Sudan University of Science and Technology

College of Graduate Studies

Assessment of Plasma Lipid Profile among Sudanese Patients With Hypo and Hyper thyroidism in Khartoum State

تقويم مستويات الدهون في بلازما الدم عند السودانيين

المصابين بنقص و فرط في الغدة الدرقية بولاية الخرطوم

Desertion submitted in partial fulfillment of the requirement for M.S.C degree in medical laboratory science (clinical chemistry)

BY:

Shadia Salah Abdelrahim Makki

B.Sc Clinical Chemistry- College of Medical Laboratory Sciences

(Khartoum College of Medical Sciences 2011)

Supervised by:

Dr.Nuha ELgaili Abu Baker

Assistant Professor of Clinical Biochemistry

(SUST)

October 2015

الآيـة

قال تعالى:

"وَاللهُ خَلَقَكُمْ مِنْ تُرَابٍ ثُمَ مِنْ نُطْفَةٍ ثُمَ جَعَلَكُمْ أَزْوٰجًا وَمَا تَحْمِلُ مِنْ أُنْثَى وَلَا تَضَعُ إِلا بِعِلْمِهِ وَمَا يُعَمَرُ مِنْ مُعَمَرٍ وَلَا يَنْقُصُ مِنْ عُمُرِهِ إِلا فِي كِتَبْ إِنَ ذَلِكَ عَلَى اللهِ يَسِيرْ "

صَدَقَ اللهُ العَظِيمْ

سوره فاطر الآية {١١}

Dedication

To those who always believe on my efforts…

To my lovingly parents who have been my constant source of inspiration ….

To my brothers and sister for their understanding support ….

To my husband ….

To all those who help me to proceed ahead ….

Acknowledgment

First of all thanks to Allah for giving me the power and willing to complete this study.

Greatest thank to Dr.Nuha ELgaili who had been a gentle supervisor and a good leader who show me the way to success.

Thank and appreciation to Mr. Osman Mohamed for providing me with reagents need for my work.

My sincerely gratitude to Miss. Suha Ahmed who help me to carry out the practical part of the study.

Also thank extend to the staff of lab of Sudan University of science and Technology and Ribat university hospital.

Special thanks to my Father Salah Abdelrahim For encouragement and my husband Moawia Ibrahim for designing this study.

Finally thank to all patients whom the blood sample had been collected from.

Abstract

This is a case - control study, conducted during the period from March to September 2015 to assess the plasma lipid profile among Sudanese patients with Hypo and Hyper thyroidism, and to determine whether the thyroid abnormalities associated with cardiovascular disease or not.

The study groups included 50 patients with thyroid disorders (25 patients with hyperthyroidism and 25 patients with hypothyroidism) and25 apparently healthy subjects as a control group (match age and sex). All participants were selected from Ribat university hospital.

A spectrophotometry was used for measurement of total cholesterol, triglycerides, high density lipoproteins, low density lipoproteins, and results were analyzed using (SPSS) computer program (Independent sample T test and person correlation).

The results of frequency showed thyroid disorders is common in ages over 40 year (less than 40 year 32%) (more than 40 year 68%).

Also this disease is common in female 37 (74%) than male13 (26%).

The study results show moderate increased in total cholesterol in hyperthyroidism patients group compared to control group (mean ± SD: 197± 23 versus173± 18 mg/dl , P- value 0.000) and LDL-c(mean ± SD: 125± 13 versus 96± 5mg/dl, P- value 0.000),while triglycerides and HDL-c were not affected

(mean± SD: 113± 13 versus 111± 11mg/dl, P-value 0.65 , mean± SD: 48 ± 9 versus 50± 9mg/dl, p- value 0.47) respectively.

In hypothyroidism patients, there were a significant increased in the plasma total cholesterol, triglycerides and LDL-c concentrations without change in HDL-c compare to control group, (mean ± SD: 212± 22 versus174± 18

mg/dl , P- value 0.000) For total cholesterol, (mean ± SD: 152± 29 versus 111± 11 mg/dl , P- value 0.000) For triglycerides, (mean ± SD: 50± 11 versus 50± 9 mg/dl , P- value 0.925) For HDL-c, (mean ± SD: 125± 21 versus 95± 5 mg/dl, P- value 0.000) For LDL-c.

Person correlation showed a significant correlation between duration of thyroid disorders and plasma levels of total cholesterol (r= 0.740, p-value=0.000), triglycerides (r= 0.457, p-value=0.001) and LDL-c (r= 0.779, p-value=0.000).

Also there was no correlation between duration of thyroid disorders and plasma level of HDL-c (r= 0.062, p-value= 0.669).

It was obvious from this study, total cholesterol and LDL-c are significant increased in patients with Hyperthyroidism, while triglyceride and HDL-c are insignificant increased, also total cholesterol, triglyceride and LDL-c are significant increased in Hypothyroidism , while HDL-c is not affected.

مستخلص الدراسة

أجريت هذه الدراسة في الفترة من مارس وحتي بداية ديسمبر ٢٠١٥ وذلك لقياس وتقييم مستوى الدهون في البلازما وسط المرضى السودانيين المصابين بخلل في الغدة الدرقية ، ولتحديد ما إذا كان للاختلال الوظيفي في الغدة الدرقية له علاقة بأمراض القلب.

تتكون مجموعة الدراسة من ٥٠ مصابين بمرض الغدة الدرقية (٢٥ مريضاً لديهم فرط نشاط الغدة الدرقية و ٢٥ مريض لديهم قصور في نشاط الغدة الدرقية) ، ٢٥ شخص من الاصحاء كمجموعه لتحكم .

جميع المشاركين في الدراسة قد تم اختيارهم من مستشفي الرباط الجامعي وقد تم التوفيق بين مجموعة المرضي ومجموعة التحكم من حيث العمر والنوع .

جهاز التحليل الكيميائي الاسبكتروفوتومتر استخدم لعمل التحاليل الخاصة بمستوى الدهون في البلازما (الكلسترول الكلي، ثلاثي الجلسرايد، البروتينات الدهنية ذات الكثافة العالية و المنخفضة) ، وتم تحليل البيانات بواسطة برنامج الحزمة الإحصائية للعلوم الإجتماعية.

أظهرت نتائج التردد أن مرض الغدة الدرقية شائع في الاعمار فوق الأربعين عاماً (اقل من ٤٠ عاماً ٣٢ %) (اكثر من ٤٠ عاماً ٦٨%).

أيضاً هذا المرض اكثر شيوعاً لدى الإناث ٣٧ (٧٤%) مقارنة بالذكور ١٣(٢٦%).

عند مقارنة متوسط مستوى الدهون لدى المرضى المصابين بفرط نشاط الغدة الدرقية بمجموعة التحكم وجد أن هنالك ارتفاع ملحوظ في مستوى الكلسترول الكلي و البروتينات الدهنية ذات الكثافة المنخفضة بينما ظل ثلاثي الجلسرايد و البروتينات الدهنية ذات الكثافة العالية دون تغيير يذكر.(المتوسط ±الإنحراف المعياري:١٩٧± ٢٣ مقابل ١٧٤± ١٨ ملجم/دسلتر،وكان الاحتمال الإحصائي للمقارنة ٠,٠٠٠) للكلسترول الكلي،(المتوسط ±الإنحراف المعياري:١١٣± ١٣ مقابل١١١± ١١ ملجم/دسلتر،وكان الاحتمال الإحصائي للمقارنة ٠,٦٥١) للثلاثي الجلسرايد،(المتوسط ±الإنحراف المعياري:٤٨± ٩ مقابل٥٠± ٩ ملجم/دسلتر،وكان الاحتمال الإحصائي للمقارنة ٠,٤٧٨) للبروتينات الدهنية ذات الكثافة العالية،(المتوسط ±الإنحراف المعياري:١٢٥± ١٣ مقابل٩٦± ٥ ملجم/دسلتر،وكان الاحتمال الإحصائي للمقارنة ٠,٠٠٠) للبروتينات الدهنية ذات الكثافة المنخفضة.

عند مقارنة متوسط مستوي الدهون لدى المرضى المصابين بقصور في نشاط الغدة الدرقية بمجموعة التحكم وجد أن هنالك ارتفاع ملحوظ وفرق معنوي في مستوى الكلسترول الكلى ، ثلاثي الجلسرايد و البروتينات الدهنية ذات الكثافة المنخفضة مع عدم تأثر البروتينات الدهنية ذات الكثافة العالية.

(المتوسط±الإنحراف المعياري: ٢١٢± ٢٢ مقابل ١٧٤± ١٨ ملجم/دسلتر، وكان الاحتمال الإحصائي للمقارنة ٠,٠٠٠) للكلسترول الكلي،(المتوسط±الإنحراف المعياري: ١٥٢± ٢٩ مقابل ١١١± ١١ ملجم/دسلتر، وكان الاحتمال الإحصائي للمقارنة ٠,٠٠٠) للثلاثي الجلسرايد،(المتوسط±الإنحراف المعياري: ٥٠± ١١ مقابل ٥٠± ٩ ملجم/دسلتر، وكان الاحتمال الإحصائي للمقارنة ٠,٩٢٥) للبروتينات الدهنية ذات الكثافة العالية،(المتوسط±الإنحراف المعياري: ١٢٥± ٢١ مقابل ٩٥± ٥ ملجم/دسلتر، وكان الاحتمال الإحصائي للمقارنة ٠,٠٠٠) للبروتينات الدهنية ذات الكثافة المنخفضة.

