

CHAPTER ONE

1.1 INTRODUCTION

Athyroid nodule is a discrete lesion within the parenchyma which can be detected either by palpation or ultrasound (Polyzos, 2007).

Thyroid nodules may be neoplastic or non- neoplastic with neoplastic nodules either benign or malignant. Non neoplastic lesions include simple cysts, haemorrhagic cysts, colloid nodules, hyperplastic nodules and palpable abnormalities related to underlying glandular pathology such as Hashimotos'thyroiditis. Colloid nodules are areas of hyperplasia within the gland which contain enlarged macrofollicles filled with colloid and lined by flattened thyroid epithelial cells eosinophilic due to the abundance of cytoplasmic mitochondria (Eszlinger et al., 2008).

Adenomas differ from hyperplastic nodules in that they are of monoclonal cellular origin and have a thick, well defined capsule. Differentiating follicular adenomas from carcinomas is impossible on cytology and can be difficult on the final histopathological specimen (Rosai, 2011) .

Benign neoplasms are most commonly follicular adenomas or Hurtle cell adenomas. Adenomas are characterised by a thick, fibrous capsule, have uniform cells of ordered architecture with few mitoses and no lymphovascular invasion. Hurtle cell adenomas differ by being extremely Well differentiated carcinomas (>90%) are papillary,

follicular carcinomas and Hurtle cell carcinomas. Anaplastic and medullary carcinomas have a completely different clinical course and treatment. Lymphoma and distant metastases may present as a primary tumour in the thyroid.

The etiology of thyroid nodules is believed to be multifactorial: age, iodine deficiency, sex and irradiation play varying roles (Wang and Lawrence, 1997).

Multinodular goitre is essential, as it is a commonly encountered endocrine problem in clinical practice. The major concern in modern thyroid gland surgery is morbidity. Besides hemorrhage and hyperparathyroidism, damage to the recurrent laryngeal nerve is the complication most feared by both patient and surgeon. It represents a serious complication inducing, when bilateral, serious functional sequelae such as phonatory, respiratory and psychological problems that limit working capacities and social relationships of the patients. Post-operative respiratory complications may need either life saving endotracheal intubation followed by tracheotomy or immediate tracheotomy. Worldwide, multinodular goitre remains a problem of enormous magnitude. It is estimated that no less than 5% of the world's population have goitres. Multinodular goitre (MNG) is more common in women than men and increases in prevalence with

age. The incidence of carcinoma in multinodular goitre has been reported as 5% to 10%. Neither a well formulated nor a simple procedure is available for the management of patients with MNG. The main reason for such situation to exist is, nodular lesions may represent one of the many different cell types that cannot be distinguished from one another without histologic study. These nodules may be benign or malignant. Ultimately, it is this threat of malignancy that poses a major problem (Stalin, 2014).

1.2. Problem statement:

Benign nodular thyroid disease constitutes a heterogeneous thyroid disorder which is highly prevalent in iodine deficient areas. On a general basis it is divided into solitary and multinodular thyroid disease

1.2. Study Objectives:

1.2.1. General Objective:

To assess the goiter using ultrasonography in Omdurman Central Military Hospital.

1.2.2. Specific Objectives:

- To measure the prevalence of multinodular goiter using ultrasonography in Omdurman Central Military Hospital
- To find number of nodule.

- To find out the association between multinodular goiter and selected study variables.

Multinodular goitre is the most prevalent thyroid pathological abnormality worldwide; although its geographical incidence varies greatly according to environmental iodization. Most countries in central and southern Europe have endemic goitre areas with a prevalence of multinodular goitre (MG) of 3-6%. In United States, the annual incidence of nodular thyroid disease is 0.1% to 1.5% and the prevalence is 4-7%. (Rios et al., 2006).

In older studies as in 1950's in Framingham, Massachusetts 1% of persons in the age 30-59 yrs had a multinodular goitre. In Wickham in northeast England, palpable goitres were detected in 10% of adult women and 2% of adult men (Hermus and Huysmans, 2005) .

Multinodular goitre refers to an enlargement of the thyroid with deformation of normal parenchymal structures by the presence of nodules. These nodules vary considerably in size, morphology and function. The development of nodular goitre is very likely a continuous process that starts with thyroid hyperplasia and simple goitre. The main epidemiological determinants are iodine deficiency, age, sex and duration of goitre in iodine deficient and also iodine sufficient areas. Thyroid nodules are discovered by palpation in 3-7% of the population. However on ultrasonography (US) it is noted in 20-76% and by autopsy in approximately 50%. (Gharib and Papini, 2007).

Increasing use of high resolution ultrasonography (HRUSG) over the last two decades has lead to an increasing prevalence of thyroid nodules in asymptomatic subjects. Moreover, 20-48% of patients with single palpable thyroid nodule are found to have additional nodules when investigated by HRUSG. (Chowdhury et al., 2006).

Prevalence increases linearly with age, exposure to ionizing radiation and iodine deficiency. Thyroid nodules are more common in women. (Gharib and Papini, 2007)

1.4. Significance of the study:

This study will provide information about assessment of goitre using ultrasonography which assist the ministry of health to determine the size of the problem.

1.5. Overview of the study:

This study deal with provide an audit of the diagnostic accuracy of multinodular goitre using ultrasonography and guide the development of appropriate, guidelines for management of nodular disease of the thyroid. This may have beneficial clinical impact and allow for better use of hospital resources.

CHAPTER TWO

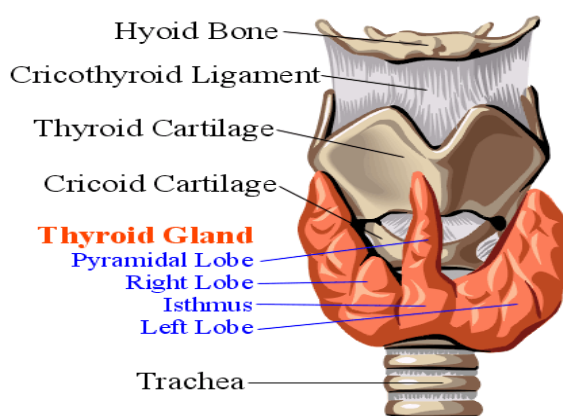
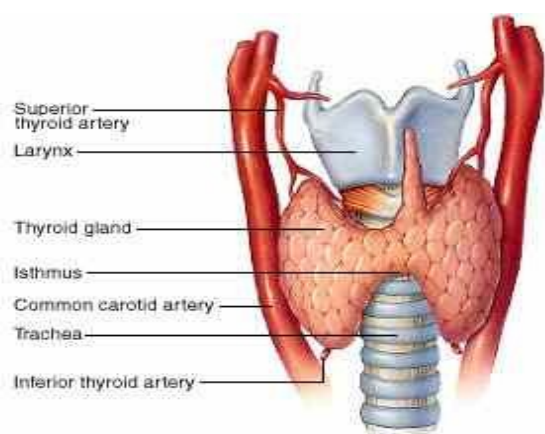
LITERATURE REVIEW

