

**Sudan University of Science and Technology**

**College of Graduate Studies**

**Classification of Thyroid Abnormalities among  
Patients Referred To the Radiation and Isotope  
Centre of Khartoum (RICK) For Thyroid Scan  
and Uptake**

تصنيف أمراض الغدة الدرقية في المرضى المحولين إلى مركز الخرطوم للعلاج  
بالأشعة والطب النووي لإجراء مسح ذري للغدة الدرقية

**A Study Submitted for Partial Fulfillment of the  
Requirements of M.Sc Degree in Nuclear Medicine  
Technology**

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الآية

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قال تعالى:

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صدق الله العظيم

سورة العلق

الآيات (1-5)

## DEDICATION

***To***

*My parents...*

*My husband...*

*My brothers ...*

*My friends ...*

*And my teachers ...*

And to all those who encouraged me to do this research, I dedicate this  
work.

## **Acknowledgment**

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## **Abstract**

The main objective of this research was to classify the thyroid abnormalities among patients referred to Radiation and Isotope Centre of Khartoum (RICK) for thyroid scan and uptake. The data was collected by using special data collecting paper among 200 patients referred to nuclear medicine department at RICK for thyroid scan and uptake, who constituted the research population . The study was conducted during a period of three months from March 2017 to May 2017, which constituted the same period during which the patients were referred.

Distribution of the study population according to gender revealed that: a percentage of 85% of the sample population were females and 15% were males.

Distribution of the study population according to age revealed that:

19 patients were < 20 years old (9% of all patients), 116 at the age of 21-40 years old (58%) , 58 patients were 41-60 years old (29%), 6 patients were of 61-80 years old (3%), and only 1 patient at the age category of 81-100 years old (0.5% of all patients).

The frequency distribution of thyroid disorders was as follows: 46 patients with multinodular goitre (MNG)( represented 23%) , 19 patients with moderate diffuse goitre( represented 9%), Graves' disease appeared on 51 patients, 31 patients with mild diffuse goitre( represented 15%), cold nodules were 37 cases( represented 19%), 5 cases of toxic adenoma (represented 3%),7 cases of hypothyroidism (represented 4%), and 4 patients with thyroiditis( represented 2%).

The percentage distribution of the thyroid disorders showed that the most common thyroid abnormalities among the study population was Graves'

disease which represented 25% of cases. The lower common thyroid disease among the study population was thyroiditis which represented 2% of the study population.

The study has come out with some recommendations and proposals which could be useful for nuclear medicine practice.

The results may also constitute a baseline for putting a map for thyroid disorders in Sudan as general.

A future studies in this field is greatly encouraged.

## ملخص الدراسة

الهدف الأساسي من هذه الدراسة هو تصنيف أمراض الغدة الدرقية في المرضى المحولين إلى مركز الخرطوم للعلاج بالأشعة والطب النووي لعمل مسح ذري للغدة الدرقية. عدد المرضى الذين شملتهم الدراسة 200 مريضا و مريضة تم تحويلهم إلى قسم الطب النووي بمركز الخرطوم للعلاج بالأشعة والطب النووي لعمل مسح ذري للغده الدرقية في ثلاثة أشهر هي الفترة من مارس 2017 إلى مايو 2017 واستغرقت الدراسة نفس الفترة المذكورة. البيانات المتضمنة في الدراسة هي تحديد نسبة كل مشكله من مشاكل الغدة الدرقية والفئات العمرية الأكثر تعرضا لها ونسبة إصابة الرجال إلى النساء. وقد خلصت الدراسة إلى أن النساء هن الأكثر إصابة بمشاكل الغدة الدرقية حيث بلغت نسبة النساء المصابات 85% بينما كانت نسبة الرجال المصابين 15%.

أما بالنسبة للفئات العمرية فكان تصنيفها كالآتي: 19 مريضا كانت أعمارهم أقل من عشرين عاما ويمثلون نسبة 9% من إجمالي المصابين، 116 مريضا تراوحت أعمارهم بين 21-40 سنة ويمثلون 58% وهي الفئة العمرية الأكثر إصابة، 58 مريضا تراوحت أعمارهم بين 42-60 عاما بنسبه بلغت 29%، 6 مرضى تراوحت أعمارهم بين 61-80 عاما ومثلوا نسبة 3% من المصابين، وكان هناك مريض واحد فقط في الفئة العمرية 81-100 عام بنسبة 1% من المصابين بمشاكل الغدة الدرقية.

خرجت الدراسة ببعض التوصيات والمقترحات التي يمكن أن تكون مفيدة في ممارسة الطب النووي. النتائج التي توصلت إليها الدراسة قد تشكل أساسا لوضع خريطة تبين اضطرابات الغدة الدرقية في السودان بشكل عام.

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## **List of Abbreviations**

RICK	Radiation and Isotope Centre of Khartoum
MNG	Multi-nodular Goitre
T3	Triiodothyronine
T4	Thyroxin
TSH	Thyroid Stimulating Hormone
TG	Thyroglobulin
TPO	Thyroid Peroxidase
HLA	Human Leukocyte Antigen
TSI	Thyroid Stimulating Immunoglobulin
TGI	Thyroid Growth-stimulating Immunoglobulin
MEN	Multiple Endocrine Neoplasia

# **Chapter One**

## **Introduction**

# Chapter One

## Introduction

### 1.1 Preamble

The thyroid gland consists of right and left lobes connected by a narrow isthmus.

It's a vascular organ surrounded by a sheath derived from the pre-tracheal layer of deep fascia. The sheath attaches the gland to the larynx and the trachea.

Each lobe is pear shaped, with its apex being directed upward as far as the oblique line on the lamina of the thyroid cartilages; its base lies below at the level of the fourth or fifth tracheal ring.

The isthmus extends across the midline in front of the second, third, and fourth tracheal rings.

A pyramidal lobe is often present, and it projects upward from the isthmus, usually to the left of the midline. a fibrous or muscular band frequently connects the pyramidal lobe to the hyoid bone ; if its muscular, it is referred to as the levator glandulae thyroideae.

Blood Supply:

The arteries to the thyroid gland are:

A. The superior thyroid artery

B. The inferior thyroid artery and sometimes the thyroidea ima.

The arteries anastomose profusely with one another over the surface of the gland.

The superior thyroid artery, a branch of the external carotid artery, descends to the upper pole of each lobe, accompanied by the external laryngeal nerve.

The inferior thyroid artery, a branch of the thyrocervica; trunk, ascends behind the gland to the level of the cricoid cartilage. It then turn medially and downward to reach the posterior border of the gland.

The veins from the thyroid gland are:

- The superior thyroid, which drains into the internal jugular vein.
- The middle thyroid, which drains into the internal jugular vein.
- The inferior thyroid.

The latter vein receives its tributaries from the isthmus and the lower poles of the gland.

The inferior thyroid veins of the two sides anastomose with one another as they descend in front of the trachea. They drain into the left brachiocephalic vein in the thorax.

Lymph Drainage:

The lymph from the thyroid gland drains mainly laterally into the deep cervical lymph nodes. A few lymph vessels descend into the Para tracheal nodes.

Development of the Thyroid Gland:

The thyroid gland develops as an endodermal outgrowth from the midline of the floor of the pharynx, between the tuberculum impar and the copula. Later, this thickening becomes a diverticulum called the thyroglossal

duct. As development continues, the duct elongates and its distal end becomes bilobed.

The duct becomes a solid cord and migrates down the neck, passing anterior to through or posterior to the developing hyoid bone, by the seventh week it reaches its final position in relation to the larynx and the trachea. Meanwhile, the solid cord connecting the thyroid gland to the tongue breaks up and disappears. The site of origin of the thyroglossal duct on the tongue remains as a pit called the foramen cecum.