تحليل إرتباط بيرسون أظهر علاقة إيجابية ذات دلاله إحصائية بين الفترة الزمنية لمرضى الغدة الدرقية ومستوى الكلسترول الكلي (معامل بيرسون للإرتباط= ٠,٧٤٠ ،القيمة المعنوية= ٠,٠٠٠)،ثلاثي الجلسرايد(معامل بيرسون للإرتباط= ٠,٤٥٧ ،القيمة المعنوية= ٠,٠٠١)،البروتينات الدهنية ذات الكثافة المنخفضة(معامل بيرسون للإرتباط= ٠,٧٧٩ ،القيمة المعنوية= ٠,٠٠٠).

أيضاً وجد أنه ليس هنالك علاقة ذات دلاله إحصائية بين الفترة الزمنية لمرضى الغدة الدرقية ومستوى البروتينات الدهنية ذات الكثافة العالية في بلازما الدم (معامل بيرسون للإرتباط= ٠,٠٦٢ ،القيمة المعنوية= ٠,٦٦٩).

يتضح من هذه الدراسة أن مستوى الكلسترول الكلي و البروتينات الدهنية ذات الكثافة المنخفضة ذات أرتفاع ملحوظ في المرضى المصابين بفرط نشاط الغدة الدرقية ، بينما ظل ثلاثي الجلسرايد و البروتينات الدهنية ذات الكثافة العالية دون أرتفاع يذكر.

أيضاً مستوى الكلسترول الكلي ، ثلاثي الجلسرايد و البروتينات الدهنية ذات الكثافة المنخفضة ذات ارتفاع ملحوظ في المرضى المصابين بقصور في نشاط الغدة الدرقية، بينما ظل البروتينات الدهنية ذات الكثافة العالية دون تغيير يذكر.

Contents

List of tables

List of figures

Abbreviations

Abbreviation	Full Term
DIT	Diiodotyrosine
HDL-c	High density lipoprotein cholesterol
HL	Hepatic lipase
IDLP	Intermediate density lipoprotein cholesterol
LDL-c	Low density lipoprotein cholesterol
LPL	Lipoprotein lipase
T_3	Triiodothyronine
T_4	Thyroxine
TBG	Thyroid binding globulin
TBPA	Thyroid binding pre-albumin
TG	Thyroglobulin
TRH	Thyroid releasing hormone
TSH	Thyroid stimulating hormone
TTR	Transthyretin
VLDL	Very low density lipoprotein cholesterol

Chapter One

Introduction

1.1 Introduction:

Diseases of thyroid gland are amongst the most abundant endocrine disorders in the world. (Heuck *et al*, 2000), Thyroid function regulates a wide array of metabolic activities. Thyroid failure is more common in women and epidemiological rate of prevalence rises with age. (Rizos *et al*, 2011).

Thyroid hormones perform a wide array of metabolic functions including regulation of lipid, carbohydrate, protein and electrolyte and minerals metabolism. (Pearce, 2004).

Excess production of thyroid hormones leads to hyperthyroidism while Diminished production leads to hypothyroidism. (Ridgway, 1996).

Lipids, commonly referred to as fats, have adual role. First, because they are composed of mostly carbon –hydrogen (C-H) bonds, they are a rich source of energy and an efficient way for the body to store excess calories. Because of their unique physical properties, lipids are also an integral part of cell membranes and, therefore, also play an important structural role in cells.

The lipids transported by lipoproteins, namely triglycerides, phospholipids, cholesterol, and cholesteryl esters, are also the principal lipids found in cells and the main focus of this section. (Bishop et al, 2010).

Thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the triglycerides - rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes high density lipoprotein 2(HDL2) to high density lipoprotein 3(HDL3) and contributes to the conversion of intermediate-density lipoproteins (IDL) to low density lipoprotein (LDL). (Kuus et al, 1980).

1.2 Rationale:

Thyroid disease is adevastating medical , social and economic problem in sudan . The thyroid gland spread in all regions of Sudan, and thyroid deployed in Sudan diseases and of up in some areas to 70% and return they spread to many factors the first of iodine deficiency Add another such as autoimmune factors in disease Acmotsy and Garivz namely cases where the gland is active and there Psychological factors appear with the proliferation of thyroid cases of thyroid and now doctors from the 14 factor which speaks of genetic factors and genetic and this linked aspect of immune and other such as the use of soy and millet and exposure, especially in the neck and neck and psychological pressure area to radiation food and the factors which affect the reproduction when increasing hormones which women infect more than It affects men to consider and eyes and heart if they are active, and when they are low excess weight and inactivity and change skin texture and shape as a result of deposits for some materials. (Vanderpump,2005).

Thyroid hormones regulate the lipid metabolism through various mechanisms. Thyroid abnormalities are associated with increased risk of cardiovascular disease (CVD) and the diagnosis of these disorders might assist to avoid cardiovascular risk.(Grogan *et al*,2008).

1.3 Objectives:

1.3.1 General objective:-

To assess the plasma levels of lipid profile among Sudanese patients with Hypo and Hyper thyroidism in Khartoum state.

1.3.2 Specific objectives:-

1-To compare the mean of plasma levels of total cholesterol, triglycerides, HDL-c and LDL-c in patients with hyperthyroidism compared to control group.

2- To compare the mean of plasma levels of total cholesterol, triglycerides, HDL-c and LDL-c in patients with hypothyroidism compared to control group.

3- To correlate between the levels of total cholesterol, triglycerides, HDL-c and LDL-c and the duration of thyroid disorders.

Chapter Two

Literature review

2. Literature review

2.1 Thyroid anatomy:

The thyroid gland is butterfly shaped and sits on the trachea, in the anterior neck. It is comprised of two lobes connected in the middle by an isthmus. Inside, the gland is made up of many hollow follicles, whose epithelial cell walls (also known as follicle cells) surround a central cavity filled with a sticky, gelatinous material called colloid. Parafollicular cells are found in the follicle walls, protruding out into the surrounding connective tissue. (Mareib *et al*, 2007).

The thyroid is the largest exclusively endocrine gland in the body. The endocrine system is the body's communication hub, controlling cell, and therefore organ, function. A primary goal of the endocrine system is to maintain homeostasis within the organism, despite external fluctuations of any sort. Hormones, which act as chemical messengers, are the mechanism for this communication .(Mareib *et al*,2007).

Two types of cells are responsible for the production of hormones by the thyroid gland; parafollicular and follicular cells. The parafollicular cells also referred to as C cells, produce calcitonin hormone, which is involved in the regulation of calcium levels in the blood. The follicular cells secrete the active hormones T4 (thyroxine or tetra iodothyronine) and T3 (triiodothyronine), as well as smaller amounts of the inactive compounds reverse T3 (rT3). (Kelly et al, 2010).

2.2 Physiology of thyroid gland:

The thyroid gland produces the hormones L-thyroxine (T4) and L-triiodothyronine (T3), which regulate metabolic body processes, cellular respiration, total energy expenditure, growth and maturation of tissues, and turnover of hormones, substrates, and vitamins. (Durmont *et al*, 2002).

The gland is composed of a uniform cluster of follicles enclosed by a thin, fibrous capsule surrounded by capillaries. The follicles are the structural, functional, and secretory units of the thyroid gland.

Release of the hormones into the bloodstream involves the negative feedback system of the hypothalamic-pituitary-thyroid axis .(Isselbacher *et al*,1994).

A low metabolic rate or a decrease in serum T3 and/or T4 levels signals the hypothalamus to secrete thyrotropin releasing hormone (TRH), which travels to the

Anterior pituitary gland and stimulates secretion of thyroid-stimulating hormone

(TSH). An elevated T3 serum level inhibits release of TRH and TSH.(Rousset *et al*, 2004).

2.2.1 Functions of thyroid gland:

Thyroid hormones have many important biological effects. A major function is their control of the basal metabolic rate and calorigenesis through increased oxygen consumption in tissues via the effects of thyroid hormone on membrane transport (cycling of Na\K-ATPase with increased synthesis and consumption of adenosine triphosphate) and enhanced mite contrail metabolism (stimulation of mitochondrial respiration and oxidative phosphorylation).

Thyroid hormones are known to:-

1-Stimulate neural development and normal growth.

2-Promote sexual maturation.

3-Stimulate adrenergic activity with increase heart rate and carbohydrate metabolism.

4-Increase the synthesis and degradation of cholesterol and triglyceride.

5-Increase the requirements for vitamins.

6-Increase the calcium and phosphorous metabolism.

7-Enhance the sensitivity of adrenergic receptor to catecholamine's.

These effects are typically magnified in patients with either an over active thyroid gland such as in hyperthyroidism or reduced in patients with a sluggish thyroid such as in hypothyroidism. (Kelly *et al*, 2010).

2.2.2 Mechanism of thyroid hormones:

Thyroid hormone regulates a wide range of genes after its activation from the Prohormone, thyroxine (T4), to the active form, triiodothyronine (T3). (Gereben *et al*, 2008).

The signaling pathway is complex and highly regulated due to the expression of cell and tissue-specific thyroid hormone transporters, multiple thyroid hormone receptor (TR) isoforms, and interactions with corepressors and coactivators (cheng *et al*, 2010).

2.3 Abnormalities of thyroid gland:

Hypothyroidism and hyperthyroidism, constitutes the most common endocrine abnormality in recent years, diagnosed either in subclinical or clinical form. (Hollowell *et al*, 2002).

Thyroid disease is associated with various metabolic abnormalities, due to the effects of thyroid hormones on nearly all major metabolic pathways. This might be a direct effect or an indirect effect by modification of other regulatory hormones such as insulin or catecholamine (Kim, 2008).