2.1. Anatomy of thyroid nodules:

The normal thyroid gland is a fairly homogenous structure, but nodules often form within its substance. These nodules may be only the growth and fusion of localized colloid-filled follicles, or more or less discrete adenomas, or cysts. Nodules larger than 1 cm may be detected clinically by palpation. Careful examination discloses their presence in at least 4% of the general population. Nodules less than 1 cm in diameter not clinically detectable unless located on the surface of the gland, are much more frequent. The terms adenomatous goiter, nontoxic nodular goiter, and colloid nodular goiter are used interchangeably as descriptive terms when a multinodular goiter is found (Geraldo, 2013).

The thyroid gland consists of two lobes lying on either side of the ventral aspect of the trachea. Each lobe is about 4 cm in length and 2 cm thickness connected together by a thin band of connective tissue called the isthmus. Weighing approximately 20 g, it is one of the largest classical endocrine glands in the body and receives a high blood flow from the superior thyroid arteries (arising from the external carotids) and the inferior thyroid arteries (arising from the subclavian arteries). The gland is so important that it takes more blood per unit

weight than the kidney and sometimes, when there is a goiter, blood flow in the gland may be heard with a stethoscope. The sound is termed a bruit. The functional unit of the thyroid gland is the follicle, a roughly spherical group of cells arranged around a protein-rich storage material called colloid. The follicular cells are orientated with their bases near the capillary blood supply and the apices abutting the colloid.



Adapted from Corel Draw 9

2.2. (BIOS Scientific Publishers Limited, 2001)

2.3. Physiology of nodular thyroid:

The function of the thyroid gland is to act as a pacemaker of metabolism. This function is performed by means of the secretory products of the gland. Kendall in 1914 isolated from the thyroid a

crystalline substance which contained from 60 to 65 percent of iodine. Tyro-substance he called thyroxin (Kendall, 1915).

Kendall was unable at the time of his first work to determine the formula of the substance and it remained to Harrington to show that the compound possessed the formula of $C_{10}H_{11}O_4I$, Kendall in his later work on the action of the substance came to the conclusion that it is the only physiologically active substance made in the thyroid gland. In contrast to Kendall's theory, Sloan believes that the action of the gland depends on the presence of more factors than thyroxine alone. The mechanism by which the colloid is

formed is still under dispute, there being two theories as to its origin, the merocrine and the holocrine. The merocrine type of secretion consists of evacuation of the contents of the cell into the follicle while the cell is not destroyed but regenerates and resumes its function. The holocrine in contrast to the merocrine theory, states that the cell ruptures and its whole structure is used in the production of the colloidal material. The discharge of the hormone of the thyroid into the blood and lymph streams is caused by deficient stimulation rather than an actual nervous stimulation. This has been shown by virtue of the fact that transplants of thyroid tissue devoid of any nervous connection, function efficiently and produce a normal product. We may state then, that the secretion is a result of a deficiency of thyroxine in

the blood and tissue in large enough quantities to promote normal metabolism. The primary function of the thyroid gland that has been found up to the present date is that of regulation of body metabolism. This was first demonstrated by Magnus Levy in 1895 using the newly developed calorimeter by which method he was able to show the heat production to be lowered as much as 40 per cent. Murray in 1891, added another bit of confirming evidence when he treated a case of Gull's disease with glycerin extract of fresh thyroid and was able to maintain the patient in perfect health for twenty-eight years. (Marine, 1937)

2.4. Pathology of thyroid nodules:

Grossly, the thyroid is enlarged and distorted. The size of the lobes differs considerably. The surface of the gland shows a knobby configuration confined by a stretched but intact capsule. The cut surfaces disclose multiple various sized nodules, some of which may be partially or completely encapsulated, others being devoid of capsules and more or less well demarcated from the surrounding parenchyma. Whitish

fibrous bands, sometimes calcified separate the nodules or traverse them. Colloid rich nodules are gelatinous with a yellowish, tanred-brown, translucent appearance. More

cellular nodules appear fleshy or rubbery. Degenerative changes like signs of fresh or old haemorrhage, necrosis with fibrosis, cholesterol deposition, calcifications and cyst formation are common (Ljunberg, 1992).

2.5. Ultrasonography

Thyroid ultrasound US is non-invasive, relatively inexpensive, and can identify nodules not apparent on physical examination, isotope scanning, or other imaging techniques. It should be performed in all patients with a suspected thyroid nodule, a nodular goiter on physical examination, or with nodules incidentally noted on other imaging studies (carotid ultrasound, CT, MRI, or 18fluorodeoxyglucose [FDG]-PET scan).

2.5.1. Ultrasound technique:

- No patient preparation.
- Patient in supine position with neck hyper extended, head may turn away from the side of interest.
- Placed a sponge, pillow, or rolled towel under the patient's shoulder to maintain hyperextension of the neck.
- High resolution, real-time, linear transducer, 7.5-10 MHz_
- 5 MHz recommended for a very muscular or fat neck.
- Doppler color flow imaging__with (low-flow filter, scale, and optimized color gain).

2.5.2. Protocol of ultrasound technique:

Longitudinal scan:



The transducer put on cross section line and slides laterally to the left or right side, the image of scan seen as oval shape this media best for wide size.

Transverse scan:



The transducer put on sagittal line on lower neck and slides laterally to the left or right side, the image of scan appear as elongated shape ,this media seen the anteroposterior and length size of thyroid gland.

Ultrasound appearance:

To assess the thyroid gland the following must be consider:

- The size of the isthmus and thyroid gland.
- The echogenicity of thyroid gland and isthmus by colour Doppler.
- The position of trachea and oesophagus not shift to left or right side.
- The cervical lymph node not enlarges.
- The carotid artery and jugular vein size.
- Muscles of the neck.