As a result of epithelial proliferation, the bilobed terminal swellings of the thyroglossal duct expand to form the thyroid gland.

Congenital anomalies:

Agenesis of the thyroid gland may occur and is the most common cause of cretinism.

Incomplete descent of the thyroid gland may occur, and the thyroid may be found at any point between the base of the tongue and the trachea.

Lingual thyroid is the most common form of incomplete descent.

A thyroglossal cyst may appear during childhood or adolescent or in young adults.

It is caused by persistence of segment of the thyroglossal duct. Such a cyst occurs in the midline of the neck at any point along the thyroglossal tract

Richard S. Snell (2000)

The thyroid secretes two major hormones, thyroxin and triiodothyronine, commonly called T4 and T3, respectively. Both of these hormones profoundly increase the metabolic rate of the body. Complete lack of thyroid secretion usually causes the basal metabolic rate to fall 40 to 50



per cent below normal, and extreme excesses of thyroid secretion can increase the basal metabolic rate to 60 to 100 per cent above normal. Thyroid secretion is controlled primarily by thyroid-stimulating hormone (TSH) secreted by the anterior pituitary gland.

The thyroid gland also secretes calcitonin, an important hormone for calcium metabolism.

### Synthesis and Secretion of the Thyroid

#### Metabolic Hormones:

About 93 per cent of the metabolically active hormones secreted by the thyroid gland are thyroxin, and 7 per cent triiodothyronine. However, almost all the thyroxin is eventually converted to triiodothyronine in the tissues, so that both are functionally important. The functions of these two hormones are qualitatively the same, but they differ in rapidity and intensity of action. Triiodothyronine is about four times as potent as thyroxin, but it is present in the blood in much smaller quantities and persists for a much shorter time than doe's thyroxin. (Guyton & Hall 2006).

## **1.2 Problem of the study**

There is no records about the classification of thyroid abnormalities among patients referred to Radiation and Isotope Centre of Khartoum (RICK) For Thyroid Scan and uptake through radionuclide images reports, to the best of the researcher's knowledge.

## **1.3 Objectives of the study**

### **1.3.1 General Objective:**

Classification of thyroid abnormalities among patients referred to radiation and isotope centre of Khartoum (RICK) for thyroid scan and uptake.

### **1.3.2 Specific Objectives:**

-To provide information about the classification of thyroid abnormalities among patients referred to radiation and isotope centre of Khartoum (RICK) for thyroid scan and uptake.

-To assist specialized authorities in making treatment plans according to these information.

-To classify the thyroid diseases among the referred patients according to gender, age and types of disease.

-To determine the most common and the less common thyroid disorders among the study population.

## **1.4 Thesis Overview**

The research was organized into the following chapters:

Chapter one dealt with the introduction about thyroid gland, problem of the study, general and specific objectives of the study and thesis overview.

Chapter two highlighted the literature review. Chapter three dealt with the materials and methods of the study. Chapter four tackled the results and discussion. Chapter five handled the conclusion, recommendations, references and appendices.

**Chapter Two**  
**Literature Review**

## **Chapter Two**

### **Literature Review**

#### **2.1 Theoretical background:**

##### **2.1.1 Anatomy of the thyroid gland:**

The thyroid is the largest single endocrine gland. It weighs 20-25 g but it varies with age, sex and physiological condition, such as pregnancy and lactation.

The thyroid gland is the only endocrine gland that does not store its hormone within the cell but in follicular cavities surrounded by the cells.

The main histological feature is the thyroid follicle, which is a spherical structure formed of a single layer of epithelial cells, which surround a cavity filled with colloid material. The type of epithelial cells forming the follicles varies according to the activity of the gland.

With normal activity the cells are cubical. With increased activity they become flat cells. The quantity of colloid material in the cavity of the follicle also varies with the activity of the gland. A few clear cells or C cells may be seen in the walls of the follicles but they have no contact with the cavity of the follicle. They are therefore also referred to as the parafollicular cells. They produce the hypocalcaemia hormone, calcitonin. (Sukkar et al 2000)

The thyroid gland is one of several glands that make up the endocrine system the thyroid gland is a small, butterfly - shaped gland found just below the Adam's apple at the base of the neck, and in front of the trachea. The gland is controlled by pituitary gland makes thyroid - stimulating hormone(TSH). The TSH stimulates thyroid gland to make thyroid hormone. (Rice, 2003)

The primary function of the thyroid is production of the hormones thyroxin ( $T_4$ ), triiodothyronine ( $T_3$ ), and calcitonin. Up to 80% of the  $T_4$  is converted to  $T_3$  by peripheral organs such as the liver, kidney and spleen.  $T_3$  is about ten times more active than  $T_4$ .

High or low TSH is usually secondary to thyroid disease. In hyperthyroidism and thyrotoxicosis the TSH levels are found to be low due to the negative feedback of the excess  $T_3$  and  $T_4$ . In hypothyroidism the levels of TSH are high due to diminished thyroid hormone and therefore absence of the negative feedback (Van Herle et al, 1982).