2.3.1 Hypothyroidism:

Decreased thyroid hormone synthesis and low levels of circulating thyroid hormones result in biochemical and/or clinical hypothyroidism. This condition occurs more frequently in women; the overall incidence is about 3% of the general population. The clinical presentation, particularly in elderly patients, may be subtle; therefore, routine screening of thyroid function tests is generally recommended for women more than 50 years of age.

Clinically, hypothyroid patients present with complaints of one or more of the following:

fatigue, weakness, lethargy, cold intolerance, dry/coarse/cold skin, coarse hair, periorbital puffiness, hoarseness, constipation, weight gain, joint pain, muscle cramps and stiffness, mental impairment, depression, and menstrual disturbances. Upon examination, the patient may also have bradycardia, prolonged relaxation of Deep-tendon reflexes, and hypercholesterolemia.

Hypothyroidism is classified as primary or secondary. Primary hypothyroidism results from diseases or treatment that directly destroy thyroid tissues or interfere

with thyroid hormone biosynthesis. Secondary hypothyroidism occurs as a results of pituitary or hypothalamic disease (Jack De Ruiter, 2002).

2.3.1.1 Primary hypothyroidism:-

Primary hypothyroidism is due to a disorder of the thyroid gland causing decreased synthesis and secretion of thyroid hormones. Hypothyroidism, which in 50% of the cases is of autoimmune etiology, is observed in chronic autoimmune thyroiditis. In the remaining 50% it is due to other causes or drugs. Recently, postpartum thyroiditis and silent thyroiditis, which may cause hypothyroidism, are considered as manifestations of chronic autoimmune thyroiditis.(Amino *et al*,1976).

Increased levels of anti-TPO antibodies are found in 95% and antithyroglonulin antibodies in 60% of the cases being higher in the atrophic than the goitrous form of the disease. The prevalence of Hashimoto's thyroiditis is great in micronodular goiter. (Yeh *et al*,1996).

Postpartum thyroiditis, which appears during the first year after delivery and affects 5%-10% of women, is due to the presence of antithyroid antibodies which increase after delivery. It presents with mild hyperthyroidism which may be transformed to hypothyroidism and may subside without therapy or may present only with hypothyroidism and should be managed by thyroxine for a duration of up to 6 months.

Silent thyroiditis presents with mild, of recent onset hyperthyroidism. It is due to the secretion of thyroid hormones in the circulation, due to cell lysis and subsides in 6-12 weeks or is transformed in 50% of the cases to transient hypothyroidism, which subsides in 2-12 weeks Iodine insufficiency is a common cause of hypothyroidism. (Andersson *et al*,2005).

These patients usually have a large goiter. Transient hypothyroidism may occur after the ingestion of large amounts of iodine and is referred to as Wolff- Chaicoff effect, due to the inhibition of hormone synthesis within the thyroid. It appears that

there is a mild enzyme disorder which is corroborated by the ingestion of iodine agents. Increased amounts of iodine are found in contrast agents and in the drug amiodarone.

In partial thyroidectomy for hyperthyroidism clinical hypothyroidism has been found in 17% and subclinical in 51.3% whereas in partial thyroidectomy for various disorders clinical hypothyroidism has been found in 27%. In Graves' disease mild and sometimes transient hypothyroidism is observed during the first 6 months after radioiodine therapy.

External radiotherapy of the head and neck, as well as whole body irradiation may cause damage to the thyroid and lead to hypothyroidism. Hypothyroidism appears after a rather large time period. (Mercado *et al*, 2001).

Various drugs may cause hypothyroidism, the commonest being the widely used drugs amiodarone and lithium. Interferon-a may also cause hypothyroidism, usually mild. The new tyrosine kinase inhibitor Sunitinib, an anticancer agent, has been shown to cause hypothyroidism. (Vetter *et al*, 2008).

Children and infants may develop hypothyroidism due to thyroid agenesis or dysgenesis and a disorder of thyroid hormone biosynthesis. Antithyroid drug therapy in pregnant women who have hyperthyroidism may lead to hypothyroidism in newborn infants.

Generalized resistance to thyroid hormones is a rare, autosomal recessive disorder caused by a mutation in the T_3receptor gene. The TSH level is usually normal and T_3 and T_4 levels are elevated. Patients are usually euthyroid and do not require thyroid hormone replacement. (Georgiou *et al*,1987).

Primary hypothyroidism may be clinical, where free T_4 (FT_4) is decreased and TSH is increased or subclinical where FT_4 is normal and TSH is increased.

The distinction between subclinical and clinical hypothyroidism is of major significance as in clinical hypothyroidism symptoms are more severe even coma may occur, while in subclinical hypothyroidism symptoms are less serious and may even be absent. (Bianco *et al*, 2002).

2.3.3.2 Secondary (central) hypothyroidism:-

Secondary hypothyroidism(central) due to the failure of adequate thyroid-stimulating hormone (TSH) secretion from the pituitary gland or thyrotrophin-releasing hormone (TRH) from the hypothalamus. Secondary hypothyroidism can be differentiated in pituitary and hypothalamic by the use of TRH test. In secondary hypothyroidism FT_4 is decreased and TSH is normal or decreased. (Bianco *et al*, 2002).

Secondary hypothyroidism is caused by a disorder of the pituitary or the hypothalamus, leading to decreased TSH secretion and consequently to decreased synthesis and secretion of thyroid hormones. Secondary hypothyroidism is also reported as central and is divided in secondary and tertiary when the causes are in the pituitary and the hypothalamus, respectively. A variety of disorders can cause secondary hypothyroidism. The most common causes are pituitary adenomas as well as surgery and/or radiotherapy, used to treat them. . (Georgiou *et al*, 1987).

2.3.2 Hyperthyroidism:-

Clinical hyperthyroidism, also called thyrotoxicosis, is the effects of excess thyroid hormone and can be triggered by different disorders. Etiologic diagnosis influences prognosis and therapy. The prevalence of hyperthyroidism in community-based studies has been estimated at 2 percent for women and 0.2 percent for men. (Turnbridge *et al*,1977).

As 15 percent of cases of hyperthyroidism occur in patients older than 60 years. (Levy, 1991).

Hyperthyroidism presents with multiple symptoms that vary according to the age of the patient ,duration of illness, magnitude of hormone excess, and presence of comorbid conditions .Symptoms are related to the thyroid hormone's stimulation of catabolic enzymopathic activity and catabolism, and enhancement of sensitivity to catecholamines. (Trivalle *et al*,1996).

Common symptoms and signs with attention to the differences in clinical presentation between younger and older patients. Older patients often present with a paucity of classic signs and symptoms, which can make the diagnosis more difficult. (Knudson, 1995).

Thyroid storm is a rare presentation of hyperthyroidism that may occur after a stressful illness in a patient with untreated or undertreated hyperthyroidism and is characterized by delirium, severe tachycardia, fever, vomiting, diarrhea and dehydration. (Fitzgerald, 2005).

The causes of hyperthyroidism:

1-Toxic adenoma, 2-Toxic multinodular goiter, 3-Subacute thyroiditis,

4-Lymphocytic thyroiditis , postpartum thyroiditis, medication-induced thyroiditis,5-Graves' disease (thyroid-stimulating antibody),6-Iodine-induced hyper functioning of thyroid gland (iodide ingestion, radiographic contrast, amiodarone [Cordarone],7-Functioning pituitary adenoma (thyroid-stimulating hormone); trophoplastictumors (human chorionic gonadotropin),8-Factitial hyperthyroidism,9-Struma ovarii; metastatic thyroid cancer(Goroll *et al*,2000).

The most common cause of hyperthyroidism is Graves' disease, a systemic autoimmune process in which the patient's body is producing autoantibodies against the thyrotropin (TSH) receptor. These autoantibodies called thyroid-

stimulating immunoglobulins (TSH [stim] Abs) are present in 95% of patients with Grave's disease and activate the thyrotropin (TSH) receptor and stimulate the Uncontrolled production and release of T4 and T3.

Measurement of the TSH level in addition to the free T4 level greatly enhances diagnostic sensitivity. The negative feedback between free thyroid hormone concentrations and TSH secretion is very sensitively regulated; as little as a 20% increase in free T4 may result in suppression of TSH secretion to undetectable levels as illustrated in subclinical hyperthyroidism. Laboratory findings in Graves' disease and other forms of thyrotoxicosis include low to undetectable (depending on the sensitivity of the radioassay) TSH levels due to feedback inhibition by high thyroid hormone levels, and increased levels of both T3 and T4, with an increased ratio of T3 relative to T3 (Jack DeRuiter, 2002).

The treatment of hyperthyroidism depends on the cause and severity of the disease, as well as on the patient's age,

Goiter size, comorbid conditions, and treatment desires (Fitzgerald, 2005).

2.4 Lipid profile:

Lipids, commonly referred to as fats, have adual role. First, because they are composed of mostly carbon –hydrogen (C-H) bonds,they are a rich source of energy and an efficient way for the body to store excess calories. Because of their unique physical properties, lipids are also an integral part of cell membranes and, therefore, also play an important structural role in cells.

The lipids transported by lipoproteins, namely triglycerides, phospholipids, cholesterol, and cholesteryl esters, are also the principal lipids found in cells and the main focus of this section. (Bishop *et al*, 2010).

The cholesterol, Highdensity lipoprotein (HDL) cholesterol, triglycerides (TG), low-density lipoprotein (LDL) particle size and blood pressure have been found to be more pronounced in women than in men. (Howard *et al*,1998).

The lipoprotein profile of a woman undergoes many changes during her lifetime because of the effects of endogenous hormones at pregnancy, the administration of oral contraceptives, and estrogen replacement at the menopause. (Miller,1990).