Sonographic appearance of the normal thyroid parenchyma has a homogenous medium to high level echogenicity as scrotum parenchyma. The strap (sternohyoid and omohyoid)m muscles are seen as thin hypoechoic band anterior to the thyroid gland (fig) . The sternocleidomastoid muscle is seen as larger oval band that lies lateral to the thyroid. The oesophagus midline structure may appear lateral and usually on the left side, trachea lies on through midline between tow lobes. The common carotid artery posteriolaterl to the lateral lobes of thyroid gland and medial to internal jugular vein if appear well defined, smooth walls with anechoic lumens. The diameter of jugular vein is greater than common carotid artery when pressed by transducer the vein appears smaller than carotid artery.

The parathyroid gland is tow pair of oval shape located postriolateral middle and lower regions of the right and left lateral thyroid lobes, with 2-4 mm diameter. They are not visible. (eMedicine.com).

Thyroid ultrasonography is used to answer questions about the size and anatomy of the thyroid gland and adjacent structures in the neck. Sonographic characteristics of a thyroid nodule associated with a higher likelihood of malignancy include hypoechogenicity, increased intranodular vascularity, irregular margins, micro calcifications, absent halo, and a shape taller than wide measured in the transverse dimension (Leenhardt *et al.*, 1999).

A Papillary Thyroid Cancer (PTC) is generally solid or predominantly solid and hypo echoic, often with infiltrative irregular margins and increased nodular vascularity. Micro calcifications, if present, are highly specific for PTC, but may be difficult to distinguish from colloid. Conversely, follicular cancer is more often iso- to hyper echoic and has a thick and irregular halo, but does not have micro calcifications (Jeh *et al.*, 2007).

Follicular cancers that are <2 cm in diameter have not been shown to be associated with metastatic disease (Machens *et al.*, 2005).

Certain sonographic appearances may also be highly predictive of a benign nodule. A pure cystic nodule, although rare (<2 % of all nodules), is highly unlikely to be malignant (Frates *et al.*, 2006).

A spongiform appearance, defined as an aggregation of multiple microcystic components in more than 50 % of the nodule volume, is 99.7 % specific for identification of a benign thyroid nodule (Moon *et al.*, 2008).

2.5.2. When to Perform Thyroid US

US evaluation is not recommended as a screening test in the general population or in patients with a normal thyroid on palpation and a low clinical risk of thyroid cancer (Grade C; BEL 3)

US evaluation is recommended for (Grade B; BEL 3)

Patients at risk for thyroid malignancy

Patients with palpable thyroid nodules or MNGs

Patients with lymphadenopathy suggestive of a malignant lesion (Weber, 2008).

2.5.3. How to Describe US Findings:

- Report should focus on risk stratification for malignancy.
- Describe position, shape, size, margins, content, echogenic pattern, and vascular features of the nodule(s) For multiple nodules, detail the nodule(s) bearing the US characteristics associated with malignancy (hypo echoic pattern and/or irregular margins, a more-tall-than-wide shape, micro calcifications, or chaotic intranodular vascular spots) rather than describing the largest (“dominant”) nodule suspicious

US criteria greatly increases the risk of thyroid cancer nodules that are hot on scintigraphy should be excluded from FNA biopsy (Weber, 2008).

2.6. Scintigraphy

Thyroid scintigraphy is used to determine the functional status of a nodule. It should be performed in patients with a low serum TSH, indicating overt or subclinical hyperthyroidism. Scintigraphy utilizes one of the radioisotopes of iodine (usually ^{123}I) or technetium-99 m pertechnetate. If available, radioiodine scanning is preferred. Normal thyroid follicular cells take up both technetium and radioiodine, but only radioiodine is organified and stored (as thyroglobulin) in the lumen of thyroid follicles (Reschini *et al.*, 2006).

Both radioisotopes are less avidly concentrated by most benign and virtually all malignant thyroid nodules than adjacent normal thyroid tissue. Patients with nodules that

are functioning on pertechnetate imaging should undergo radioiodine imaging to confirm that they are actually functioning as 5 percent of thyroid cancers concentrate pertechnetate but not radioiodine (Reschini *et al.*, 2006).

2.7. Other Imaging Techniques

MRI and CT should not be used routinely in nodular thyroid disease because they are rarely diagnostic for malignant lesions except in very advanced cases (Shetty *et al.*, 2006, Razek *et al.*, 2008).

MRI and CT may be having value, however, if assessment of size or substernal extension of a nodular goitre is desired for clinical management. CT contrast medium usually contains iodine decreases

subsequent uptake of radioiodine, and may also induce hyperthyroidism, especially in iodine deficient geographic areas (Weber, 2008).

2.8. Previous studies:

Thyroid nodules are extremely common. The first population based report on the incidence of thyroid nodules in the normal population comes from the small town of Framingham, 21 km from Boston, Massachusetts in 1948 (Dawber *et al.*, 1951).

This town was selected for an epidemiology study on CVS disease and included 6600 participants. Palpation of the thyroid gland was part of the clinical examination and results showed that 4.2% of the normal, asymptomatic population had palpable thyroid nodules (6.4% in females, 1.5% in males). The next population study commonly quoted was in Whickham, UK where the prevalence of all types of thyroid disease was assessed. Closely reproducing the results of the Massachusetts study, 5.3% women and 0.8% men

In the normal population had palpable thyroid nodules (Tunbridge *et al.*, 1977).

Later studies have confirmed the rate of palpable nodules to range from 3 – 7% with an average of 5% depending on the iodine deficiency history of the region. (Gharib *et al.*, 2010).

The use of high resolution ultrasound has caused an explosion in the detection of thyroid nodules. The presence of incidental thyroid nodules on ultrasound varies from study to study, ranging from 17– 48%. Improvements in imaging has revealed that up to 48% of patients who were thought to have solitary nodules on clinical examination, in fact have multiple nodules on ultrasound (Ross, 2002) .

Autopsy studies are the gold standard for assessing the true prevalence of thyroid nodules. The first recorded autopsy study was conducted at the Mayo clinic in 1955 by Mortenssen and colleagues. A total of 821 thyroid glands in patients with no clinical thyroid disease were evaluated. 50.5% had thyroid nodules of which 4.2% were malignant (Davies *et al.*, 2010)

Subsequent autopsy studies showed a prevalence of between 37 – 57% (.Thus thyroid nodules are present in at least 50% of the adult population, approximately 5% of asymptomatic individuals will have a palpable nodule and the percentage detected with high resolution ultrasound continues to rise. Without rational criteria regarding fine-needle aspiration biopsy (FNA), ultrasound and surgery, there is a risk of being overwhelmed by this avalanche of thyroid nodules. In sharp contrast to the prevalence of thyroid nodules, thyroid cancer is a rare disease. The annual incidence is 1-2/100000 though this accounts for

90% of the total malignancies of the endocrine system (Hegedus, 2004) .