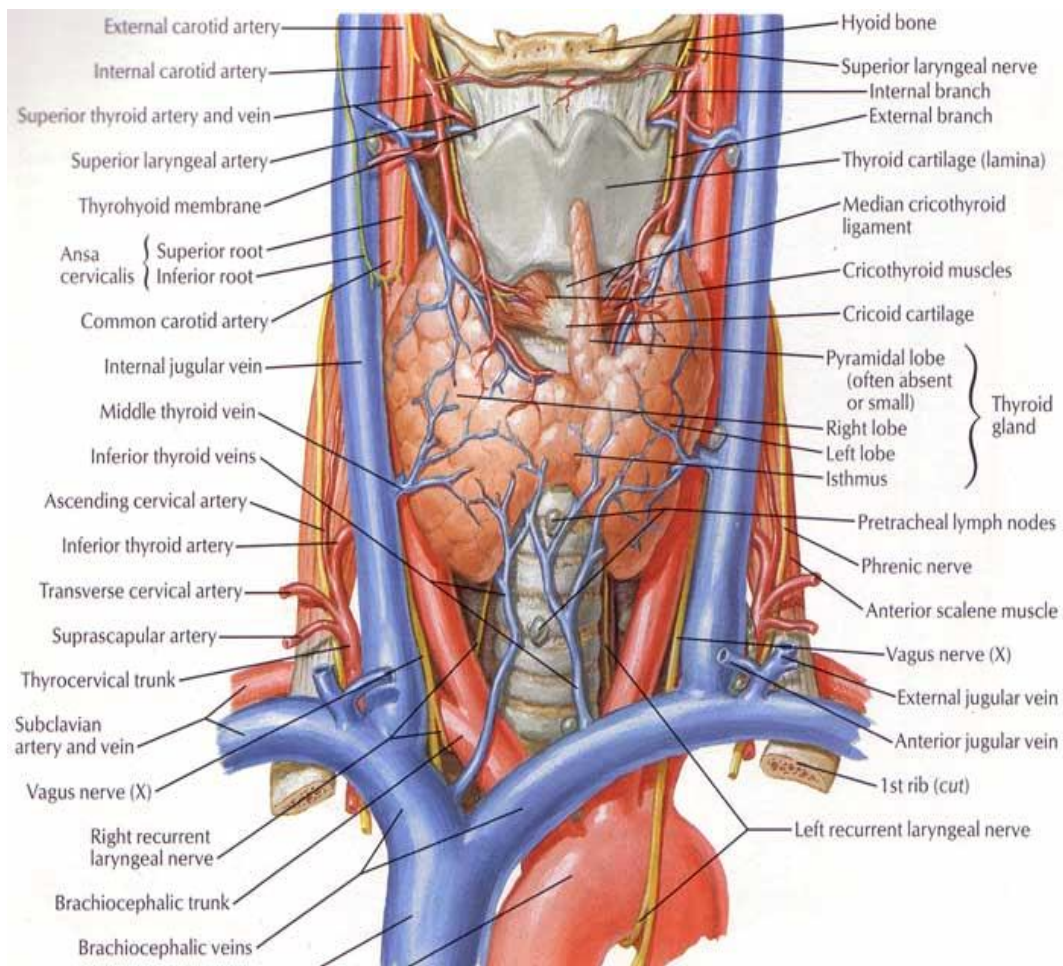


Figure 2.1 shows anatomy and blood supply of the thyroid gland

## **2.1.2 Physiology of the thyroid gland**

### **2.1.2.1 T<sub>3</sub> and T<sub>4</sub> production and Action:**

Thyroxin is synthesized by the follicular cells from free tyrosine and on the tyrosine residues of the protein called thyroglobulin (TG). Iodine is captured with the " iodine trap " by the hydrogen peroxide generated by the enzyme thyroid peroxidase (TPO) and linked to the 3` and 5` sites of the benzene ring of the tyrosine residues on TG, and on free tyrosine. Upon stimulation by the thyroid - stimulating hormone (TSH), the follicular cells reabsorb TG and proteolytically cleave the iodinated tyrosine from TG, forming T<sub>4</sub> and T<sub>3</sub>(in T<sub>3</sub> one iodine is absent compared to T<sub>4</sub>), and releasing them into the blood. Deiodinase enzymes convert T<sub>4</sub> to T<sub>3</sub>. Thyroid hormone that is secreted from the gland is about 90% T<sub>4</sub> and about 10% T<sub>3</sub>.

Cells of the brain are a major target for the thyroid hormones T<sub>3</sub> and T<sub>4</sub> l. Thyroid hormones play a particularly crucial role in brain development during pregnancy (Van Herle et al, 1982)

### **2.1.2.2 Action of thyroid hormones:**

- Increase metabolism and protein synthesis.
- Necessary for growth and development in children including mental development and attainment of sexual maturity.

## **2.3 Pathology of the Thyroid gland:**

### **2.3.1 Hyperthyroidism**

Thyrotoxicosis is a hypermetabolic state caused by elevated circulating levels of free T<sub>3</sub> and T<sub>4</sub>. Because it is caused most commonly by hyperfunction of the thyroid gland, it is often referred to as hyperthyroidism. However, in certain conditions the oversupply is related

either to excessive release of preformed thyroid hormone (e.g., in thyroiditis) or to an extrathyroidal source, rather than to hyperfunction of the gland. Thus, strictly speaking, hyperthyroidism is only one (albeit the most common) category of thyrotoxicosis.

The clinical manifestations of thyrotoxicosis are truly protean and include changes referable to the hypermetabolic state induced by excess thyroid hormone as well as those related to overactivity of the sympathetic nervous system.

Hyperthyroidism could be treated in three ways: medical therapy with anti-thyroid drugs, radioiodine therapy and surgery (Francklyn, 1996).

In many clinics, radioiodine treatment is the most commonly used method for adult with hyperthyroidism and is generally accepted as safe, convenient and of low cost (Francklyn, 1996).

### **2.3.2 Hypothyroidism**

Hypothyroidism is caused by any structural or functional derangement that interferes with the production of adequate levels of thyroid hormone. As in the case of hyperthyroidism, this disorder is sometimes divided into primary and secondary categories, depending on whether the hypothyroidism arises from an intrinsic abnormality in the thyroid or results from hypothalamic or pituitary disease.

The clinical manifestations of hypothyroidism include cretinism and myxedema. Cretinism refers to hypothyroidism developing in infancy or early childhood. In the past, this disorder was fairly common in areas of the world where dietary iodine deficiency is endemic, including the Himalayas, inland China, Africa, and other mountainous areas. It has now become much less frequent because of the widespread supplementation of foods with iodine. On rare occasions, cretinism may also result from inborn errors in metabolism (e.g., enzyme deficiencies) that interfere with

the biosynthesis of normal levels of thyroid hormone (sporadic cretinism). Clinical features of cretinism include impaired development of the skeletal system and central nervous system, with severe mental retardation, short stature, coarse facial features, a protruding tongue, and umbilical hernia. The severity of the mental impairment in cretinism appears to be directly influenced by the time at which thyroid deficiency occurs in utero. Normally, maternal hormones, including T<sub>3</sub> and T<sub>4</sub>, cross the placenta and are critical to fetal brain development. If there is maternal thyroid deficiency before the development of the fetal thyroid gland, mental retardation is severe. In contrast, reduction in maternal thyroid hormones later in pregnancy, after the fetal thyroid has developed, allows normal brain development.

Hypothyroidism developing in older children and adults results in a condition known as myxedema. Myxedema, or Gull disease, was first linked with thyroid dysfunction in 1873 by Sir William Gull in a paper addressing the development of a "cretinoid state" in adults. Manifestations of myxedema include generalized apathy and mental sluggishness that in the early stages of disease may mimic depression. Patients with myxedema are listless, cold intolerant, and often obese. Mucopolysaccharide-rich edema accumulates in skin, subcutaneous tissue, and a number of visceral sites, with resultant broadening and coarsening of facial features, enlargement of the tongue, and deepening of the voice. Bowel motility is decreased, resulting in constipation. Pericardial effusions are common; in later stages the heart is enlarged, and heart failure may supervene.

### **2.3.3 GRAVES DISEASE**

In 1835, Robert Graves reported on his observations of a disease characterized by "violent and long continued palpitations in females"



associated with enlargement of the thyroid gland. Graves' disease is the most common cause of endogenous hyperthyroidism. It is characterized by a triad of manifestations:

-Thyrotoxicosis caused by hyperfunctional, diffuse enlargement of the thyroid is present in all cases.

-An infiltrative ophthalmopathy with resultant exophthalmos is noted in up to 40% of patients.

-A localized, infiltrative dermopathy (sometimes designated pretibial myxedema) is seen in a minority of cases.

Graves' disease occurs primarily in younger adults, with a peak incidence between the ages of 20 and 40. Women are affected up to seven times more often than men. An increased incidence of Graves' disease occurs among family members of affected patients, with a 50% concordance among identical twins. The occurrence of this disorder is strongly associated with the inheritance of human leukocyte antigen (HLA)-DR3.

### **2.3.3.1 Pathogenesis**

Graves' disease is an autoimmune disorder in which a variety of autoantibodies may be present in the serum. These include antibodies to the TSH receptor, thyroid peroxisomes, and thyroglobulin; of these, the TSH receptor is the most critical auto antigen against which antibodies develop; the effects of the generated antibody vary depending on which TSH receptor epitope it is directed against. For example, one such antibody, termed thyroid-stimulating immunoglobulin (TSI), binds to the TSH receptor to stimulate the adenylate cyclase/cyclic AMP pathway, with resultant increased release of thyroid hormones. Another class of antibodies, also directed against the TSH receptor, has been implicated in the proliferation of thyroid follicular epithelium (thyroid growth-

stimulating immunoglobulins, or TGI). Still other antibodies, termed TSH-binding inhibitor immunoglobulins (TBIs), prevent TSH from binding normally to its receptor on thyroid epithelial cells. In so doing, some forms of TBI mimic the action of TSH, resulting in the stimulation of thyroid epithelial cell activity, while other forms may actually inhibit thyroid cell function. It is not unusual to find the coexistence of stimulating and inhibiting immunoglobulins in the sera of the same patient, a finding that may explain why some patients with Graves' disease spontaneously develop episodes of hypothyroidism.

