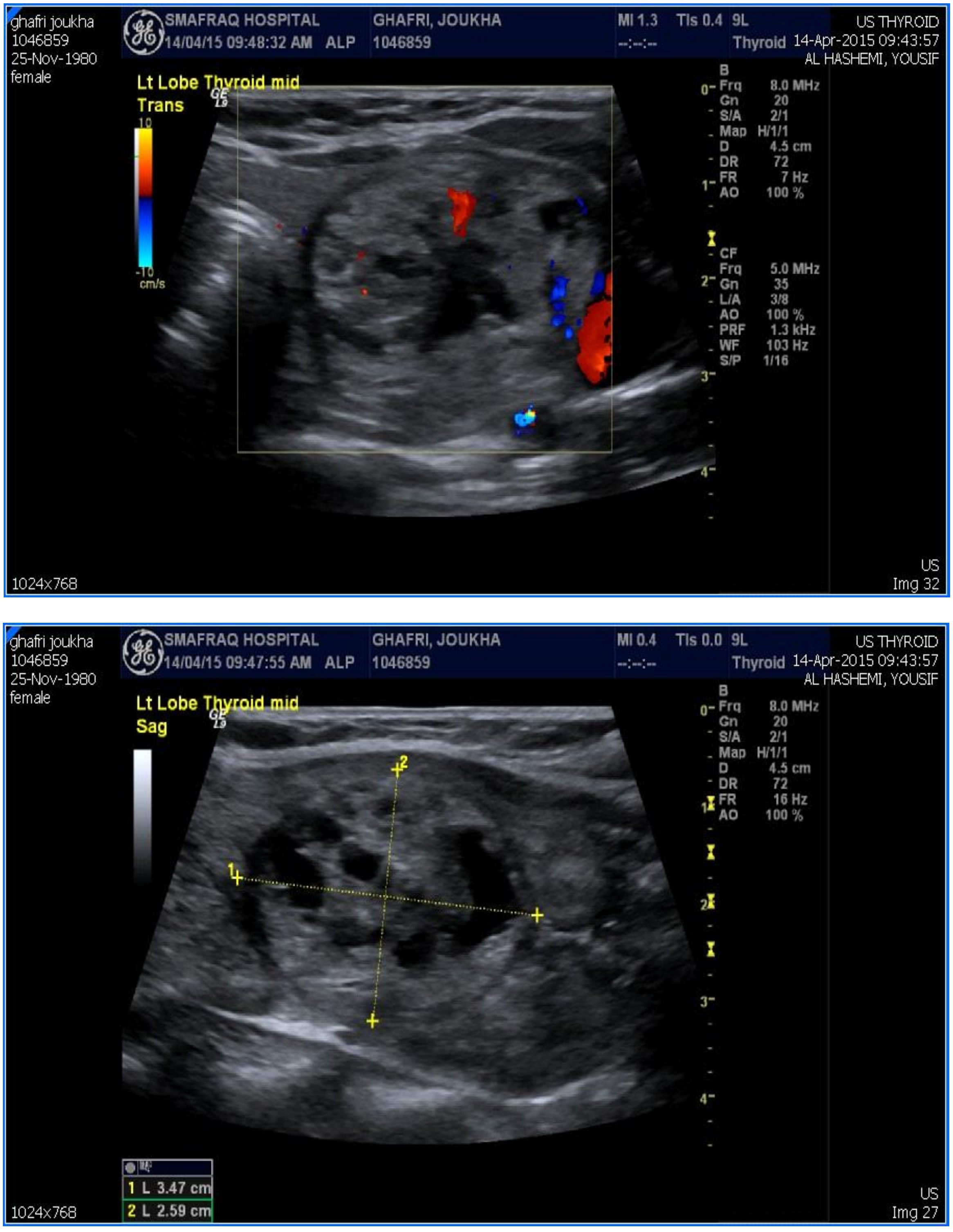
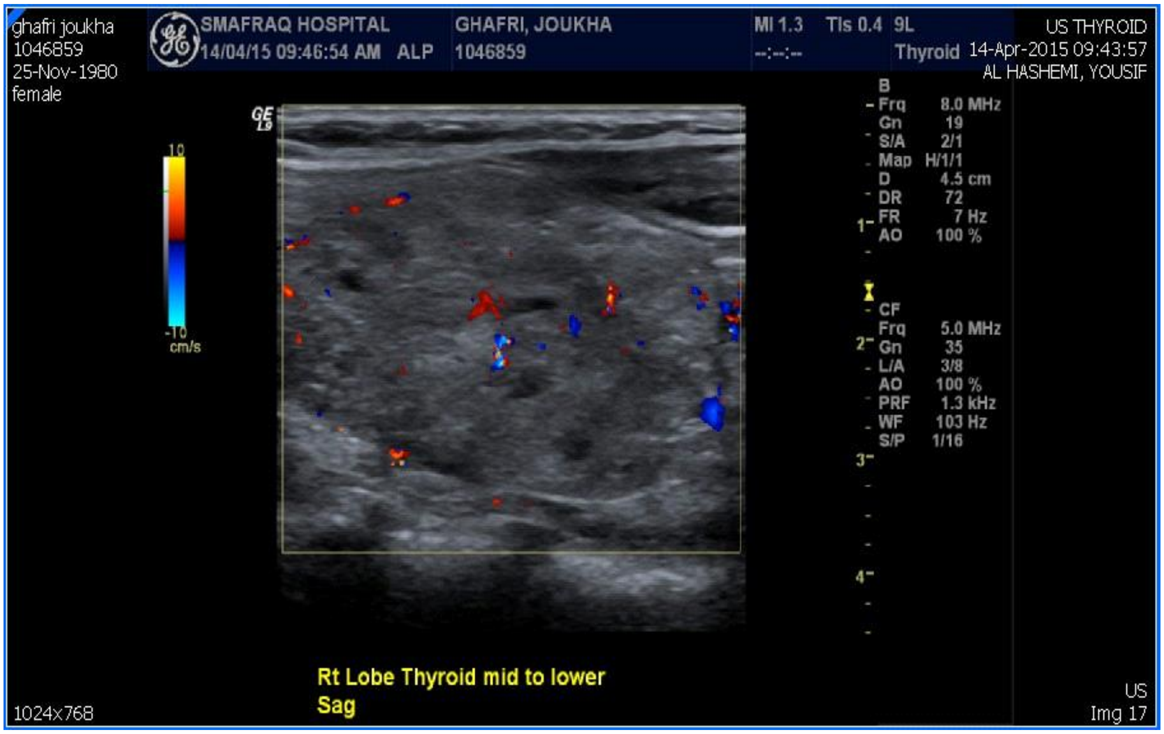