Most thyroid cancers are well differentiated (90%) with a relatively good prognosis. In fact autopsy studies show that between 5 and 13% of thyroid glands harbour thyroid cancer clinically undetected during the patients' lifetime .(Ward *et al.*, 2007)

The world-wide incidence of thyroid cancer is rising and has almost doubled in the last 30 years but mortality from thyroid cancer has remained unchanged. This may be because small papillary carcinomas of less than 2cm constitute 87% of this rise. In fact the increase may only be due to improvements in the detection of sub clinical and probably insignificant small cancers. These increasing numbers of patients are being subjected to surgery, long term follow up and the psychological burden of a cancer diagnosis. Thus John Cronan in a recent editorial appeals for the research focus to move from the diagnosis of small, impalpable thyroid nodules and shift to identifying the small subset of thyroid cancers that behave aggressively and have a poor prognosis (Cronan, 2008) .

The incidence of goiter, diffuse and nodular, is very much dependent on the status of iodine intake of the population. In areas of iodine deficiency, goiter prevalence may be very high and especially in goiters of longstanding, multinodularity develops frequently. (Geraldo, 2013).

The incidence of multinodular goiter in areas with sufficient iodine intake has been documented in several reports. In a comprehensive population survey of 2,749 persons in northern England, Tunbridge *et al.* found obvious goiters in 5.9% with a female/male ratio of 13:1. Single and multiple thyroid nodules were found in 0.8% of men and 5.3% of women, with an increased frequency in women over 45 years of age (Tunbridge *et al.*, 1977; Beckers and Cornette, 1971)

Routine autopsy surveys and the use of sensitive imaging techniques produce a much

higher incidence. In three reports nodularity was found in 30% to 50% of subjects in autopsy studies, and in 16% to 67% in prospective studies of randomly selected subjects on ultrasound (Tassi *et al.*, 1999).

In Framingham the prevalence of multinodular goiter as found in a population study of 5234 persons over 60 years was 1% (Sawin *et al.*, 1990)

Results from Singapore show a prevalence of 2.8% (Wang *et al.*, 1990).

In an evaluation in 2,829 subjects, living in southwestern Utah and Nevada (USA, between 31 and 38 years) of age, 23% had non-toxic goiter, including 18 single nodules, 3 cysts, 38 colloid goiters and 7 without a histological diagnosis. No mention was made of multinodular

goiters, although some might have been present in the colloid and unidentified group (Rallison *et al.*, 1991).

In general, in iodine sufficient countries the prevalence of multinodular goiter is not higher than 4% (Pinchera *et al.*, 1996).

In countries with previous deficiency that was corrected by universal salt iodination, elderly subjects may have an incidence of, approximatively, 10% of nodular and multinodular goiter, attributed to lack of nutritional iodine in early adult life (Pinchera *et al.*, 1996).

In 2006 Frates *et al* conducted a retrospective study 1985 patients to look at the prevalence of malignancy in multinodular goitres. The study included 1181 patients with a solitary nodule and 804 with multiple nodules. The rate of malignancy was 14.8% in patients who had a solitary nodule and 14.9% in patients with a multiple nodules. Solitary nodules had a higher likelihood of malignancy than each nodule in a multinodular goitre but the overall risk per patient was the same, in their study, up to four nodules greater than 10mm in size and with suspicious US findings were biopsied. It is interesting to note

that only 72.5% of cancers occurred in the largest nodule. (Frates *et al.*, 2006)

Similar results were found in retrospective studies by Gandolphi *et al* (2006) , and Tollin *et al* (2000). In a large prospective study done by Papinni *et al* in Italy, the rate of malignancy was 6.3% for solitary

nodules and 9.2% of patients with multinodular goitre. This was not a statistically significant difference. This study also demonstrated that size criteria to determine which nodule to biopsy detected only 5.8% malignancies whereas using suspicious ultrasound criteria increased the diagnostic rate to 21.7% (Papini *et al.*, 2002) . In the work done by Cappelli *et al* (2006), malignancy was slightly higher in the MNG group than in the solitary nodule group.

Multinodularity can therefore no longer be viewed as decreasing the risk of cancer. The practice of assessing the largest nodule or dominant nodule in a multinodular goitre is not only inaccurate but probably also increases the number of unnecessary procedures performed. Nodules in MNG should be assessed according to the ultrasound characteristics and identified for FNA on the basis of suspicious features and not size alone. More than one nodule may need to be biopsied if these criteria are applied.

CHAPTER THREE

MATERIAL AND METHODS

3. Material and methods:

3.1. Study design:

A descriptive cross sectional design.

3.2. Study area:

Omdurman Central Military Hospital.

3.3 duration of study:

Three month.

3.4. Sample size:

The sample were includes all patients with enlargement of thyroid gland, with more than one nodule palpable or enlarged thyroid gland with nodular surface. Both toxic and nontoxic multinodular goitres were included in the study during a period of 3 months.

3.4. Inclusion criteria:

Enlarged thyroid gland, with more than one nodule palpable or enlarged thyroid gland with nodular surface even toxic and nontoxic multinodular goitres were included in the study.

3.5. Exclusion criteria:

- Patients who will not willing to participate in the study.

- Those having thyroid surgery, medication or any illness affecting thyroid profile.

3.6. **Method of data collection:**

3.6.1. Clinical and laboratory diagnosis:

All newly patients referred to Omdurman Central Military Hospital were recruited for the study during 3 months period. Those having thyroid surgery, medication or any illness affecting thyroid profile were excluded. The patients were interviewed by qualified physician regarding necessary information pertaining to thyroid.

Each patient history was noted on a Performa. It will include age, sex, thyroid age and signs and symptoms associated with thyroid dysfunction. Local examination of thyroid gland was included inspection and palpation of the thyroid and neck. Goitre size was graded according to WHO criteria (grade 0: absent goitre, grade 1: goitre palpable but invisible with neck in a normal position, grade II: goitre visible with neck in a normal position and grade III: large goitre perceptible at a distance).

3.7 Ultra sound:

Machine manufactured by semen's company. colour Doppler with high resolution transducer 7.5-10 MHz.

3.8 **Data analysis:**

Data was analyzed using SPSS version 15.0. Descriptive statistic was used hence chi-square test was applied to test the significance of

difference between two arbitrary groups. A value of $P < 0.05$ was considered significant.

3.9 **Ethical considerations:**

Ethical clearance was obtained from University of Sudan for Technology and Sciences and verbal permission for implementing the study was sought from Omdurman Central Military Hospital. Informed written consent was obtained from participants prior to the study. Privacy, confidentiality and anonymity were guarded. Scientific objectivity of the study was maintained with honesty and impartiality.