Although the role of antibodies in the causation of Graves' disease seems established, what propels B cells to make autoantibodies is not clear. There is little doubt that the antibody secretion by B cells is triggered by CD4<sup>+</sup> helper T cells, many of which are found within the thyroid. Intrathyroidal helper T cells are also sensitized to thyrotropin receptor, and they secrete soluble factors such as interferon- $\gamma$  and tumor necrosis factor. These in turn induce expression of HLA class II molecules and T-cell costimulatory molecules on thyroid epithelial cells, thus allowing presentation of thyroidal antigen to other T cells. This may sustain the activation of TSH-receptor-specific cells within the thyroid. In keeping with the primacy of helper T-cell activation in thyroid autoimmunity, Graves' disease shows an association with certain HLA-DR alleles and polymorphisms of the cytotoxic T-lymphocyte antigen 4 (CTLA-4). Activation of the latter normally dampens the T-cell response, and perhaps some alleles allow uncontrolled T-cell activation against autoantigens.

It is likely that autoantibodies to the TSH receptor also play a role in the development of the infiltrative ophthalmopathy characteristic of Graves' disease. It is postulated that certain extrathyroidal tissues (e.g., orbital

fibroblasts) aberrantly express the TSH receptor on their surface. In response to circulating anti-TSH receptor antibodies and other cytokines from the local milieu, these fibroblasts undergo differentiation into mature adipocytes and also secrete hydrophilic glycosaminoglycans into the interstitium, both of which contribute to the orbital protrusion (exophthalmos) seen in Graves ophthalmopathy. A similar mechanism has been proposed for the development of Graves's dermopathy, with TSH receptor-bearing pretibial fibroblasts secreting glycosaminoglycans in response to stimulatory autoantibodies and cytokines. Robbins (2007)

### **2.3.3.2 Characteristics of Grave's disease**

-Grave's disease affects women much more often than men (about 8:1 ratio, thus 8 women get Grave's disease for every man that gets it).

-Grave's disease is often called diffuse toxic goiter because the entire thyroid gland is enlarged, usually moderately enlarged, and sometimes quite big.

-Grave's disease is uncommon over the age of 50 (more common in the 30s and 40s).

Grave's disease tends to run in families (not known why) (Norman 2009). Grave's disease was the commonest cause of thyrotoxicosis accounting for 63% of patients also Toxic thyroid adenoma, Toxic multinodular goiter and Inflammation (thyroiditis) (Mir et al. 2004)

### **2.3.4 Diffuse Nontoxic Goiter and Multinodular Goiter**

Goiter, or simple enlargement of the thyroid, is the most common thyroid disease. The disorder is endemic in certain areas of the world and may also occur sporadically. Whether sporadic or endemic, the presence of goiter reflects impaired synthesis of thyroid hormone, most often caused by dietary iodine deficiency. Impairment of thyroid hormone synthesis leads to a compensatory rise in the serum TSH level, which in turn causes

hypertrophy and hyperplasia of thyroid follicular cells and, ultimately, gross enlargement of the thyroid gland.

Endemic goiter occurs in geographic areas where the soil, water, and food supply contain low levels of iodine. The term endemic is used when goiters are present in more than 10% of the population in a given region. Such conditions are particularly common in mountainous areas of the world, including the Himalayas and the Andes. With increasing dietary iodine supplementation, the frequency and severity of endemic goiter have declined significantly. Sporadic goiter occurs less commonly than endemic goiter. The condition is more common in females than in males, with a peak incidence in puberty or young adult life, when there is an increased physiologic demand for thyroxine. Sporadic goiter may be caused by a number of conditions, including the ingestion of substances that interfere with thyroid hormone synthesis at some level, such as excessive calcium and vegetables belonging to the Brassica and Cruciferae groups (e.g., cabbage, cauliflower, Brussels sprouts, and turnips). In other instances, goiter may result from hereditary enzymatic defects that interfere with thyroid hormone synthesis. In most cases, however, the cause of sporadic goiter is not apparent.

#### **2.3.4.1 Clinical Features:**

The dominant clinical features of goiter are those caused by the mass effects of the enlarged gland. In addition to the obvious cosmetic effects of a large neck mass, goiters may also cause airway obstruction, dysphagia, and compression of large vessels in the neck and upper thorax. In a significant minority of patients, a hyperfunctioning ("toxic") nodule may develop within the goiter, resulting in hyperthyroidism. This condition, known as Plummer syndrome, is not accompanied by the infiltrative ophthalmopathy and dermopathy of Grave's disease. Less

commonly, goiter may be associated with clinical evidence of hypothyroidism. Goiters are also clinically significant because of their ability to mask or to mimic neoplastic diseases arising in the thyroid.

### **2.3.5 Thyroiditis**

Inflammation of the thyroid gland, or thyroiditis, can occur in a number of different settings. Most of the common entities included under thyroiditis can be distinguished using a combination of two criteria: (1) the rapidity of onset or the duration of disease (acute, subacute, or chronic) and (2) the predominant inflammatory response (polymorphonuclear, lymphocytic, or granulomatous). For example, acute suppurative thyroiditis associated with microbial infections and polymorphonuclear inflammation is quite uncommon. The more common types of thyroiditis, including chronic lymphocytic (Hashimoto) thyroiditis, subacute granulomatous (de Quervain) thyroiditis, and subacute lymphocytic thyroiditis. Robbins (2007).

### **2.3.6 Neoplasms of the thyroid**

The thyroid gland gives rise to a variety of neoplasms, ranging from circumscribed, benign adenomas to highly aggressive, anaplastic carcinomas. From a clinical standpoint, the possibility of neoplastic disease is of major concern in patients who present with thyroid nodules. Fortunately, the overwhelming majority of solitary nodules of the thyroid prove to be benign lesions, either follicular adenomas or localized, non-neoplastic conditions (e.g., nodular hyperplasia, simple cysts, or foci of thyroiditis). Carcinomas of the thyroid, in contrast, are uncommon, accounting for well under 1% of solitary thyroid nodules. Several clinical criteria provide a clue to the nature of a given thyroid nodule:

-Solitary nodules, in general, are more likely to be neoplastic than are

multiple nodules.

-Solid nodules, in general, are more likely to be neoplastic than are cystic nodules.

-Nodules in younger patients are more likely to be neoplastic than are those in older patients.

-Nodules in males are more likely to be neoplastic than are those in females.

-Nodules that do not take up radioactive iodine in imaging studies ("cold" nodules) are more likely to be neoplastic; "hot" nodules are almost always benign.

### **2.3.7 Adenomas**

Adenomas of the thyroid are benign neoplasms derived from follicular epithelium. As in the case of all thyroid neoplasms, follicular adenomas are usually solitary. Clinically and morphologically, they may be difficult to distinguish, on the one hand, from hyperplastic nodules or, on the other hand, from the less common follicular carcinomas.

### **2.3.8 Carcinomas**

Carcinomas of the thyroid are relatively uncommon in the United States, being responsible for less than 1% of cancer-related deaths. Most cases occur in adults, although some forms, particularly papillary carcinomas, may present in childhood. A female predominance has been noted among patients developing thyroid carcinoma in the early and middle adult years, probably related to the expression of estrogen receptors on neoplastic thyroid epithelium. In contrast, cases presenting in childhood and late adult life are distributed equally among males and females, largely related to exogenous influences. The major subtypes of thyroid

carcinoma and their relative frequencies are as follows:

-Papillary carcinoma (75% to 85% of cases)

-Follicular carcinoma (10% to 20% of cases)

-Medullary carcinoma (5% of cases)

-Anaplastic carcinomas (<5% of cases)

### **2.3.8.1 Papillary Carcinoma**

Papillary carcinomas represent the most common form of thyroid cancer (80% of all cases). They may occur at any age, and they account for the vast majority of thyroid carcinomas associated with previous exposure to ionizing radiation.