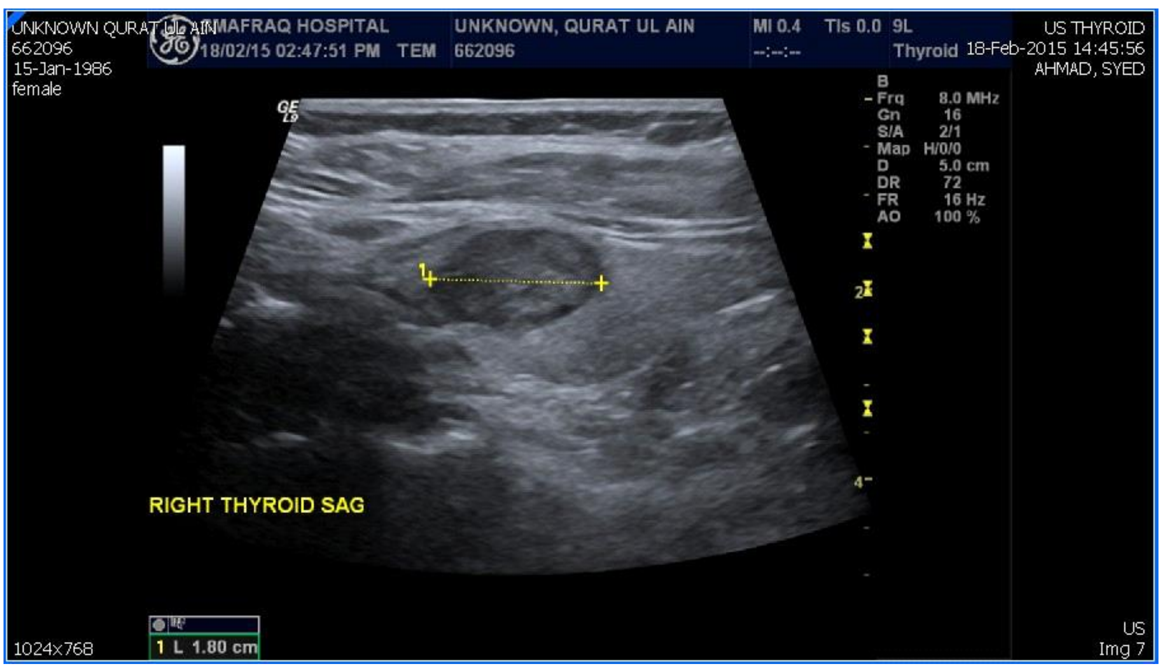