CHAPTER FOUR

RESULTS

Table 4-1 One-Sample Statistics of patient's age:

	N	Mean	Std. Error Mean
Age	36	43.5556	2.31539

Fig4-2 Distribution of patients according to age group (n=36)

Table 4-3 Distribution of patients age group according to gender (n=36)

			Age					Total
			< 20	20-30	31-40	41-50	> 50	
Gender	Male	N	0	1	2	0	0	3
		%	.0%	25.0%	22.2%	.0%	.0%	8.3%
	Female	N	1	3	7	11	11	33
		%	100.0%	75.0%	77.8%	100.0%	100.0%	91.7%
Total		N	1	4	9	11	11	36
		%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

P-value considered significant at less than 0.05 levels; P-value=.213 (Not significant)

Fig. 4-4 Distribution of patients according to residence (n=36)

Fig. 4-5 Distribution of patients by gender (n=36)

Fig. 4-6 Distribution symptoms among patients (n=36)

Fig. 4-7 Distribution signs among patients (n=36)

**Fig4-8 Distribution of MNG among patients according to
Ultrasound results (n=36)**

Fig. 4-9 Classification of MNG according to WHO (n=36)

Table 4-10 Association between MNG grades and patients residence

			Classification of MNG according to WHO			Total
			Grade I	Grade II	Grade III	
Residence	Khartoum	N	2	5	6	13
		%	50.0%	31.3%	37.5%	36.1%
	Out of Khartoum	N	2	11	10	23
		%	50.0%	68.8%	62.5%	63.9%
	Total	N	4	16	16	36
		%	100.0%	100.0%	100.0%	100.0%

P-value considered significant at less than 0.05 levels; P-value=.774 (Not significant)

Table 3-11 Association between MNG grades and patients gender

			Classification of MNG according to WHO			
			Grade I	Grade II	Grade III	Total
Gender	Male	N	2	1	0	3
		%	50.0%	6.3%	.0%	8.3%
	Female	N	2	15	16	33
		%	50.0%	93.8%	100.0%	91.7%
Total		N		4	16	16
		%		100.0%	100.0%	100.0%

P-value considered significant at less than 0.05 levels; P-value=.005 (Significant)

Table 4-12 Association between MNG grades and patients age

			Classification of MNG according to WHO			
			Grade ^{HH}	Grade ^Π	Grade ^Ш	Total
Age	< 20	N	0	0	1	1
		%	.0%	.0%	6.3%	2.8%
	20-30	N	0	3	1	4
		%	.0%	18.8%	6.3%	11.1%
	31-40	N	3	5	4	12
		%	75.0%	31.3%	25.0%	33.3%
	41-50	N	1	5	4	10
		%	25.0%	31.3%	25.0%	27.8%
	> 50	N	0	3	6	9
		%	.0%	18.8%	37.5%	25.0%
Total		N	4	16	16	36
		%	100.0%	100.0%	100.0%	100.0%

P-value considered significant at less than 0.05 levels; P-value=.465 (Not significant)

CHAPTER FIVE

DISCUSSION

A descriptive cross sectional study was conducted among 36 patients attended Omdurman Military Hospital during the period of three months started from September -December 2015.

Patients with enlargement of thyroid gland, with more than one nodule palpable or enlarged thyroid gland with nodular surface even toxic and nontoxic multinodular goitres were included in the study.

The findings of the study resulted that; the mean age of patients was 43.5 years with Std. Error Mean of 2.3. More than one third of the patients aged between 31-40 years. Also the study indicated that the majority of patients were females with ratio male: female (1:11). However similar study conducted by Sunil *et al.*, 2011, showed that there were 52 females and four males with age range of 23-63 years (n=56) .

The majority of patients were from out of Khartoum 23 (63.9%) mainly Kordofan and Darfur States and 13(36.1%) were from Khartoum State. This may be because the majority of cases from other Sudan States referred to Khartoum and specialized governmental hospitals such as Omdurman Military Hospital, hence the military hospital served all families of military peoples from all Sudan.

The study revealed that the most symptoms of MNG patients were incidental 9 (25%). The finding of the study in line with other studies showed that; the two most common

complications of thyroid resection include recurrent laryngeal nerve injury and

hypocalcemia. These and other major complications typically occur in less than 5% of the cases.[1,2](#) In the 21st century, thyroidectomy has become safe and effective with improved outcomes and minimal morbidity. (Friguglietti *et al.*, 2003, Koyuneu *et al.*, 2003). This is in part due to the awareness of the anatomical relationship of the parathyroid gland to the thyroid, which is important in preventing postoperative hypocalcemia. Nonetheless, the incidence of hypocalcemia following thyroidectomy remains significantly high in the range of 1.6% to 50%, with permanent hypocalcemia occurring in 1.5% to 4% of the cases. Friguglietti *et al.*, 2003; Kupferman *et al.*, 2002 Regardless of surgeon experience, an incidental parathyroid gland features.

The current study showed that almost the majority of patients signs 29 (80.6%) were resulted in MNG, 4 (11.1%) were solitary nodules, 2 (5.6%) were MNG and metastases and 1 (2.8%) were MNG and lymphadenopathy. Multinodular goitre extending to supra sternal notch in 96 patients (16%), solitary thyroid nodule in 30 patients (5%), simple goitre (2.5%), Multi nodular goitre (1.5%) and Diffuse goitre extending to SSN in 6 patients(1.0%) (mohammed *et al.*, 2012).

The study showed that all patients 36 (100) exposed to ultrasound were diagnosed as MNG. However MNG is said to be endemic when it affects more than 10% of a given population (Studer and Gebel, 1986)

Annual incidence in non endemic regions is 0.1% to 1.5% and prevalence remains between 4 - 6%. Non endemic goiter is more common in women and elderly (Hurley and Gharib, 1996).

The present study indicated that Grade II 16 (44.4%) and Grade III 16 (44.4%) were the common MNG detected among patients followed by Grade IV 4 (11.2%) according to WHO classification. However dissimilar study found that the results of goiter size showed that 42 patients had grade(0) (7%),grade(1) goiters in 390 patients(65 %),, while 168 patients (28 %) presents with grade(2) (mohammed *et al.*, 2012).