### **2.3.8.2 Follicular Carcinoma**

Follicular carcinomas are the second most common form of thyroid cancer (15% of all cases). They usually present at an older age than do papillary carcinomas, with a peak incidence in the middle adult years. The incidence of follicular carcinoma is increased in areas of dietary iodine deficiency, suggesting that, in some cases, nodular goiter may predispose to the development of the neoplasm. There is no compelling evidence that follicular carcinomas arise from preexisting adenomas.

### **2.3.8.3 Medullary Carcinoma**

Medullary carcinomas of the thyroid are neuroendocrine neoplasms derived from the parafollicular cells, or C cells, of the thyroid. Like normal C cells, medullary carcinomas secrete calcitonin, the measurement of which plays an important role in the diagnosis and postoperative follow-up of patients. In some cases, the tumor cells elaborate other polypeptide hormones such as carcinoembryonic antigen, somatostatin, serotonin, and vasoactive intestinal peptide (VIP).

Medullary carcinomas arise sporadically in about 80% of cases. The remaining 20% are familial cases occurring in the setting of multiple endocrine neoplasia (MEN) syndromes 2A or 2B or familial non-MEN medullary thyroid carcinoma. Germ-line mutations in the RET proto-oncogene play an important role in the development of both MEN and non-MEN familial cancers. Somatic RET proto-oncogene mutations have also been identified in sporadic cases. Sporadic medullary carcinomas, as well as familial non-MEN cancers, occur in adults, with a peak incidence in the fifth to sixth decades. Cases associated with MEN 2A or 2B, in contrast, occur in younger patients and may even arise in children.

#### **2.3.8.4 Anaplastic Carcinoma**

Anaplastic carcinomas of the thyroid are among the most aggressive human neoplasms. They occur predominantly in elderly patients, particularly in areas of endemic goiter. Robbins (2007).



## **2.4 Previous studies**

Woodman (1952) was a medical officer at Lirangu Hospital in Azande Area. He described an endemic area approximately 200 miles long and 60 miles wide extending between lat. 5-6 No and long. 27-29 Eo, its southern limit being the Nile- Congo watershed. In this area Woodman examined several hundred individuals and found (3%) of them to be goitrous and (85%) of all goitrous subjects were females. He noted the striking absence of cretinism and myxedema, and the rarity of exophthalmic goitre of which he has seen only two cases. Although Woodman presumed that iodine deficiency is the main causative factor he was puzzled as to the abrupt disappearance of the endemic to the east, south and west of this area although, according to him all environmental conditions, soil, vegetation, tribes, habits etc...

Smith (1957), the pioneer of goiter study in Sudan. He was the dean of Physiology department, University of Khartoum. During the year 1957 he visited three suspected goiter area in Sudan and recorded his most enlightening observations.

Smith and Abdallatif (1957), circumvented Jebal Marra in Darfur Province and examined 1838 individuals, mainly schoolchildren. They found that (70%) of those examined had goitre. Smith speculated that a goitre belt might extend through Southern Darfur into Kordofan Province and thus account for the cases seen around Mujlad.

Smith and Khogali (1957), examined over 3000 individuals during a sleeping-sickness inspection in an area 30 miles north and west of Nzara, in the center of Woodman's goitre area. A goitre incidence of (37%) was found, with (69%) of the adolescent females affected.

Smith explained the disparity between his figures and those of Woodman by the fact that latter considered as goitrous classify as grade 2 (WHO simplified classification of goitre).

Smith and Khogali were of opinion that iodine deficiency is the cause of goitre in this area. They pointed out that the people in the area consume very little, if any red-sea salt, which they consider, contains adequate amounts of iodine.

They recommended the prophylactic use of iodine at regular intervals, a recommendation which will be easy to carry out in this area in view of the already established system of regular gathering for sleeping-sickness inspection.

Another area studied by smith was Ingessana Roseiris and Kurmuk, not far from the Ethiopian borders. The incidence of goitre patient was unlikely to exceed (5%).

Kambal (1968) has chosen endemic goitre as a subject because it was a common condition in Sudan.

The records of goitre admission of the University Department of Surgery, Khartoum Hospital during the three years 1965-1968 showed that no less than (9.5%) of the non-urgent admission were duo to thyroid disease, mostly simple goitre . The same records indicated that a large portion of these patients were derived from Darfur, especially those with large goitres.

The objective of Kambal's study was to determine the incidence of goitre in various parts of Darfur Province and to map out the boundaries of the endemic area.

By the other hand, to elucidate the etiological factors underlying the state of endemicity and to outline the most suitable method by means of which goitre can be controlled.

Results of Kambal's study:

-Kambal reported that in the Province of Darfur the prevalence of goitre was (58%), and that of large goitre (19%).

-Kambal reported that goitre in all its clinical types constituted an incidence of (12.2%) at Khartoum region.

-Kambal reported one malignant thyroid nodule among a series of 76 patients (1.3%).

-Kambal considered Khartoum to be an endemic area according to the WHO committee which regarded any area in which the frequency of goitre exceeding (10%) to be considered as an endemic area.

-Kambal believed that endemic goitre in Darfur is due to iodine deficiency.

-Kambal pointed that salt iodization is the only rational method for goitre control.

El-daw Mukhtar (1974), reported that congenital dyshormonogenesis is likely to be an important contributory factor in the development of some cases of goitre in Sudan.

The most likely defect is an abnormal secretion of iodoproteins for big families from different non-endemic areas were selected for Mukhtar's study.

Most of them either were born with a goitre or developed it a few months later. The parents of all these families were first-degree cousins. There was a wide spectrum in the clinical presentation. Some patients were euthyroid with either nodular or diffuse soft tissues. One patient presented with huge nodular goitre, she was clinically euthyroid, but mentally defect.

Four patients presented with typical goitrous cretinism, with mental, physical and sexual retardation.

The recognition of these cases is very important as surgical removal is invariably followed by recurrent of the goitre. Thyroxin treatment will cause disappearance of the goitres.

A. HIDAYATALLA et al (1974) reported that radioiodine is a cheap, effective and easy method of treatment of thyrotoxicosis. The indication and method of therapy of 80 patients treated by radioiodine were presented in Khartoum Teaching Hospital. The immediate and late complications of therapy were discussed. The most serious side effect is the rising incidence of hypothyroidism

El-DAW MUKHTAR (1981) reported that TSH index correlated with the degree of hyperthyroidism, patients with moderate to severe hypothyroidism had high values while those with mild hyperthyroidism had lower limits. There was no correlation between the level of TSH and the degree of ophthalmopathy.

Some patients with autoimmune thyroiditis, ophthalmic Graves' disease and thyroid carcinoma had detectable level of TSH.

Treatment with radioiodine for patients with hyperthyroidism due to Graves' disease resulted initially in a sharp rise in thyroid Stimulating Immunoglobulin TSI in susceptible individuals (21).

EL.gizouli (1987) performed a prospective study comprised 103 patients presented with clinically solitary thyroid nodule at the thyroid clinic in Khartoum Teaching Hospital during the period from March 1985-March 1987.