The lipids are transported by lipoproteins, namely fatty acid, phospholipids, cholesterol and cholesteryl ester are the principal lipids found in the cells. Men and women both show tendency toward increased total cholesterol, LDL-c and triglyceride concentration with age. HDL-c concentration generally remains stable after the onset of puberty. (Bishop *et al*, 2005).

Circulating levels of total cholesterol, LDL-c and triglyceride in young children are generally much lower than those seen in adults. In addition concentrations do not differ significantly between boys and girls, and HDL-c level for both boys and girls are comparable to those of adult women. At the onset of puberty however HDL-c concentration in boys fall to adult male level, adrop of approximately 20%

whereas those of girl do not change. It is account for much of the observed association with increased risk of premature heart disease. (Bishop *et al*, 2005).

2.4.1 Triglycerides:

Triglycerides are another fat in the bloodstream. The most common type of fat in the body. Normal triglyceride levels vary by age and sex. High levels of triglycerides is also linked to heart disease. (Stryer, 1988).

Triglycerides in plasma are derived from fats eaten in foods or made in the body from other energy source like carbohydrates. Calories ingested in meal and not used immediately by tissues are converted to triglycerides and transported to fat cells to be stored. Hormones regulate the release of triglycerides from fat tissue so they meet the body needs for energy between meals. (Tietz *et al*, 2010).

High blood levels of triglycerides, the most abundant fatty molecule in most organisms. Elevated levels of triglycerides are associated with atherosclerosis, even in the absence of hypercholesterolemia (high cholesterol levels), and predispose to cardiovascular disease. Very high triglyceride levels also increase the risk of acute pancreatitis. (Berglund et al, 2012).

Causes of high serum triglycerides:-

Condition that may cause high serum triglycerides includes:-

1\ Obesity.

2\ poorly controlled diabetes.

3\ an under active thyroid.

4\ renal failure.

5\ Excessive intake of carbohydrates.

6\ Drinking a lot of alcohol.

Certain medicine may also raise triglyceride e-g: steroid, beta-blockers, diuretics and birth control pills. (Tietz et al, 2010).

2.4.2 Cholesterol:

Cholesterol is a waxy substance made by animal liver and also supplied in diet through animal products such as meats, poultry, fish and dairy products. Cholesterol is needed in the body to insulate nerves, make cell membranes and produce certain hormones, and it is an important lipid in some membranes.

Cholesterol plays a major role in human heart health. (Tabas , 2002).

Cholesterol is an important precursor molecule for synthesis of vitamin D and the steroid hormones. Human breast milk also contain significant quantities of cholesterol. Cholesterol is not present in plant based food source unless it has been added during the foods preparation .(Tietz *et al* ,2010).

2.4.2.1 Hypercholesterolemia:

High plasma cholesterol level (Hypercholesterolemia) or more correctly higher Concentrations of LDL-c and lower concentration of functional HDL-c are strongly associated with cardiovascular disease because these promote atheroma Development in arteries (atherosclerosis).

This disease process leads to myocardial infarction, stroke and prepheral vascular disease. Cholesterol can be both good and bad. High-density lipoprotein (HDL) is good cholesterol because they remove cholesterol from the cells and atheroma and low-density lipoprotein (LDL) is bad cholesterol because they have been linked to atheroma formation (Tietz *et al*,2010).

Causes of high serum cholesterol:

Hypercholesterolemia may be associated with:-

1-A diet high in saturated fat and cholesterol.

2- Lack of exercise – this can increase the LDL-c level and decrease the HDL-c level.

3- Overweight.

4- Age and gender –cholesterol level generally rise with increasing age and men are more likely to be affected than women.

5- Excessive intake of alcohol.

Rarely, high cholesterol can be caused by a condition which may runs in family, this called (family hypercholesterolemia).

Other condition such as poorly controlled diabetes, certain kidney and liver diseases and an underactive thyroid may also cause high cholesterol.

Some medicine such as beta-blockers, steroids or thiazides may also affect blood lipid level (Tietz *et al*, 2010).

2.4.2.2 Hypocholesterolemia:

Abnormally low levels of cholesterol are termed hypocholesterolemia.

Research into the causes of this state is relatively limited, but some studies suggest a link with depression, cancer and cerebral hemorrhage. Generally, the low cholesterol level seems to be a consequence of underlying illness, rather than a cause (Tietz *et al*, 2010).

2.4.3 Lipoproteins:

Lipoproteins are soluble complexes of proteins (apolipoproteins) and lipids that transport lipids in the circulation of all vertebrates and even insects. Lipoproteins are synthesized in the liver, in the intestines, arise from metabolic changes of precursor lipoproteins, or are assembled at the cell membranes from cellular lipids

and exogenous lipoproteins or apolipoproteins. In the circulation, lipoproteins are highly dynamic. They undergo enzymatic reactions of their lipid components, facilitated and spontaneous lipid transfers, transfers of soluble apolipoproteins, and conformational changes of the apolipoproteins in response to the compositional changes. Finally, lipoproteins are taken up and catabolized in the liver, kidney, and peripheral tissues via receptor-mediated and other mechanisms (Barklay, 1972).

2.4.3.1 Classification of lipoproteins:

According to density:-

Lipoproteins may be classified as follows, listed from larger and less dense one to smaller and denser ones. Lipoproteins are larger and less dense, if they consist of more fats than of proteins.

1-Chylomicrons: carry triacylglycerol (fat) from the intestine to the liver, skeletal muscle and to adipose tissue.

2- Very low density lipoprotein (VLDL): carry (newly synthesized) triacylglycerol from liver to adipose tissue.

3- Intermediate density lipoprotein (IDL): are intermediate between VLDL and LDL. They are not usually detectable in the blood.

4- Low density lipoprotein (LDL): carry cholesterol from the liver to cells of the body.

5- High density lipoprotein (HDL): collect cholesterol from the body tissues and bring it back to the liver. (Bishop *et al* ,2005).

2.4.3.2 Chylomicrons:

Chylomicrons, which contain apo B- 48, are the largest and the least dense of the lipoprotein particles, having diameters as large as 1200 nm. Because of their large size, they reflect light and account for the turbidity of postprandial plasma . Because they are so light, they also readily float to the top of stored plasma and form a creamy layer, which is a hallmark for the presence of chylomicrons.

Chylomicrons are produced by the intestine, where they are packaged with absorbed dietary lipid. Once they enter the circulation, triglycerides and cholesteryl esters in chylomicrons are rapidly hydrolyzed by lipases and, within a few hours, they are transformed into chylomicron remnant particles, which are recognized by proteoglycans and remnant receptors in the liver, facilitating their uptake. The principle role of chylomicrons is the delivery of dietary lipids to hepatic and peripheral cells (Bishop *et al*, 2010).

2.4.3.3 Very Low Density Lipoproteins (VLDL):

VLDL is produced by the liver and contains apo B-100, apo E and apo Cs; like chylomicrons, they are also rich in triglycerides. They are the major carriers of endogenous (hepatic-derived) triglycerides and transfer triglycerides from the liver to peripheral tissue. Like chylomicrons, they also reflect light and account for most of the turbidity observed in fasting hyperlipidemic plasma specimens, although they do not form a creamy top layer like chylomicrons, because they are smaller and less buoyant. Excess dietary intake of carbohydrate, saturated fatty acids, and trans fatty acids enhances the hepatic synthesis of triglycerides, which in turn increases VLDL production (Bishop *et al*, 2010).

2.4.3.4 Low Density Lipoproteins (LDL):

LDL-c primarily contains apo B-100 and is more cholesterol rich than other apo B-Containing lipoproteins. They form as a consequence of the lipolysis of VLDL.

LDL-c carry cholesterol from the liver to cells of the body. there has been great interest in measuring LDL-c subfractions, because small, dense, LDL-c particles have been shown to be more proatherogenic and may be a better marker for coronary heart disease risk (Bishop *et al*, 2010).

2.4.3.5 High density lipoprotein (HDL):

HDL-c the smallest and most dense lipoprotein particle, is synthesized by both the liver and intestine. There are two major types of spherical HDL-c based on density

difference: HDL_2 and HDL_3. HDL_2 particles are larger in size and richer in lipid than HDL_3 and may reflect better efficiency in delivering lipids to the liver (Bishop *et al*, 2010).

2.5 Relationship between thyroid disorder and lipids:

It is well known that alterations in thyroid function result in changes in the composition and transport of lipoproteins. (Duntas,2002).

These changes in the lipid profile are explained by the regulatory effect of thyroid hormones on the activity of some key enzymes of lipoprotein metabolism. Specifically, the thyroid hormone stimulates the hepatic de novo cholesterol synthesis by inducing the 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase that catalyzes the conversion of HMG-CoA to mevalonate, the first step in the biosynthesis of cholesterol. (Ness *et al*,1973).

Additionally, thyroid hormones activate the LDL-c receptors; the promoter of the LDL-c receptor gene contains a thyroid hormone responsive element (TRE) which allows the triiodothyronine (T3) to upregulate the gene expression of the LDL-c receptor. (Bakker *et al*, 1998).

Thyroid hormones stimulate the cholesteryl ester transfer protein (CETP), an enzyme which transports cholesteryl esters from HDL2 to the very low density lipoproteins (VLDL) and triglycerides in the opposite direction .(Lagrost,1994).

Finally, thyroid hormones stimulate the lipoprotein lipase (LPL), which catabolizes the triglyceride-rich lipoproteins, and the hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 .(Kussi *et al*,1980).