Also the study failed to found an association between residence and prevalence of MNG. However other studies succeeded and stated that numerous factors should be considered in the decision making process for the management of thyroid nodules. Particularly, natural history of the lesion, the age and gender of the patient, family history, and the geographic area of the patient's residence provide important clues. However, the pathogenesis of the disease is still debated ^(75, 76). The study proved there was association between Patients gender and MNG. The finding in agreement with Cxıkım *et al.*, 2004. Non endemic goiter is more common in women and elderly (74). An average figure for sex distribution in both endemic and non endemic regions is 3:1 (Female: Male) (Hurley and Gharib, 1996). This finding is typically matched the study results.

The study illustrated that there was no association between patient's age and MNG. MNG was not significantly ($p > 0.05$) prevalent among the age group ranged 31-40 years, 12 933.3%) followed by the age group 41-50 years. Other study consistent to the study stated that Nodules appear early in endemic goiter and later in sporadic goiters

although patient may be unaware of the goiter until his or her late 40s and 50s (Krukowski *et al.*, 2004)

Dissimilar study obtained by Baier *et al.* ([2009](#)) evaluated the US data and the clinical and laboratory characteristics of 944 patients with thyroid nodules and noted an association between malignant solid nodules and patient age younger than 45 years.

CONCLUSION

The study concluded the following;

- Grade II 16 (44.4%) and Grade III 16 (44.4%) were the common MNG detected among patients followed by Grade IV 4 (11.2%) according to WHO classification.
- The vast majority of patients in this study were young females 33 (91.7%) and 3 (8.3%) were males with MNG.

- The most of symptoms prevalent among patients were incidental 9 (25%), airway.
- The majority of patients signs 29 (80.6%) were resulted in MNG, 4 (11.1%) were solitary nodules, 2 (5.6%) were MNG and metastases and 1 (2.8%) were MNG and lymphadenopathy.
- There was association between MNG Grades and patient's gender.

RECOMMENDATIONS

- Active surveillance should be implemented out of Khartoum mainly Kordofan and Darfur States for MNG.

- Ultrasound suggested being valuable for differentiating between nodules types.
- Establishment of nodules centers in the head of Sudan States to facilitate the process of diagnosis and management.
- Additional studies are needed to identify specific risk factors of MNG.

REFERENCES

Baier ND, Hahn PF, Gervais DA, Samir A, Halpern EF, Mueller PR. 2009; Fine-needle aspiration biopsy of thyroid nodules: experience in a cohort of 944 patients. *AJR Am J Roentgenol.* 193(4):1175-9.

Beckers C, Cornette C, 1971: TSH production rate in nontoxic goiter. *J Clin Endocrinol Metab* 32:852.

BIOS Scientific Publishers Limited. Chapter 3 ,2001: The thyroid gland. Bookshelf ID: NBK28.

Cappelli C, Castellno M, Pirola I, Gandssi E, De Martino E, Cumetti D,2006. Thyroid nodule shape suggests malignancy. *European Journal of Endocrinology*; 155:27-31.

Chowdhury S.,Mukherjee S., Mukhopadhyay S,2006: The Thyroid Nodule-Evaluation and Management *J Indian Med Assoc*; 104: 568-573.

Cronan J. Thyroid Nodules: Is it Time to turn off the US Machines? *Radiology* 2008; 247:602-604.

Cxıkim G, Ozan G, Gu Icu F,2004. Toksik multinoduler guatrılı olgularda homosistein duzeyi ve lipid peroksidasyonu. *Firat Tıp Dergisi.* 9:116-119.

Davies L, Ouellette M, Hunter M, Welsh G,2010. The Increasing Incidence of Small Thyroid Cancers: Where Are the Cases Coming From? *The Laryngoscope*;120:2446-2451.

Dawber TR, Gilcin FM, Moore FE, 1951. Epidemiological Approaches to Heart Disease: The Framingham Study. *American Journal of Public Health*;41:279-286.

Dean DS, Gharib H, 2008. Epidemiology of Thyroid Nodules. *J Clin Endocrinol Metab*; 22:901-911.

Eszlinger M, Krohn K, Hauptmann S, Dralle H, Giordano TJ and Paschke R ,2008. Perspectives for Improved and More Accurate Classification of Thyroid Epithelial Tumors. *J Clin Endocrinol Metab*;93: 3286-3294.

Frates MC, Benson CB, Doubilet PM,2006. The Prevalence and Distribution of Carcinoma in Patients with Solitary and Multiple Thyroid Nodules on Sonography. *J Clin Endocrinol Metab*;91:3411-3417.

Friguglietti CU, Lin CS, Kulesar MA,2003. Total thyroidectomy for benign thyroid disease. *Laryngoscope.* ; 113:1820-6.

Gandolfi PP, Frisna A, Raffa M,2004. The Incidence of Thyroid Cancer in Multinodular Goitre: retrospective analysis. *Acta Bio Medica AteneoParmense*;75:114-117.

Geraldo, M.N, 2013. Multinodular Goiter. Thyroid Research Laboratory (LIM-25), University of São Paulo Medical School.

Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L, Vitti P. AACE/AME/ETA ,2010,Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. *Endocrine Practice*;16:Suppl. 1.

Gharib H., Papini E, 2007: Thyroid Nodules: Clinical Importance, Assessment, and Treatment: *Endocrinol Metab Clin N Am*: 36: 707-735.

Hermus A R., Huysmans D A, 2005: Pathogenesis of Nontoxic Diffuse and Nodular goitre in Werner and Ingbar's The Thyroid A Fundamental and Clinical Text . (eds): Braverman L E., Utiger R D 9th ed.,Lippincott Williams & Wilkins Philadelphia, , : 873- 878.

Hurley DL, Gharib H, 1996. Evaluation and management of multinodular goiter. *Otolaryngol Clin N Am*; 29(4): 527-540.

Jeh SK, Jung SL, Kim BS, Lee YS,2007. Evaluating the degree of conformity of papillary carcinoma and follicular carcinoma to the reported ultrasonographic findings of malignant thyroid tumor. *Korean J Radiol.* 8:192-7.

Kendall, E. C,1915. The in the erystalline form of the compound containing iodine which occurs in the thyroid. *Tans. Ass. Am. Phys.* 30:420.

Koyuneu A, Dokmetas HS, Turan M, Aydin C, Karadayi K, Budak E,2003. Comparison of different thyroidectomy techniques for benign thyroid disease. *Endocr J* ; 50:723-7.

Krohn K., Fuhrer D., Bayer,2004-2005. Molecular Pathogenesis of Euthyroid and Toxic Multinodular Goitre. *Endocrine Reviews*, 26: 504-524.