The objectives of El.gizouli's study was to determine the prevalence of the solitary thyroid nodule among other thyroid diseases in Sudan. Since a solitary thyroid nodule is the earliest and most common presentation of thyroid carcinoma, and to obtain on the usefulness of the medical history, physical examination, thyroid isotope scan and sonographic scan for predicting or ruling out malignancy in clinically solitary thyroid nodule.

Results of El.gizouli's study:

-The solitary thyroid nodule was found to affect females in the reproductive age group i.e. less than 40 years of age (60%), with a female to male ratio of 10:1.

-Patients reported from all parts of the country. (42%) were from Khartoum region, (25%) from central Sudan, while (18%) came from known goitre endemic areas (Kordofan and Darfur).

-Hypo-functioning (cold) nodules were found in (68%) of cases, the rest had functioning warm nodules.

-Simple nodular goitre formed (77%) of surgical removed specimens.

-The incidence of malignancy among solitary thyroid nodules was found to be (6.8%), all were cold on isotopic scans. Papillary carcinoma was the most common type of malignancy (66.7%).

-Ultrasound was helpful in differentiating cystic from solid nodules and the mixed types as well.

Alnagar (1996) study was carried out in the village of Soga; a goitre endemic area located in western Sudan and comprised 165 adults'

subjects, all with visible goitre, aged 15-35 years.

Alnagar calculated the optimum dose of massive oral iodine and determined the feasibility of using sugar and water as vehicles for iodine supplementation for public health purpose. He also studied the effects of pregnancy on thyroid function in relation to maternal iodine status.

# **Chapter Three**

## **Methodology**

## Chapter Three

### Materials and Methods

#### 3.1 Materials

##### - Gamma camera

A gamma camera, also called a scintillation camera or Anger camera, is a device used to image gamma radiation emitting radioisotope, a technique known as scintigraphy. The applications of scintigraphy include early drug development and nuclear medical imaging to view and analyse images of the human body or the distribution of medically injected, inhaled, or ingested radionuclides emitting gamma rays.

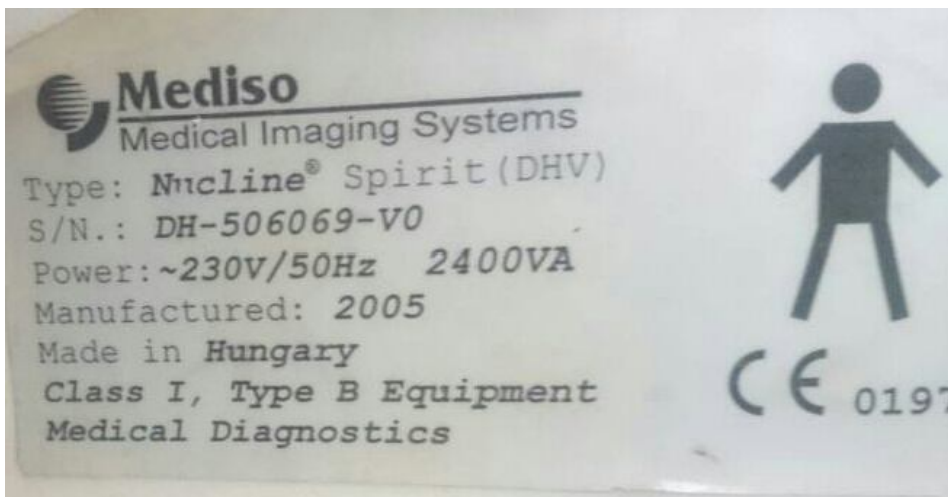


Fig. 3.1 shows the type of gamma camera at RICK



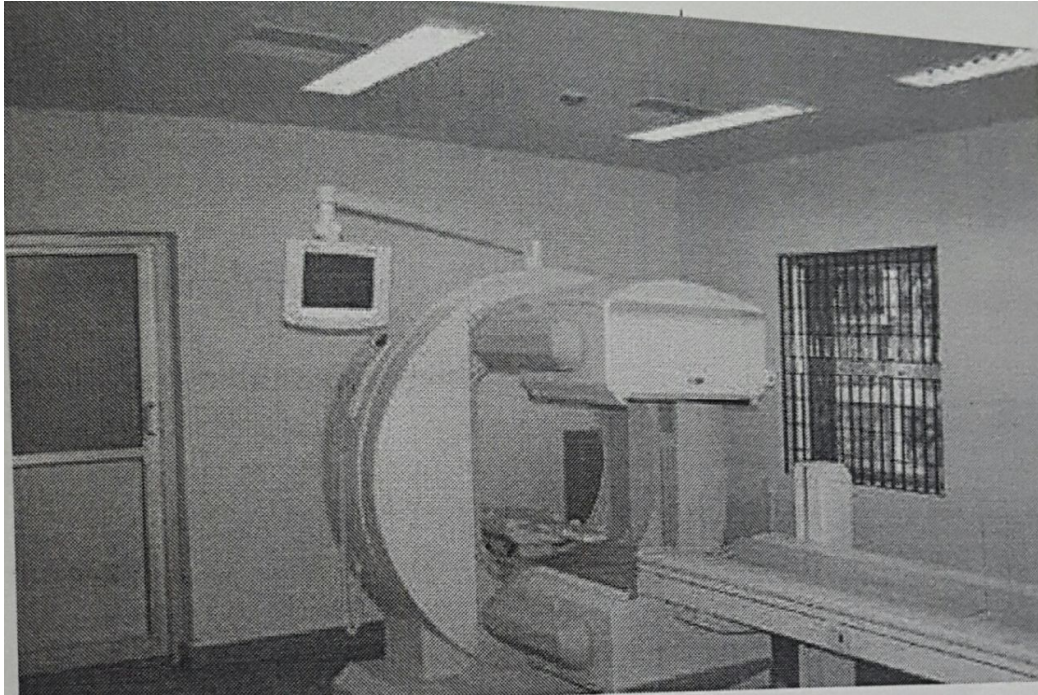


Figure 3.2 shows a dual head scintillation gamma camera

-computer

-dose calibrator

**-<sup>99</sup>Mo/ <sup>99m</sup>Tc generator**

A technetium-99m generator, or colloquially a technetium cow or moly cow, is a device used to extract the metastable isotope  $Tc^{99m}$  of technetium from a source of decaying molybdenum-99.  $Mo^{99}$  has a half-life of 66 hours and can be easily transported over long distances to hospitals where its decay product technetium-99m (with a half-life of only 6 hours, inconvenient for transport) is extracted and used for a variety of nuclear medicine diagnostic procedures, where its short half-life is useful.

## **3.2 Methods**

### **3.2.1 Methods of data collection:**

The data were collected for this study by a "Data Collecting Sheet", which was designed especially for the study.

### **3.2.2 Sample Selection:**

The data were collected from 200 patients with different ages and gender who were suffering from thyroid disorders.

Those patients were selected randomly when attending the department of nuclear medicine at Radiation and Isotope Center of Khartoum (RICK) for a Tc<sup>99m</sup>thyroid scan and uptake.

### **3.2.3 Area of the Study:**

Nuclear medicine department at Radiation and Isotope Center of Khartoum (RICK), Khartoum State, Sudan.

### **3.2.4 Duration of the Study:**

The study was carried out from March 2017 up to May 2017.

### **3.2.5. Method of Data Analysis:**

The data were firstly summarized into master sheet, and then analyzed by using Statistical Package for the Social Sciences (SPSS), and then Microsoft excel for graphical presentation was used.

### **3.2.6. Data Storage and Ethical Issue:**

Patient's data sheets were kept in locked cabinet, and all data were stored on personal computer. No individual patient's details throughout this study were revealed.