Chapter Three

Materials and Methods

3. Materials and Methods

3.1 Materials

3.1.1 Study approach

A quantitative method was used to measure total cholesterol, triglycerides, HDL-c and LDL-c in Sudanese patients with Hypo and Hyper thyroidism in Khartoum state, during the period from March to September 2015.

3.1.2 Study design

This is a case- control study.

3.1.3 Study area:

This study was conducted in Ribat university hospital in Khartoum state.

3.1.4 Target population:

The study included patients with Hypo and Hyper thyroidism (males and females).

3.1.5 Sample size:

A total of 50 patients with thyroid dysfunction (25 hyperthyroidism and 25 hypothyroidism patients) were enrolled in this study and (25) apparently healthy volunteers (age and sex matched with the test group) were included to serve as control.

3.1.6 Inclusion and Exclusion criteria:

Sudanese patients with thyroid dysfunction and apparently healthy volunteers were included, while patients with diabetes mellitus, hypertension and cardiac disease were excluded.

3.1.7 Ethical consideration:

Verbal consent was taken regarding acceptance to participate in the study and reassurance of confidentiality. Before the specimen was collected, the donor knew that this specimen was collected for research purpose.

3.1.8 Data collection:

The clinical data were obtained from history, clinical examination and hospital follow up records and were recorded on aquestionnaire sheet.

3.1.9 Sample collection and processing:

Local 70% antiseptic for the skin was used , 3 ml of venous blood (fasting sample) was collected from the arm of each patient and control by syringe (3ml) using venipuncturing directly into centrifuge tube which contained heparin as anticoagulant for plasma preparation. Plasma was separated from blood cells after centrifugation for 5 minutes at 5000 r.p.m at room temperature and the sera were used immediately for estimation of lipid profile.

3.1.10 Requirement:

Sterile needle

70% alcohol, Cotton

Plan and heparinize container

Constant temperature

Cuvette, Test tubes.

Biosystem (spectrophotometer)

Automatic pipette

Blue and yellow tip.

Disposable plastic dropper.

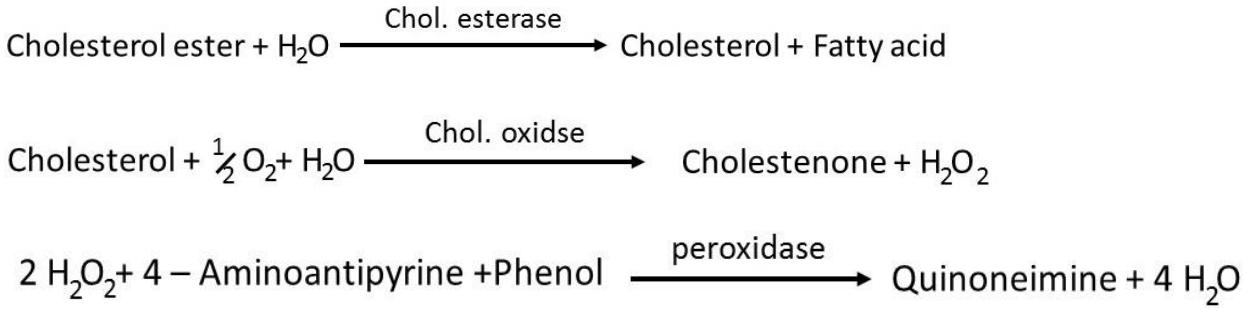
Centrifuge.

3.2 Methods

3.2.1 Estimation of total cholesterol:

3.2.1.1 Principle of total cholesterol:

Free and esterified cholesterol in the sample originates, by means of the coupled reactions described below a colored complex that can be measured by spectrophotometry.



3.2.1.2 Reagent preparation and stability:

The reagent and Standard are provide ready to use and are stable for 7 days at 2-8 ˚c.

3.2.1.3 Procedure of total cholesterol:

The reagents were first brought to room temperature then the following amount were pipetting according to the table below.

	Blank	Standard	Sample
Working reagent(ml)	1.0	1.0	1.0
Sample		——	0.01
standard(ml)		0.01	——

- Reagents were mixed and incubated for 10 min at room temperature.
- The absorbance (A) of the Standard and the sample were read at 500 nm against the blank.

3.2.1.4 Calculation:

The Cholesterol concentration in the sample was calculated using the following general formula.

Cholesterol (mg/dl) = (A° sample/A° stander) * conc. Stander

A =absorbance

Conc= concentration

Reference values:

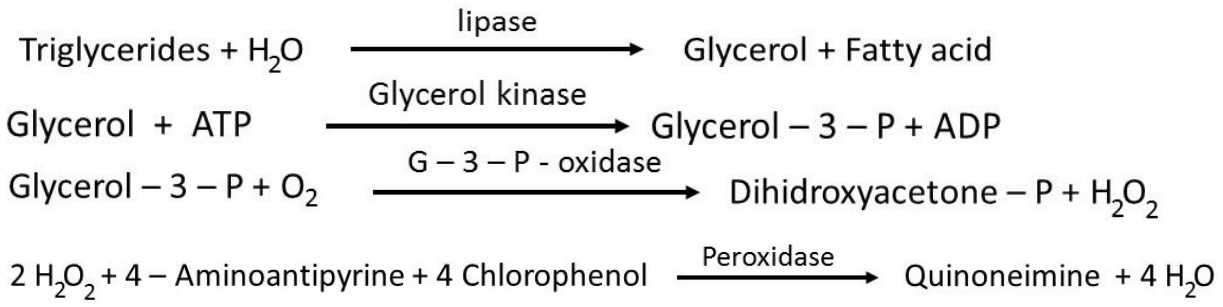
Serum or plasma

Up to 200 mg/dl = 5.2 mmol/l (Bishop *et al*, 2010).

3.2.2 Estimation of triglycerides:

3.2.2.1 Principle of triglycerides:

Triglycerides in the sample originates, by means of the coupled reactions described below, a coloured complex that can be measured by spectrophotometry.



3.2.2.2 Reagent preparation and stability:

The reagent and Standard are provide ready to use and are stable for 5days at2-8˚c.

3.2.2.3 Procedure of triglycerides:

The reagents were first brought to room temperature then the following amount were pipetting according to the table below.

	Blank	Standard	Sample
Working reagent(ml)	1.0	1.0	1.0
Sample		——	0.01
standard(ml)		0.01	——

- Reagents were mixed and incubated for 15 min at room temperature or for 5 minutes at 37˚c.
- The absorbance (A) of the Standard and sample were read at 500 nm gainst blank.

3.2.2.4 Calculation:

The triglycerides concentration in the sample was calculated using the following general formula.

(A° sample/A° stander) * Conc. Stander

A =absorbance

Conc = concentration

Reference values:

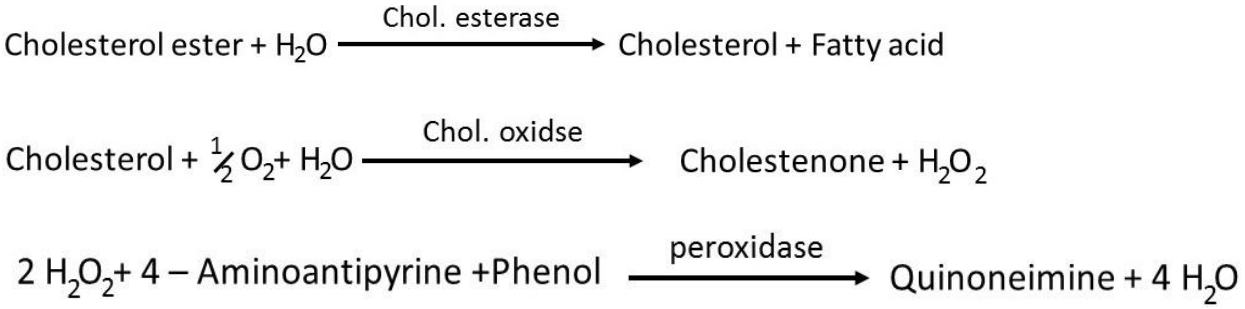
Serum or plasma

Up to 150 mg/dl = 1.7 mmol/l (Bishop *et al*, 2010).

3.2.3 Estimation of High density lipoprotein (HDL):

3.2.3.1 Principle of HDL:

Very low density lipoproteins (VLDL) and low density lipoproteins (LDL) in the sample precipitate with phosphotungstate and magnesium ions. The supernatant contains high density lipoproteins (HDL). The HDL-c cholesterol is then spectrophotometrically measured by means of the coupled reactions described below.



3.2.3.2 Reagent preparation and stability:

The reagent and Standard are provide ready to use and are stable for 7 day's

at 2-8˚c.

3.2.3.3 Procedure of HDL-c:

Precipitation:

1-Reagent were pipetting into labelled centrifuge tubes:

Sample	0.2ml
Reagent(Cholesterol HDL kit)	0.5ml

2-Mixed thoroughly and let stand for 10 minutes at room temperature.

3-Centrifuge at a minimum of 4000r.p.m for 10 minutes.

4-The supernatant were collected carefully.

Colorimetry:

5- The reagents were brough at room temperature.

6-Pipette into labelled test tubes:

	Blank	Standard	Sample
Cholesterol working reagent(ml)	1.0	1.0	1.0
Sample supernatant		——	0.1
HDL-c standard(ml)		0.1	——
D.W (ml)	0.1	——	——

- Reagents were mixed and incubated for 30 min at room temperature or for 10 minutes at 37˚c.
- The absorbance (A) of the Standard and the sample were read at 500 nm against blank.

3.2.3.4 Calculation:

The HDL-c cholesterol concentration in the sample was calculated using the following general formula.