Krukowski Z H. The thyroid and the thyroglossal tract. In: Russell RCG, Williams NS, **Bulstrode CJK (eds).** Bailey and Love's short practice of surgery 24th edition. London; *Arnold*,

Kupferman ME, Mandel SJ, DiDonato L, Wolf P, Weber RS,2002. Safety of completion thyroidectomy following unilateral lobectomy for well-differentiated thyroid cancer. *Laryngoscope* ;112:1209-12.

Leenhardt L, Hejblum G, Franc B, Fediaevsky LD, Delbot T, Le Guillouzie D, 1999. Indications and limits of ultrasound-guided cytology in the management of nonpalpable thyroid nodules. *J Clin Endocrinol Metab*; 84:24-8.

Ljunberg O,1992. Non toxic goiter. In: Biopsy pathology of the thyroid and parathyroid, 12th edition, London: Chapman Hall Medical, p. 75-102.

Machens A, Holzhausen HJ, Dralle H,2005. The prognostic value of primary tumor size in papillary and follicular thyroid carcinoma. *Cancer*; 103:2269-73.

Marine, David,1937. Physiology and interrelations of Gull's disease. J. A. M. A. Vol.104, 2249-2256.

Mohammed, A, S, Nagi I, .A, .Hassanand Khalid, H,2012.

Characterization of radioimmunoassay and diagnostic tools for Goitre in Sudanese. *Ozean Journal of Applied Sciences* 5(2).

Moon WJ, Jung SL, Lee JH, Na DG, Baek JH, Lee YH,2008. Thyroid Study Group, Korean Society of Neuro- and Head and Neck Radiology. Benign and malignant thyroid nodules: US differentiation— multicenter retrospective study. *Radiology*; 247:762-70.

Papini E, Guglielmi R, Bianchini, 2002. Risk of Malignancy in Nonpalpable Thyroid Nodules: Predictive Value of Ultrasound and Color-Doppler Features. *J Clin Endocrinol Metab* ;87:1941-1946.

Pinchera A, Aghini-Lombardi F, Antonangeli L, Vitti P, 1996. Multinodular goiter. Epidemiology and prevention. *Ann Ital Chir* 67:317-325.

Polyzos SA, Kita M, Avramidis A,2007. Thyroid nodules - Stepwise diagnosis and management. *Hormones*;6:101-119.

Rallison ML, Dobyns BM, Meikle AW,1991. Natural history of thyroid abnormalities: prevalence, incidence, and regression of thyroid diseases in adolescents and young adults. *Am J Med* 91:363-370.

- Razek AA, Sadek AG, Kombar OR, Elmahdy TE, Nada N**, 2008. Role of apparent diffusion coefficient values in differentiation between malignant and benign solitary thyroid nodules. *AJNR.Am.J.Neuroradiol*;29:563-568.
- Reschini E, Ferrari C, Castellani M, Matheoud R, Paracchi A, Marotta G**,2006. The trapping-only nodules of the thyroid gland: prevalence study. *Thyroid*; 16:757.
- Rios A., Rodriguez J. M., Moya M R**, 2006: **Association of HLA- C** alleles with Multinodular Goitres- Study in a population from Southeastern Spain. *Arch Surg*, 141, 123-128.
- Rosai, A, 2002**. 10th Edition 2011. Thyroid Gland 448 – 494.
Ross DS. Non palpable Thyroid Nodules – Managing and Epidemic. *J Clin Endocrinol Metab*;87:1938-1940.
- Shambaugh 3rd GE, Quinn JL, Oyasu R, Freinkel N**,1974. Disparate thyroid imaging. Combined studies with sodium pertechnetate Tc 99 m and radioactive iodine. *JAMA*;228:866.
- Shetty SK, Maher MM, Hahn PF, Halpern EF, Aquino SL**,2006. Significance of incidental thyroid lesions detected on CT: Correlation among CT, sonography, and pathology. *AJR. Am. J Roentgenol*; 187:1349-1356.
- Sloan, E. P**,1936. The thyroid. Charles c. Thomas, Baltimore, Kd.
- Stalin , C. R. , Karthick, P. .2014**. Clinical study of multi nodular goitre in a rural hospital. International Journal of Research in Medical Sciences Stalin Raja C et al. *Int J Res Med Sci.*;2(4):1350-1354.

Studer H, Gebel F,1986. Sporadic goiter in: Ingbar SH, Breverman LE (eds). *Werner's The thyroid, A fundamental and clinical text* 5th edition, Philadelphia; *Lippin Lippin Cott*, p. 1311-1315.

Sunil K Menon, Varsha S Jagtap, Vijaya Sarathi, Anurag R Lila, Tushar R Bandgar, Padmavathy S Menon, Nalini S Shah .2011. Prevalence of upper airway obstruction in patients with apparently asymptomatic euthyroid multi nodular goitre. *Indian Journal of Endocrinology and Metabolism*, Vol. 15, No. 6, pp. 127-131

Tassi V, Di Cerbo A, Porcellini A, Papini E, Cisternino C, 1999. Screening of thyrotropin receptor mutations by fine-needle aspiration biopsy in autonomous functioning thyroid nodules in multinodular goiters. *Thyroid* 9:353-357.

Tollin SR, Mery GM, Jelveh N, 2000. The Use of Fine-Needle Aspiration Biopsy Under Ultrasound Guidance to Assess the Risk of Malignancy in Patients with a Multinodular Thyroid Goitre;10:253-242.

Tunbridge VMG, Evered DC, Hall R,1977. The Spectrum of Thyroid Disease in a Community: The Whickham Survey. *Clin Endocrinol*; 7:481-515.

Tunbridge WGM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Evans JG, 1977: The spectrum of thyroid disease in a community: The Whickham survey. *Clin Endocrinol* 7:481.

Wang C, Lawrence MC,1997;. The Epidemiology of thyroid disease and implications for screening. *Endocrin Metab Clin* 26:190-218.

Ward LS, Morari EC, Leite JL, Bufalo NE, Guilhen ACT, Araujo PP,2007. Identifying a Risk Profile for Thyroid Cancer. *Arq Bras Endocrine Metab*;51:713-722.

Weber AL, Randolph G, Aksoy FG, 2000. The thyroid and parathyroid glands: CT and MR imaging and correlation with pathology and clinical findings. *Radiol Clin North Am*; 38:1105-1129.

Appendix 1: Standardized Proforma

Personal Details

Thyroid Data Sheet

Patient name

Gender

Age.....