Figure 5 : A 35 , F , patient with multiple nodules , the result of FNAB was negative of malignancy.


ghafri joukha
1046859
25-Nov-1980
female
SMAFRAQ HOSPITAL
14/04/15 09:46:54 AM ALP
GHAFRI, JOUKHA
1046859
MI 1.3 TIs 0.4 9L
Thyroid
US THYROID
14-Apr-2015 09:43:57
AL HASHEMI, YOUSIF
10
-10
cm/s
B
Frq 8.0 MHz
Gn 19
S/A 2/1
Map H/1/1
D 4.5 cm
DR 72
FR 7 Hz
AO 100 %
CF
Frq 5.0 MHz
Gn 35
L/A 3/8
AO 100 %
PRF 1.3 kHz
WF 103 Hz
S/P 1/16
Rt Lobe Thyroid mid to lower
Sag
1024x768
US
Img 17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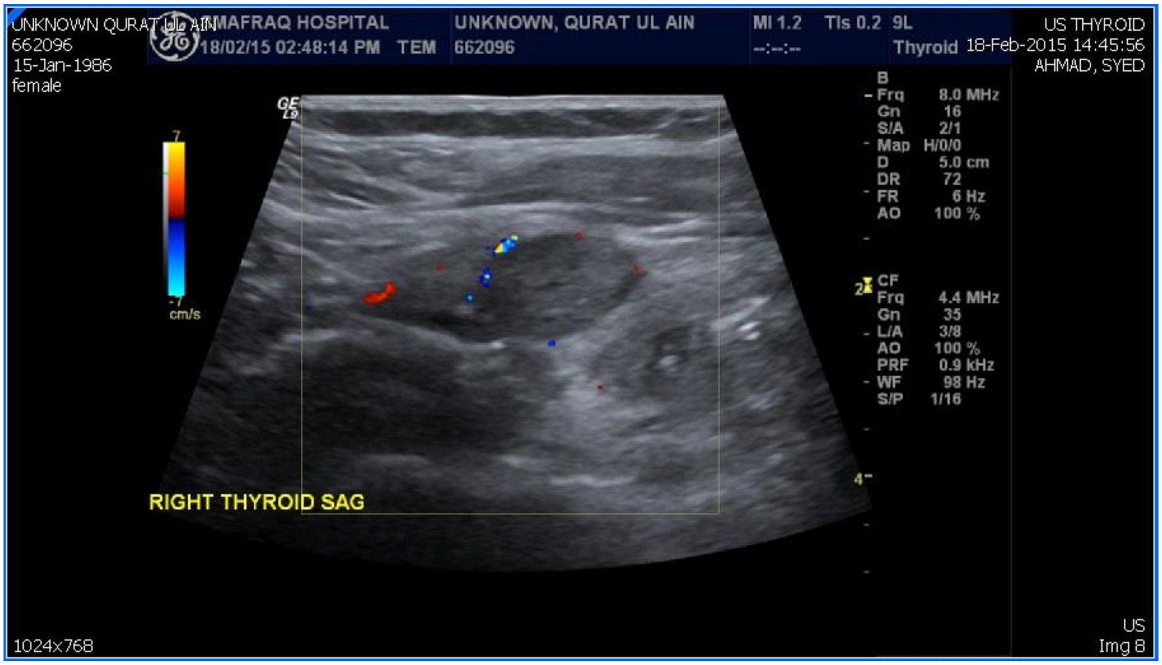
662096
15-Jan-1986
female
SMAFRAQ HOSPITAL
18/02/15 02:47:51 PM TEM
UNKNOWN, QURAT UL AIN
662096
MI 0.4 TIs 0.0 9L
Thyroid
US THYROID
18-Feb-2015 14:45:56
AHMAD, SYED
B
Frq 8.0 MHz
Gn 16
S/A 2/1
Map H/0/0
D 5.0 cm
DR 72
FR 16 Hz
AO 100 %
RIGHT THYROID SAG
1 L 1.80 cm
1024x768
US
Img 7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662096
15-Jan-1986
female
MAFRAQ HOSPITAL
18/02/15 02:48:14 PM TEM
UNKNOWN, QURAT UL AIN
662096
MI 1.2
TIs 0.2
9L
Thyroid
US THYROID
18-Feb-2015 14:45:56
AHMAD, SYED
B
Frq 8.0 MHz
Gn 16
S/A 2/1
Map H/0/0
D 5.0 cm
DR 72
FR 6 Hz
AO 100 %
CF
Frq 4.4 MHz
Gn 35
L/A 3/8
AO 100 %
PRF 0.9 kHz
WF 98 Hz
S/P 1/16
7
-7
cm/s
RIGHT THYROID SAG
1024x768
US
Img 8