(A° sample/A° stander) * Conc. Stander* DF

A =absorbance

Conc = concentration

DF = dilution factor

Reference values:

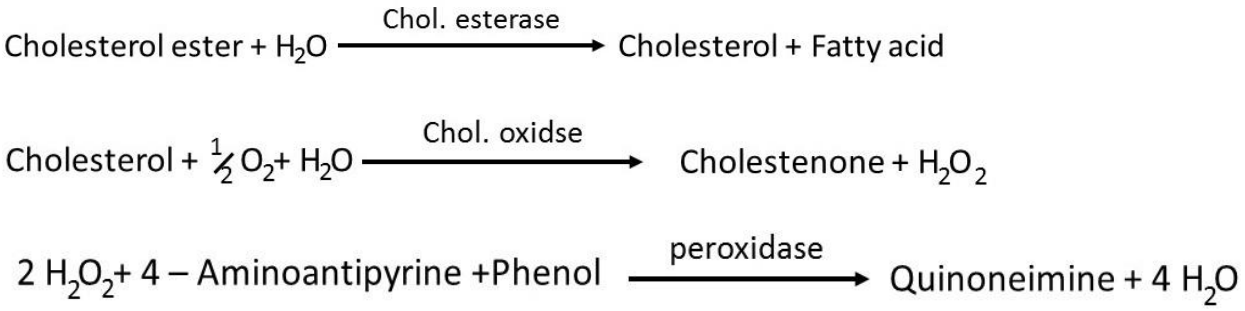
Serum or plasma

Up to 35mg/dl = 0.91 mmol/l (Bishop *et al*, 2010).

3.2.4 Estimation of Low density lipoprotein (LDL):

3.2.4.1 Principle of LDL-c:

Low density lipoproteins (LDL) in the sample precipitate with polyvinyl sulphate. Their concentration is calculated from the difference between the serum total cholesterol and the cholesterol in the supernatant after centrifugation. The cholesterol is spectrophotometrically measured by means of the coupled reactions described below.



3.2.4.2 Reagent preparation and stability:

The reagent and Standard are provide ready to use and are stable for 24 hours at 2-8 ˚c.

3.2.4.3 Procedure of LDL-c:

Precipitation:

1- Reagent were pipetting into labelled centrifuge tubes:

Sample	0.2ml
Reagent(Cholesterol LDL kit)	0.2ml

2-Mixed thoroughly and let stand for 15 minutes at room temperature.

3-Centrifuge at a minimum of 4000r.p.m for 15 minutes.

4-The supernatant were collected carefully.

Colorimetry:

5- The reagents were brough at room temperature.

6-Pipette into labelled test tubes:

	Blank	Standard	Sample
Cholesterol working reagent(ml)	1.0	1.0	1.0
Sample supernatant		——	0.02
Cholesterol standard(ml)		0.02	——
D.W (ml)	0.02	——	——

- Reagents were mixed and incubated for 30 min at room temperature or for 10 minutes at 37˚c.
- The absorbance (A) of the Standard and the sample were read at 500 nm against blank.

3.2.4.4 Calculation:

The cholesterol concentration in the supernatant was calculated using the following general formula.

(A° sample/A° stander) * conc. Stander* DF

A =absorbance

Conc= concentration

DF = dilution factor

The LDL-c cholesterol concentration in the sample is calculated as follows:

LDL-c cholesterol = total cholesterol- cholesterol in supernatant.

Reference values:

Serum or plasma

Optimal: Up to 100 mg/dl = 2.59 mmol/l (Bishop *et al*, 2010).

3.3 Quality control

The precision and accuracy of all methods used in this study were checked by commercially prepared control sample before application for the measurement of test and control samples.

3.4 Data analysis

data was analyzed using SPSS computer program, the mean and standard deviation of total cholesterol, triglycerides, HDL-c and LDL-c were obtained and the independent 't.test' used for comparison (p value of ≤ 0.05) was consider significant.

Chapter Four

Results

4. Results

The results of the biochemical determinant serum lipid profile (total cholesterol, triglycerides, HDL-c and LDL-c) are given in tables and figures.

Table (4-1) shows ages and gender of patients with thyroid disorders. The result showed that the patients whose ages over forty years were more susceptible for thyroid disorders with the percentage of 68% compared to those with age below forty years (32%).

The number of males in patients was 13(26%), while the numbers of females was 37(74%).

Table (4-2): shows the mean of plasma levels of total cholesterol, triglycerides, HDL-c and LDL-c in hyperthyroidism patients compared to control group.

The plasma levels of total cholesterol and LDL-c were significantly increased in hyperthyroidism patients compared to control group. Total cholesterol (mean ± SD: 197± 23 versus173± 18 mg/dl , P- value 0.000) .

LDL-c (mean ± SD: 125± 13 versus 96± 5mg/dl, P- value 0.000).

No significant different between the mean of plasma levels of triglycerides and HDL-c in both study groups.

Triglycerides (mean ± SD: 113± 13 versus 111± 11mg/dl, P-value 0.65).

HDL-c (mean± SD: 48 ± 9 versus 50± 9mg/dl, p- value 0.47).

Table (4-3): illustrate the mean of plasma levels of total cholesterol, triglycerides, HDL-c and LDL-c in hypothyroidism patients compared to control group.

The plasma levels of total cholesterol, triglyceride and LDL-c were significantly increased in hypothyroidism patients compared to control group.

Total cholesterol (mean ± SD: 212± 22 versus174± 18 mg/dl , P- value 0.000) .

Triglycerides (mean ± SD: 152± 29 versus111± 11 mg/dl , P- value 0.000).

LDL-c (mean ± SD: 125± 21 versus 95± 5 mg/dl , P- value 0.000).

No significant different between the mean of plasma level of HDL-c in both study groups.

HDL-c (mean ± SD: 50± 11 versus50± 9 mg/dl , P- value 0.925).

Figure (4-1): a scatter plot shows the correlation between total cholesterol level and duration of thyroid disorders. Showed significant correlation between total cholesterol level and increased duration of thyroid disorders (r= 0.740, p-value=0.000).

Figure (4-2): a scatter plot shows the correlation between triglycerides level and duration of thyroid disorders. Showed significant correlation between triglycerides level and increased duration of thyroid disorders (r= 0.457, p-value=0.001).

Figure (4-3): a scatter plot shows the correlation between HDL-c level and duration of thyroid disorders. Showed no correlation (insignificant) between

HDL-c level and increased duration of thyroid disorders (r= 0.062,

p-value=0.669).

Figure (4-4): a scatter plot shows the correlation between LDL-c level and duration of thyroid disorders. Showed significant correlation between LDL-c level and increased duration of thyroid disorders (r= 0.779, p-value=0.000).

Table (4-1): Ages and gender of patients with thyroid disorders:

Variable	Number	%
Age 20-40 years	16	32%
Age 41-60 years	34	68%
Sex Male	13	26%
Sex Female	37	74%

Table (4-2):

The comparison between levels of total cholesterol, triglycerides, HDL-c and LDL-c (mg/dl) in hyperthyroidism patients and control group:

Variable	**Case (hyperthyroidism)** **Mean ± SD**	**Control** **Mean± SD**	**P-value**
Total cholesterol	197 ± 23	173.6 ± 18.5	0.000
Triglycerides	112.9 ±13.2	111.3 ±11.5	0.651
HDL-c	48.3 ± 9.3	50.2 ± 9.2	0.478
LDL-c	124.6 ± 13.5	95.8 ± 4.6	0.000

- Results given in mean ± SD.
- P-value ≤ 0.05 consider significant.

Table (4-3):

The comparison between levels of total cholesterol, triglycerides, HDL-c and LDL-c (mg/dl) in hypothyroidism patients and control group:

Variable	**Case (hypothyroidism)** **Mean ± SD**	**Control** **Mean± SD**	**P-value**
Total cholesterol	211.9 ± 22.1	173.6 ± 18.5	0.000
Triglycerides	152.0 ±29.0	111.3 ±11.5	0.000
HDL-c	50.4 ± 11.5	50.2 ± 9.2	0.925
LDL-c	125.0 ± 20.8	95.8 ± 4.6	0.000

- Results given in mean ± SD.
- P-value ≤ 0.05 consider significant.