Symptoms:

1. Incidental
2. Airway
3. Dysphagia
4. Systemic/LOW
5. Voice Change
6. Nil

Signs:

1. Solitary Nodule
2. MNG
3. Lymphadenopathy
4. Metastases

Ultrasound Report:

1. MNG
2. Dom nod MNG (Susp)
3. Solitary Nodule (Not sups)

4. Solitary Nodule (Sups)

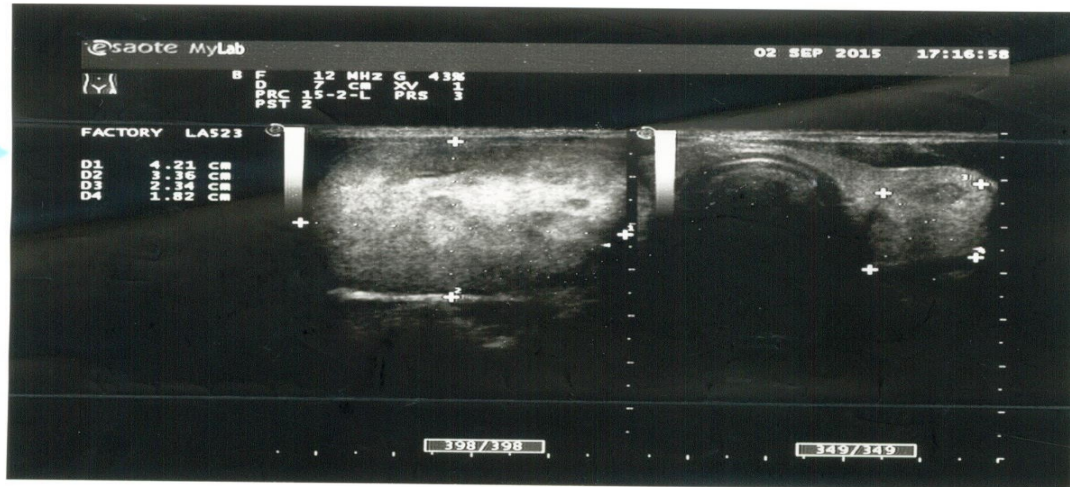
5. Size SN or DN in MNG

***Investigations results:* (classification of multindural goiter according to WHO):**

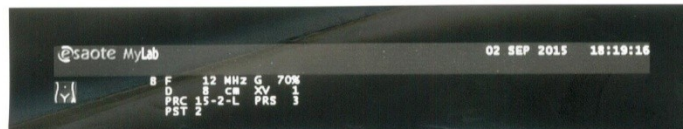
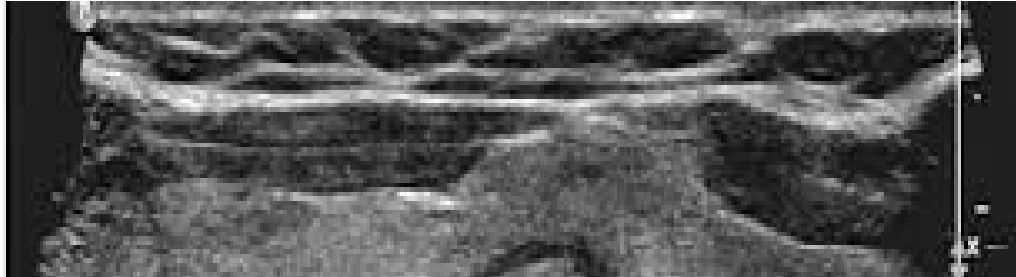
Grade 1

Grade II

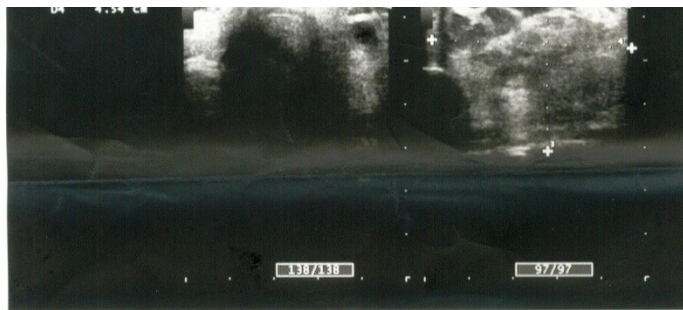
Grade ⇒ ⇒ ⇒

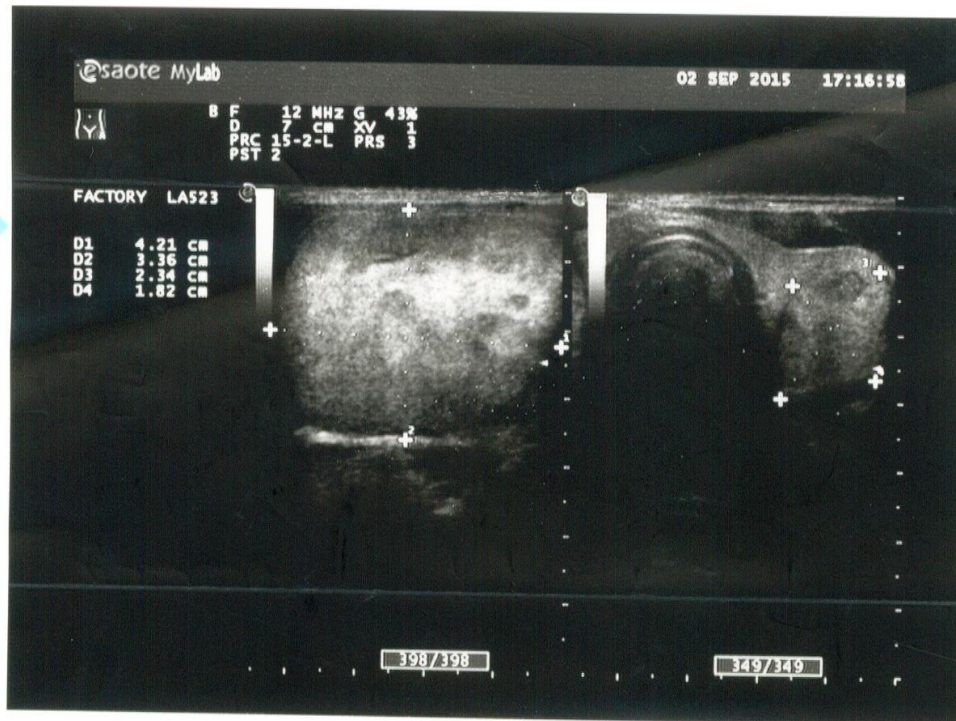


Female 45 years old complained of palpable tumour front of her neck



Male 36 years old have athyroid giotre





Female 55 years old have multiple nodular



Female 70 years old have thyroid giotre