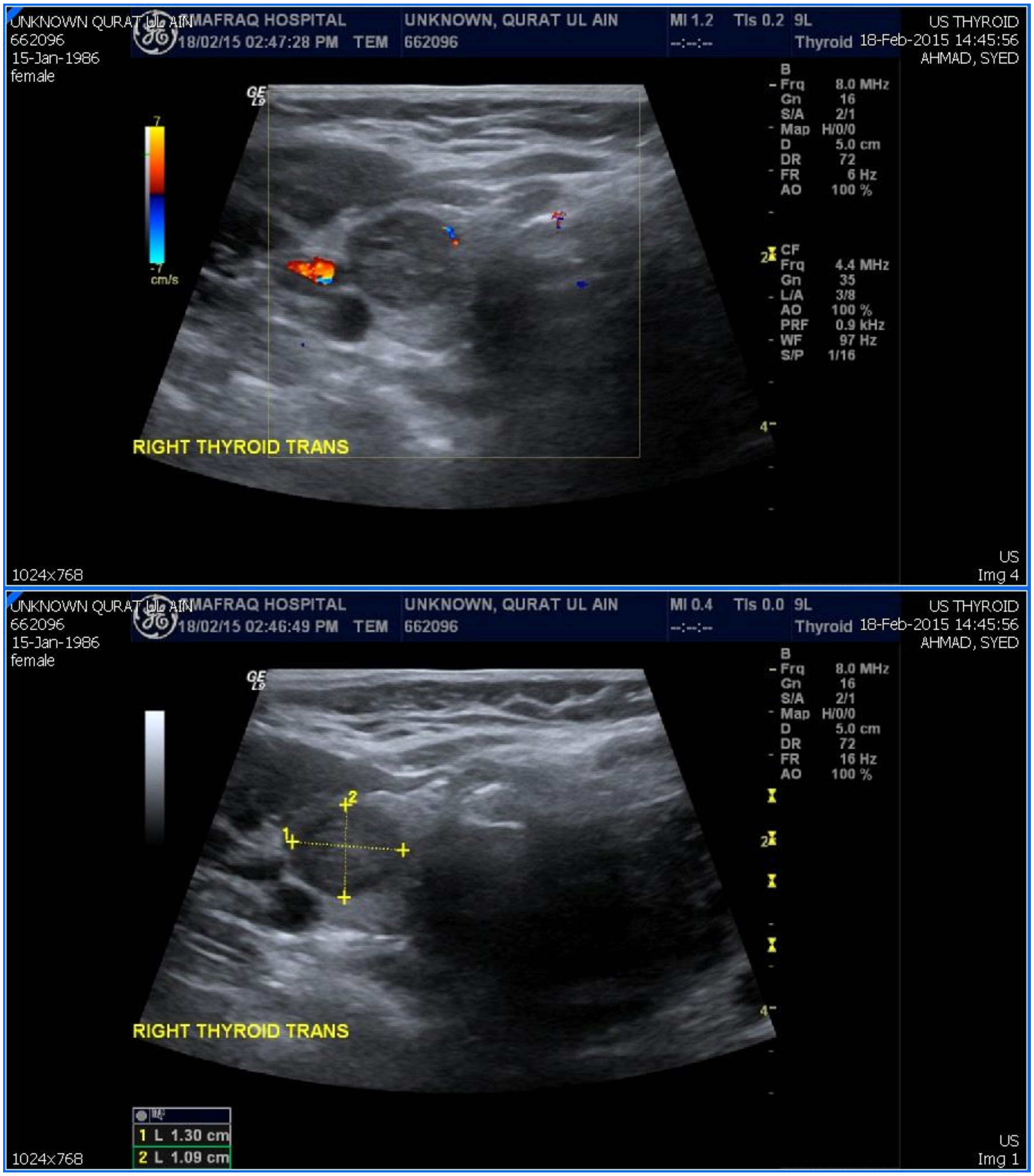