### 3.3. Imaging Protocol

#### 3.3.1 Patient Preparation:

Careful interviewing of patients undergoing the scanning was applied to determine whether there was a history of anti-thyroid drugs, thyroid hormones, or radiographic contrasts used in gall bladder, kidneys and myelographic studies because numerous medications and iodinated contrast agents affect Tc99m concentration (Table 1). To perform a successfully study, those medications were withheld for appropriate periods of time before attempting the imaging procedure.

Table 1.1 Thyroid gland drugs preparation

Medication	Time*
Triiodothyronine (Cytomel) Thyroid Extract (Synthroid)	3 weeks
Intravenous contrast agents	1-2 months
Oral cholecystographic agents Oil-based iodinated contrast agents	3-6 months
Bronchographic agents	6-12 months
Myelographic agents	2-10 years
Anti-thyroid drug (Newmercazole)	2 weeks

\*: Time that patient should wait after medication is discontinued before the scan.

Source: Fred A. Mattler et al., Essentials of Nuclear Medicine Imaging, W.B. Saunders Company, 4<sup>th</sup> edition, P109.

### **3.3.2 Route of Administration:**

Each patient was injected intravenously. The vein puncture site was even antecubital or median cubical vein on the anterior surface of the elbow or the medial basilica or cephalic veins or veins of the anterior wrist and posterior hand.

### **3.3.3 Administered Activity:**

The usual dose injected to the patients under study ranged between (3 – 5 mCi) of Tc99m Pertechnetate, depending on the patients age and weight.

# **Chapter Four**

## **Results**

## Chapter Four

### Results

Table 4.1 a frequency distribution according to gender

Gender	Frequency distribution
Female	171
Male	29
Total	200

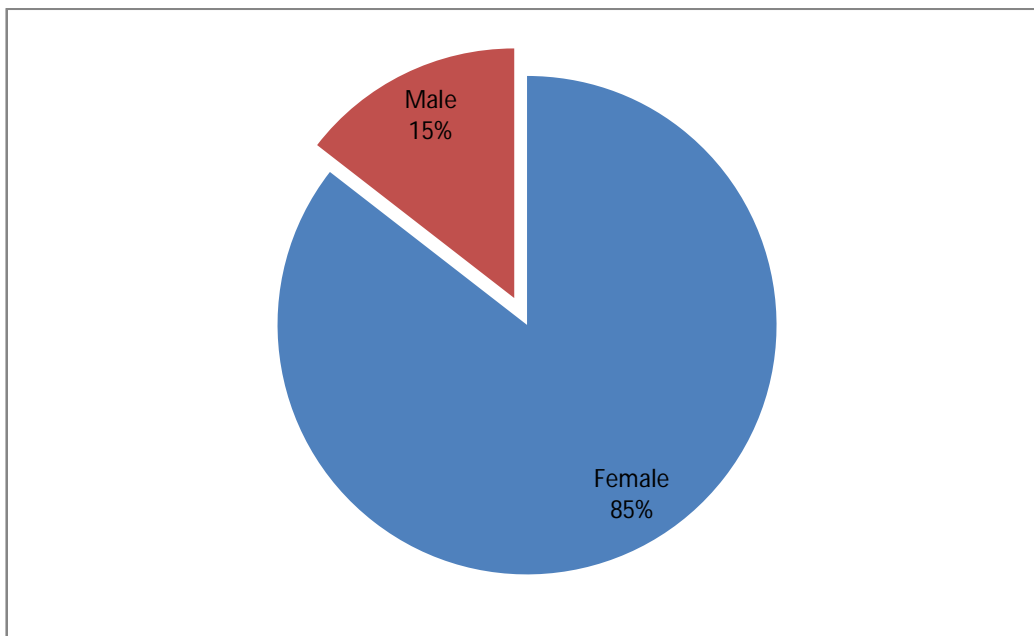


Figure 4.1a pie chart shows the percentage distribution of gender

Table 4.2 a frequency distribution according to age

Age (years)	Frequency distribution	%
<20	19	9%
21-40	116	58%
41-60	58	29%
61-80	6	3%
81-100	1	0.5%

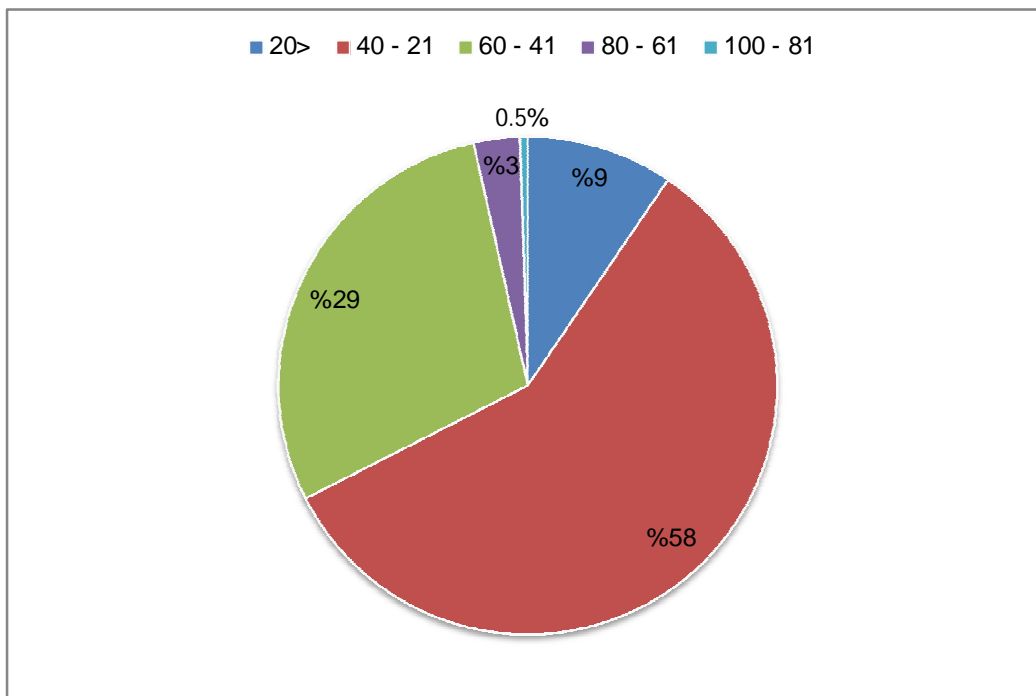


Figure 4.2a pie chart shows the percentage distribution of the age groups

Table 4.3 the frequency distribution of thyroid disorders

Thyroid disorder	Frequency distribution	%
Multinodular goitre (MNG)	46	22%
Moderate diffuse goitre	19	10%
Graves' disease	51	25%
Mild diffuse goitre	31	15%
Cold nodule	37	19%
Toxic adenoma	5	3%
Hypothyroidism	7	4%
Thyroiditis	4	2%