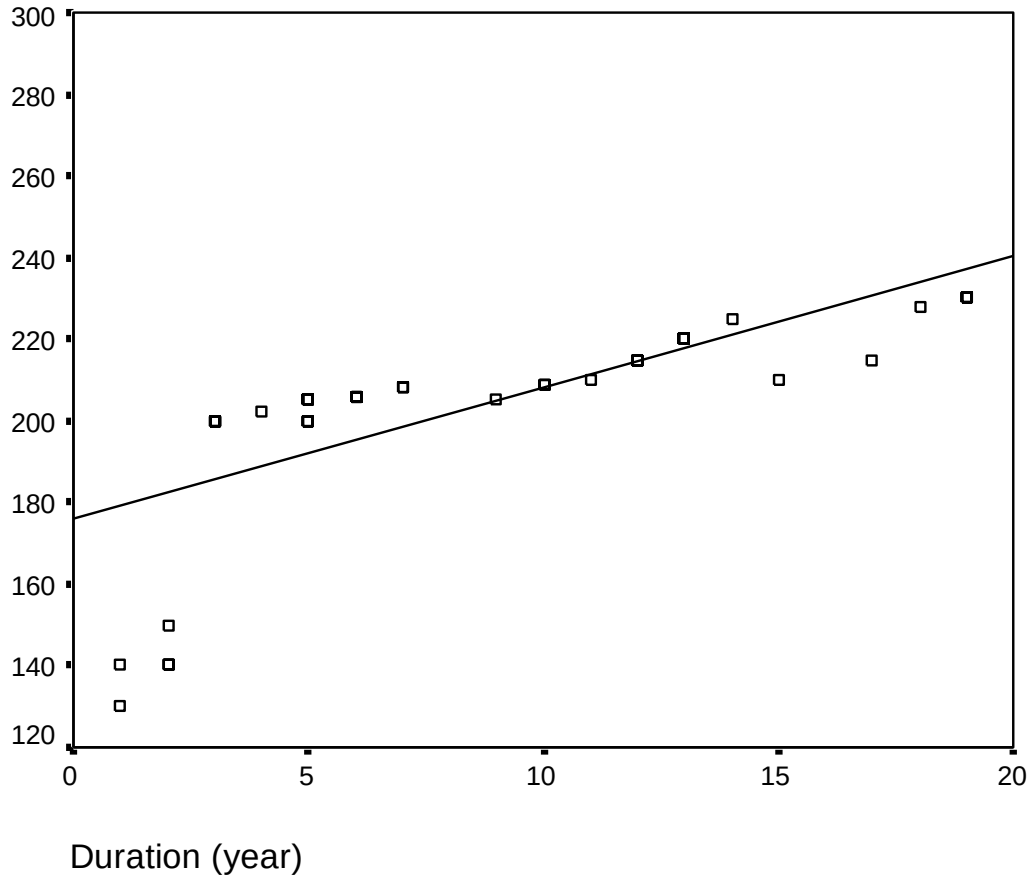


Figure (4-1): scatter plot of correlation between total cholesterol level and duration of thyroid disorders: (r= 0.740, p-value=0.000).

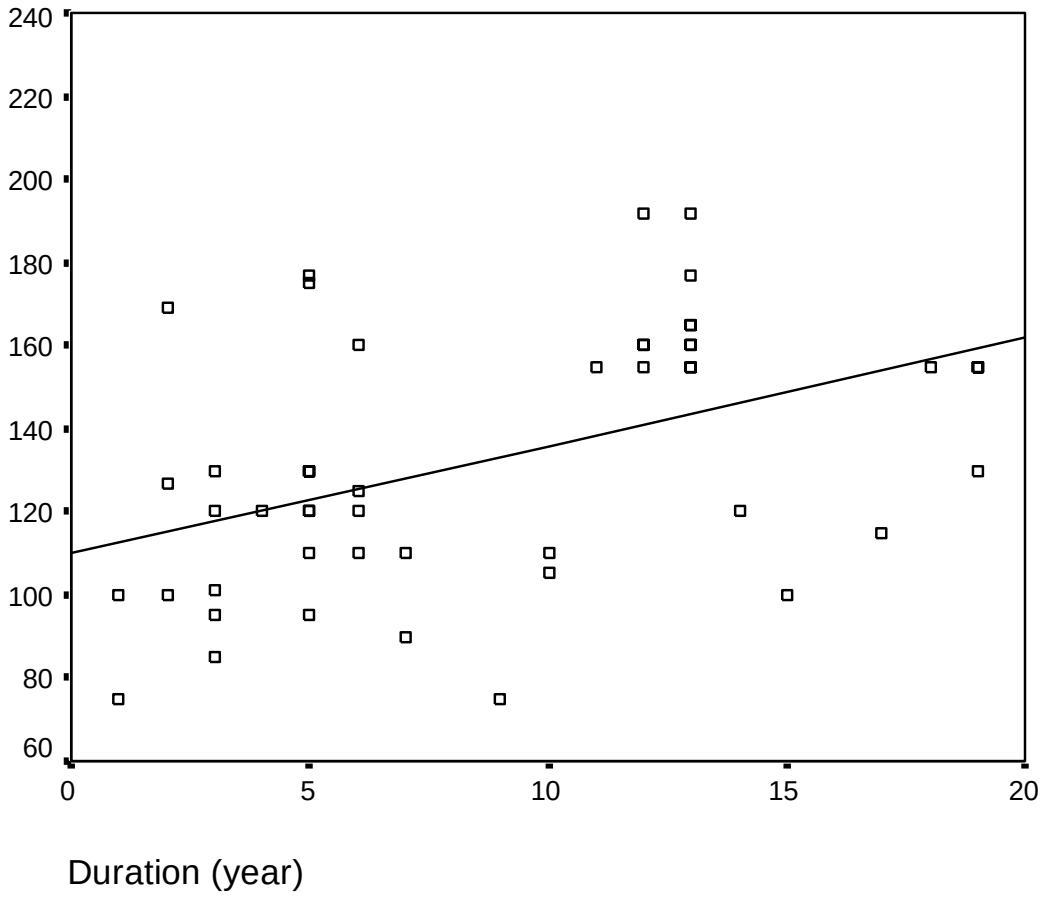


Figure (4-2): scatter plot of correlation between triglycerides level and duration of thyroid disorders: (r= 0.457, p-value=0.001).

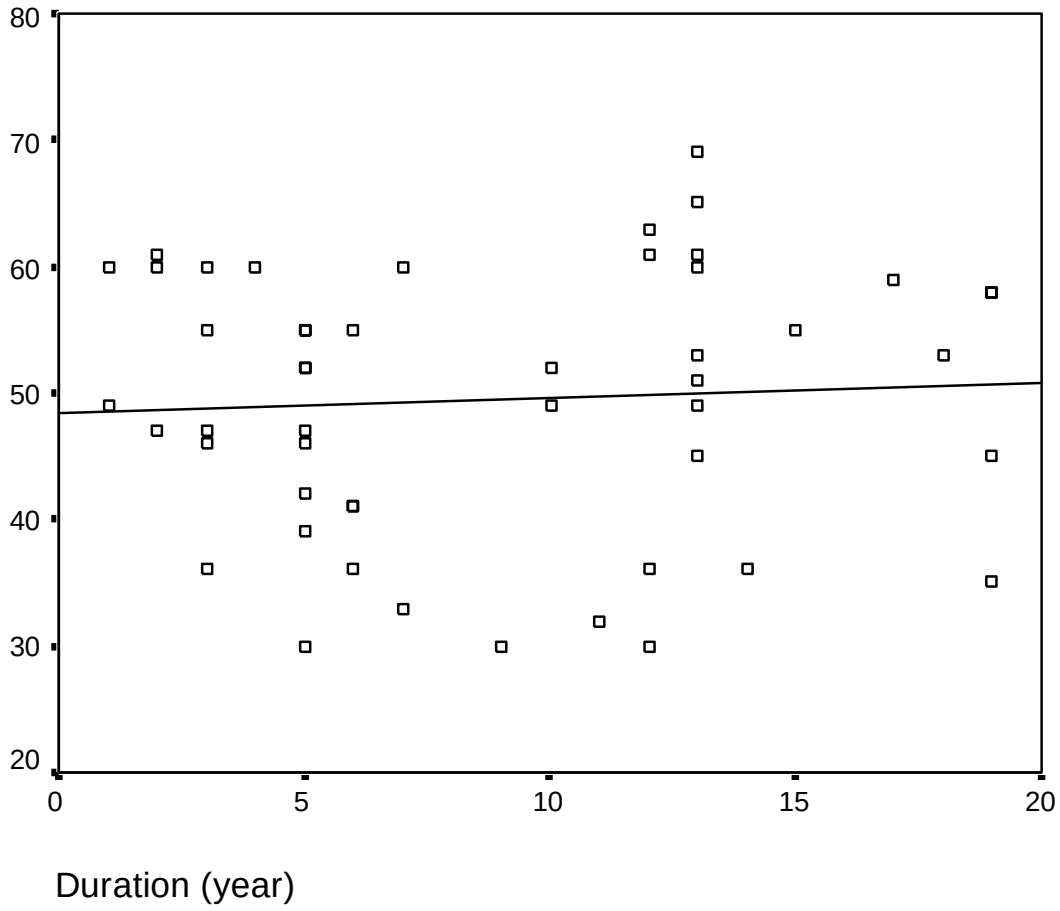


Figure (4-3): scatter plot of correlation between HDL-c level and duration of thyroid disorders: (r= 0.062, p-value=0.669).