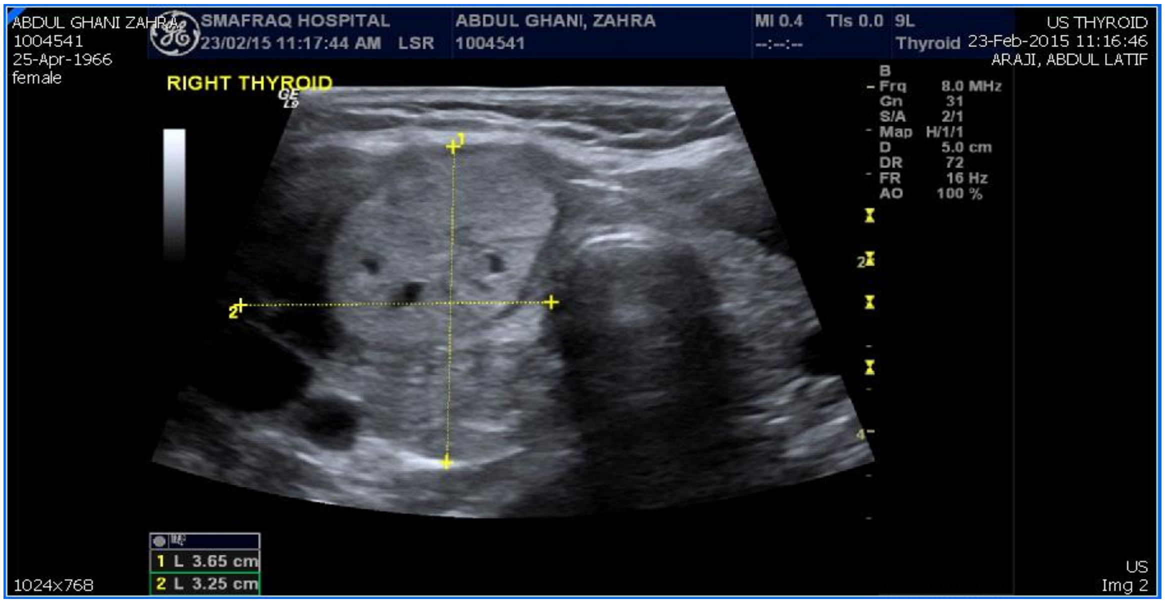