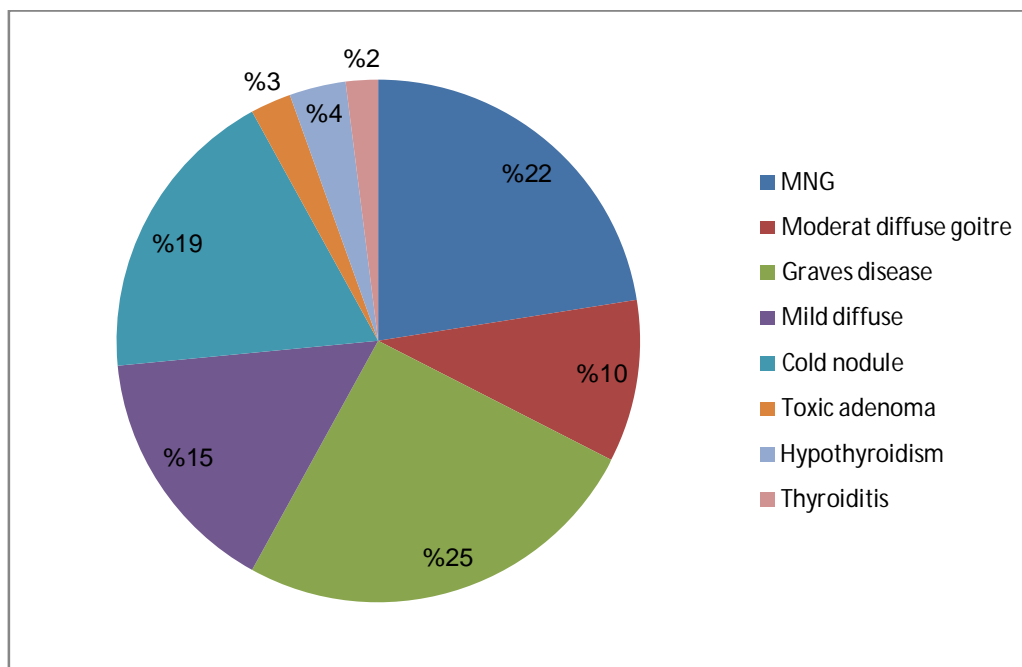


Figure 4.3 a pie chart shows the percentage distribution of the thyroid disorders



Table 4.4 cross tabulation between thyroid and age group

Diagnosis	<20	21 - 40	41 - 60	61 - 80	81 - 100	Total
MNG	1	28	17			47
Moderate diffuse goitre	4	13	2			19
Graves' disease	4	35	12			51
Mild diffuse	8	14	9			31
Cold nodule	2	18	12	4	1	37
Toxic adenoma		2	3			5
Hypothyroidism		5	2			7
Thyroiditis		1	1	2		4

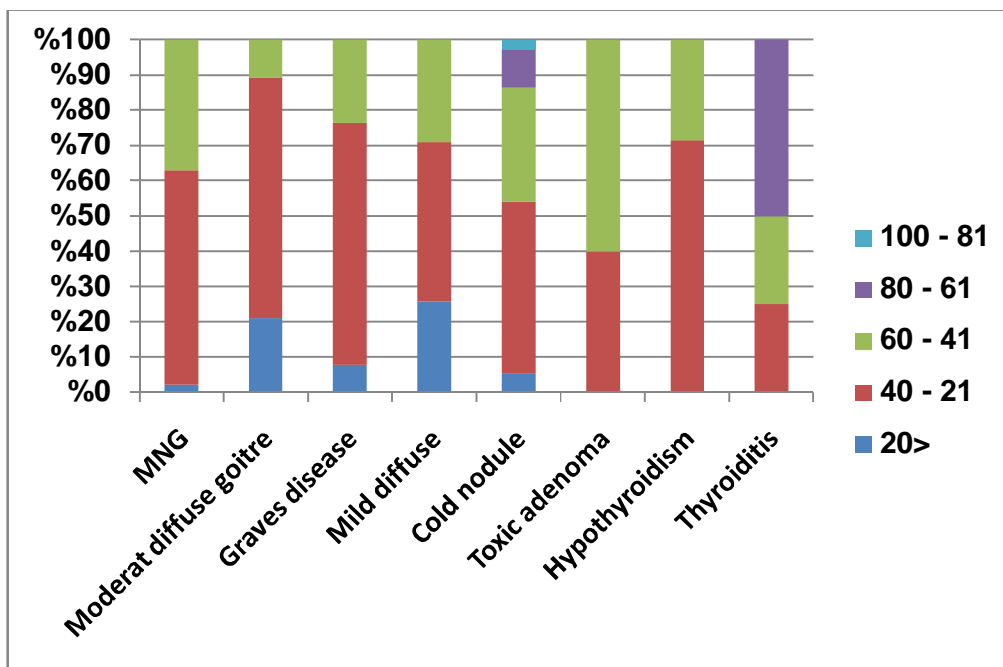


Fig 4.4 shows the thyroid disorders according to age category

**Chapter Five**  
**Discussion, Conclusion and Recommendations**

## Chapter Five

### Discussion, Conclusion and Recommendations

#### 5.1 Discussion

Distribution of the study population according to gender revealed that: a percentage of 85% of the sample population were females and 15% were males. This results matched the information stated by Norman (2009), and also agreed with Woodman (1952). (Grave's disease affects women much more often than men (about 8:1 ratio, thus 8 women gets Grave's disease for every man that gets it).

Distribution of the study population according to age revealed that:

19 patients were < 20 years old (9% of all patients), 116 at the age of 21-40 years old (58%), 58 patients were 41-60 years old (29%), 6 patients are of 61-80 years old (3%), and only 1 patient at the age category of 81-100 years old (0.5% of all patients). These results showed that thyroid disorders affect the youth (21-40 years old) more than other ages, as showed in table 4.2 and figure 4.2. This result agreed with the result of El.gizouli in which 60% of the study population was less than 40 years old.

The frequency distribution of the thyroid disorders was as follows:

46 patients with Multinodular goitre (MNG), 19 patients with moderate diffuse goitre, Graves' disease appeared on 51 patients, 31 patients with mild diffuse goitre, Cold nodules was 37 cases, 5 cases of Toxic adenoma, 7 cases of hypothyroidism, and 4 patients with Thyroiditis, the result shown in table 4.3 confirm this statement.

The percentage distribution of the diagnosis of thyroid disorders showed that the most common thyroid abnormalities among patients referred to radiation and isotope centre of Khartoum (RICK) for thyroid scan and uptake was Graves' disease which represented 25% of cases, Multinodular goitre represented 23%, Cold nodule represented 19%, Mild diffuse goitre represented 15%, 9% of abnormalities were moderate diffuse goitre, Thyroiditis represented 4% of thyroid abnormalities, 3% Toxic adenoma, and Thyroiditis represented only 2% of thyroid abnormalities, as showed in figure 4.3.

## **5.2 Conclusion**

The main objective of this study was to classify the thyroid abnormalities among patients referred to Radiation and Isotope Centre of Khartoum (RICK) for thyroid scan and uptake. The data were collected by using special data collecting paper among 200 patients referred to nuclear medicine department at RICK for thyroid scan and uptake during a period of three months from March 2017 to May 2017.

The study revealed that the thyroid abnormalities was associated with female gender with 85% as compared to 15% among males.

The most common affected age was the category of 21-40 years old. This agreed with the information given by Norman2009 (Grave's disease is uncommon over the age of 50 more common in the 30 and 40 years.

The most common thyroid abnormality was Graves' disease which represented 25% of the study population.

The lower common thyroid disease among the study population was thyroiditis which represented 2% of the study population.

### **5.3 Recommendations:**

Diet with rich iodine should be taken by all people especially people of west Sudan, where there are no river or sea water which is usually rich of iodine.

Encouragement of adding iodine to drinking water, particularly in the areas which lack iodine.

Standard dose, technique and position of patient should always be adopted in thyroid imaging in order to have good images and good diagnosis of thyroid disorders

More diagnostic centers of thyroid studies should be established in Sudan to meet the increasing number of patients with thyroid abnormalities.

Most recent equipment and techniques(SPECT and PET) should be available at the nuclear medicine centers to obtain more reliable and accurate results of thyroid studies.

Future studies on the same topic should be encouraged using larger sample and different techniques.

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## Appendices



Appendix 1 shows the dose calibrator



Appendix 2 shows the scintillation gamma camera



Appendix 3 shows  $\text{Mo}^{99}\text{-Tc}^{99\text{m}}$  generator