Figure 6 : A 34 , F , patient with multiple nodules , the result of FNAB was positive for malignancy, (papillary carcinoma).



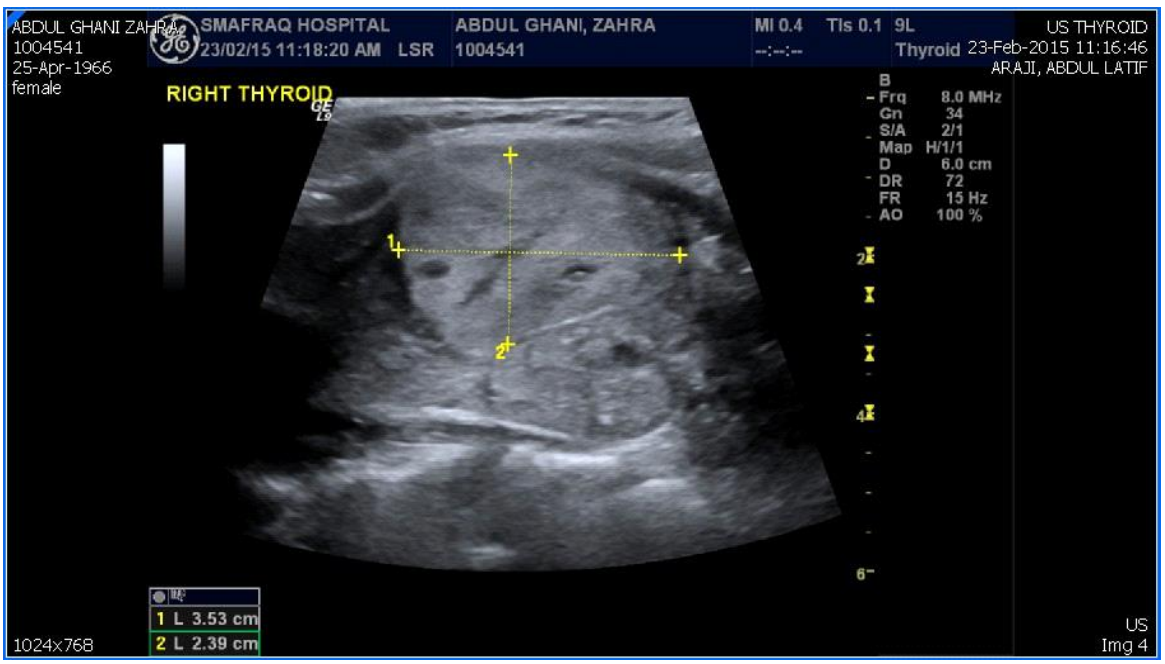


Figure 7 : A 49 , F , patient with multiple nodules , the result of FNAB was positive for malignancy, (papillary carcinoma).

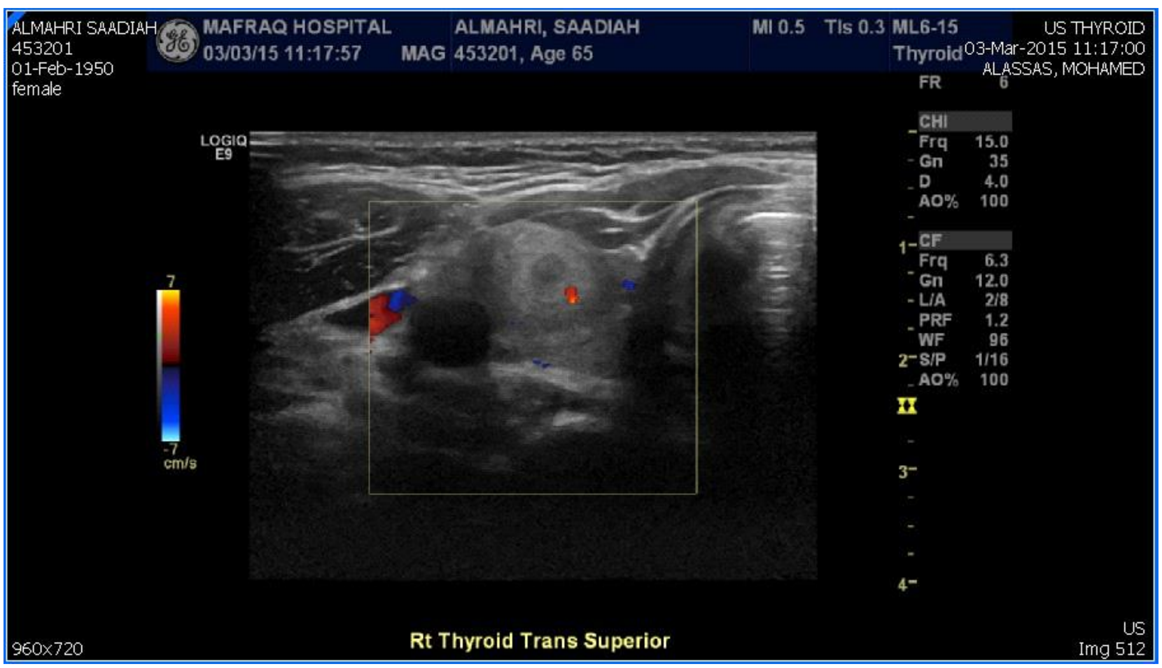


Figure 8 : A 65 , F , patient with multiple nodules , the result of FNAB was positive for malignancy, (folicullar carcinoma).

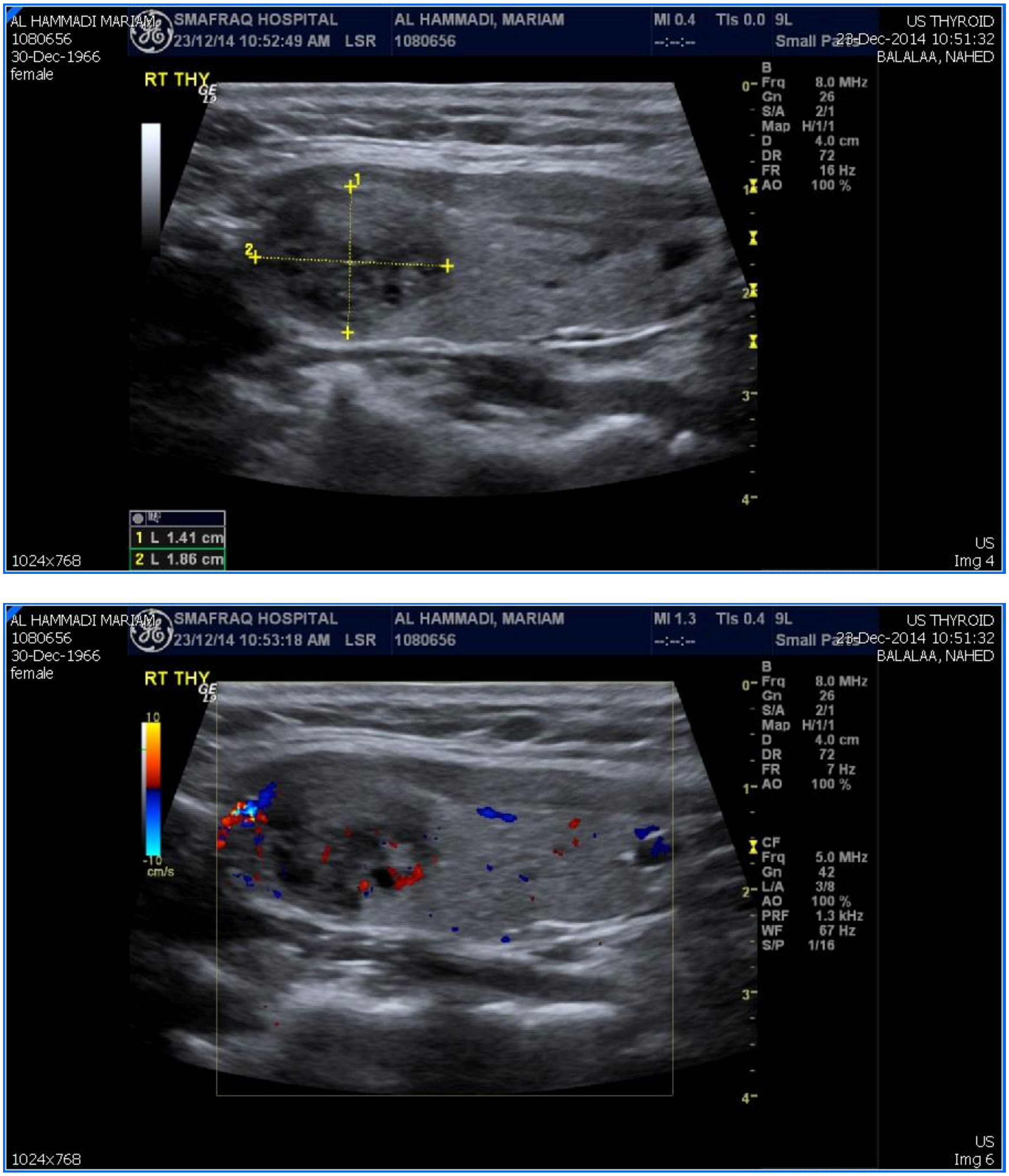


Figure 9 : A 49 , F , patient with multiple nodules , the result of FNAB was positive for malignancy, (papillary carcinoma).

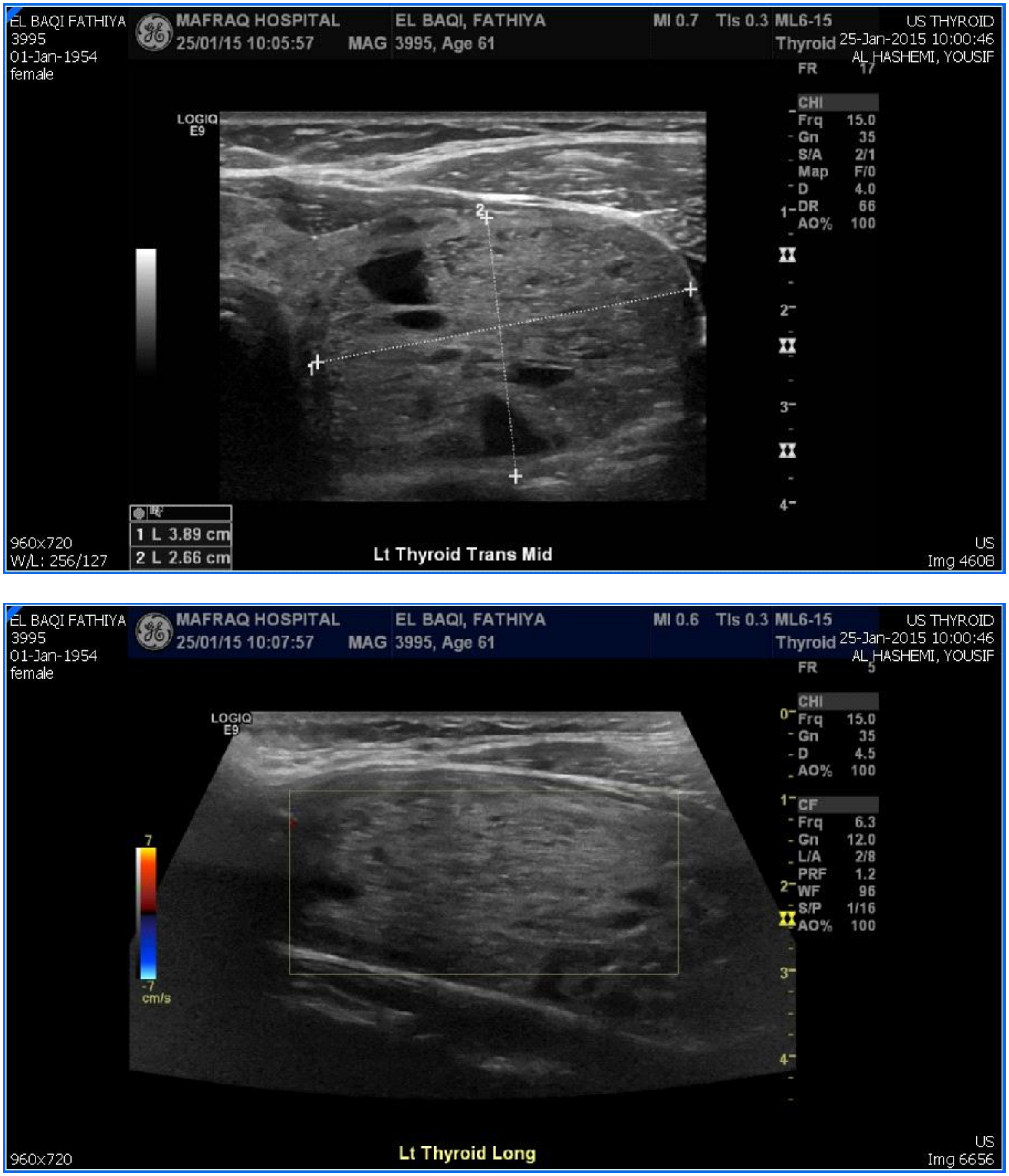


Figure 10 : A 61 , F , patient with multiple nodules , the result of FNAB was positive for malignancy, (folicullar carcinoma).

MASTER DATA SHEET

No.	File No.	Age	Gender	Nodule site			Size		Solitary	Multiple
				Rt lope	Lt lope	Isthmus	0 - 2 cm	> 2 cm		
1	215330	38	F	**1**				1	1	
2	238125	50	F	1				1	1	
3	504450	51	F	1	1.0					1
4	1084945	37	F	1			1			1
5	898721	33	F	1	1		1.0			1
6	1107755	34	M	1	1		1			1
7	58417	67	F	1	1		1.0			1
8	865526	40	F	1			1			1
9	1104340	39	F	1	1.0		1.0			1
10	812023	42	F	1	1			1		1

A vascular	Vascular		Echchotexture			
	Central	periphral	Solid	Cystic	Mixed	Calcifed
1			**1**			**1**
	1				**1**	
		1		**1**		
1					**1**	**1**
1				**1**		
		1		**1**		
		1			**1**	
		1	**1**			
		1			**1**	
		1			**1**	**1**

Echogenecity			lymph nodes involvment	Biopsy result	
Hyperechoic	Hypoechoic	Isoechoic		Benign	Malignant
1					1
1				1	
1				1	
	1				1
	1		1	1	
	1		1	1	
		1		1	
		1		1	
1				1	
	1			1	