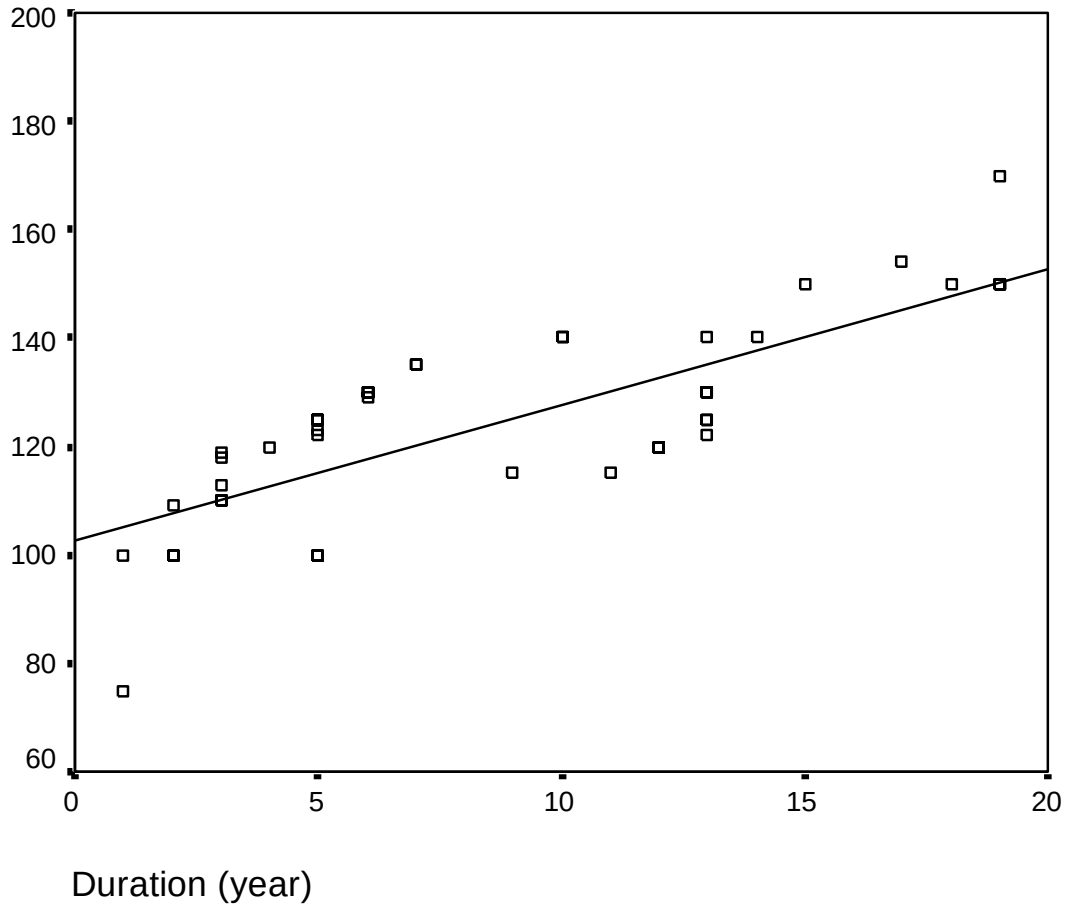


Figure (4-4): scatter plot of correlation between LDL-c level and duration of thyroid disorders: (r= 0.779, p-value=0.000).

Chapter Five

- **Discussion**
- **Conclusion**
- **Recommendations**

5.1 Discussion

Alterations in lipid profile are well known phenomena in thyroid dysfunction. Thyroid hormones regulate lipid metabolism through various mechanisms (regulate activity of some key enzymes of lipoprotein metabolism). (Bishop *et al,* 2005).

The present study was carried out to assess plasma lipids among Sudanese patients with Hypo and Hyper thyroidism in Khartoum state.

The findings obtained from specially designed questionnaire revealed that, the majority of patients with thyroid disease participated in this study over forty years. This result agreed with previous published results of many authors. (Hollowell *et al*, 1994), which showed thyroid disorders is more common in old ages.

Sex distribution in patients with thyroid disease in this study revealed that 74% were females. This results agreed with result carried out by (Bell et al, 2007),which showed female will be more likely to have thyroid dysfunction , that may be due to a sex difference in the prevalence of autoimmune diseases.

The results of present study revealed that there were significant increased in mean concentration of plasma total cholesterol (p- value 0.000) and LDL-c(p- value 0.000) in hyperthyroidism patients group when compared with control group.

These results are in agreement with study carried out by (Duntas , 2002), Which showed that hyperthyroidism exhibits an enhanced excretion of cholesterol and increased turn over of LDL-c, where as HDL-c is decreased or not affected. This contraversary result may be due to the thyroid treatment or the status of the disease weather it was overt or mild hyperthyroidism.

The findings of this study showed that, there were no significant difference in the mean of triglyceride and HDL-c between hyperthyroidism patients and control group, (p-value 0.65, p-value 0.47) respectively. These results were agreed with another study carried out by

(Duntas, 2002), Which showed that the HDL-c may not be affected. But these results were disagree with the study carried out by (Evagelos N *et al*, 2002), Which showed that hyperthyroidism a companied by a decrease in serum levels of total cholesterol and HDL-c.

In comparison the mean of lipid profile in hypothyroidism patients and control group, the study showed that there was a significant increased in the levels of total cholesterol, LDL-c and triglyceride , and no significant difference in HDL-c (p-value 0.92). These results were agree with the study carried out by (Elizabeth P *et al*, 2008), which showed there was statistically significant gradual increase in fasting total cholesterol , triglyceride and LDL-c as thyroid function declined . Also these findings were agree with the study carried out by

(Evagelos N *et al*, 2002), which showed that hypothyroidism was associated with high total cholesterol , LDL-c, while HDL-c was usually normal or elevated.

Also in this study as appeared in figure (4-1),(4-2)and (4-4) there were a significant correlation between duration of thyroid disorders and plasma total cholesterol , triglycerides and LDL-c levels in patients with thyroid disorders, (r= 0.740, p-value=0.000), (r= 0.457, p-value=0.001), (r= 0.779, p-value=0.000) respectively.

This result agreed with result done by (Duntas, 2002),Which found significant correlation between duration of thyroid disorders and plasma total cholesterol, triglycerides and LDL-c levels in patients with thyroid disorders.

The finding of this study showed that no correlation between duration of thyroid disorders and plasma HDL-c level (r= 0.062, p-value=0.669).This results agreed

with result carried by (Elizabeth P *et al*, 2008), Which found no correlation between HDL-c and duration of thyroid disorders.

5.2 Conclusion:

From the results and findings of this study, It is concluded the following :-

1-Thyroid disorders affected by ages and gender.

2-Total cholesterol and LDL-c are significantly increased in hyperthyroidism , while triglycerides and HDL-c are insignificant increased in hyperthyroidism.

3- Total cholesterol, triglycerides and LDL-c are significantly increased in hypothyroidism while HDL-c is insignificant increased in hypothyroidism.

4-There are significant correlation between duration of thyroid disorders and plasma levels of total cholesterol, triglycerides and LDL-c, and no correlation between duration of thyroid disorders and plasma level of HDL-c.

5.3 Recommendations:

1- Lipid profile should be done for patients with thyroid disorders routinly to avoid risk of cardiovascular disease.

2- More studies should be carried out on the effect of thyroid disorder in all lipid profile except Total cholesterol, triglycerides, HDL-c and LDL-c.

References

References

- Amino N, Hagen SR, Yamada N and Refetoff S . (1976). Measurement of circulating thyroid microsomal antibodies by the tanned red cell haemagglutination technique: its usefulness in the diagnosis of autoimmune thyroid diseases. Clin Endocrinol (Oxf); 5:115–125.
- Andersson M, Takkouche B, Egli I, Allen HE and Benoist B. (2005). Current global iodine status and progress over the last decade towards the elimination of iodine deficiency. Bull World Health Organ; 83:518–525.
- Bakker O, Hudig F, Meijssen S and Wiersinga WM.(1998). Effects of triiodothyronine and amiodarone on the promoter of the human LDL receptor gene. Biochem Biophys Res Commun; 240: 517-521.
- Barklay M. (1972). Lipoprotein class distribution in normal and disease states. In: G.J. Nelson. (Ed.). Blood Lipids and Lipoproteins: Quantitation, Composition, and Metabolism. Wiley-Interscience, New York; 587-603.
- Bell RJ, Davison SL, Topliss DJ, Donath S and Davis SR. (2007) . Wellbeing, health related quality of life and cardiovascular diseaserisk profile in women with subclinical thyroid disease- acommunity based study. *Clin Endocrinol*; 66: 548-56.
- Berglund L, Brunzell JD and Goldberg AC . (2012)."Evaluation and treatment of hypertriglyceridemia: an endocrine society clinical practice guideline". J. Clin. Endocrinol. Metab; 97 (9): 2969–89.
- Bishop M L ,Fody P E and Schoeff E L. (2005).Clinical chemistery-5th edition. Lippincott W illiams and Wilkins; 283-290.
- Bishop M L ,Fody P E and Schoeff E L. (2010).Clinical chemistery-6th edition. Lippincott Williams and Wilkins; 328-335.

- Bianco A, Salvatore D, Gereben B ,Berry MJ and Larsen PR. (2002). Biochemistry, cellular and molecular biology, and physiological roles of the iodothyronine selenodeiodinases. Endocr Rev; 23:38–89.
- Cheng SY, Leonard JL and Davis PJ. (2010). Molecular aspects of thyroid hormone actions. Endocr Rev; 31(2):139–170.
- Durmont JE, Corvilain B, Maenhaut C, Dunn JT, Refetoff S and Hennemann G. (2004) . The phylogeny, ontogeny, anatomy, and metabolic regulation of the thyroid. In Thyroid disease manager (chap. 1), August 2002. Available from: http://www.thyroidmanager.org/thyroidbook.htm.
- Duntas LH . (2002). Thyroid disease and lipids. Thyroid;12: 287-293.
- Elizabeth P and Pearce Peter W.F. (2008). Thyroid function and lipid subparticle sizes in patients with short-term hypothyroidism J Clin Endocrinol Metab; 93(3):888-94.
- Evagelos N Liberoboulos. (2002). Moses S Elisaf Dyslipidemia in patients with thyroid disorder. Hormones; 1(4):218-223.
- Fitzgerald PA . (2005). Endocrinology. In: Tierny LM, McPhee SJ, Papadakis MA. Current medical diagnosis and treatment. 44th ed. New York:McGraw- Hill; 2005:1102-10.
- Gereben B, Zavacki AM, Ribich S, Kim BW, Huang AS, Simonides WS, Zeold A and Bianco AC. (2008). Cellular and molecular basis of deiodinase-regulated thyroid hormone signaling. Endocr Rev; 29(7):898–938.

- Georgiou E, Ntalles K ,Proukakis Ch and Anousis ST. (1987). Clinical manifestations and use of microcomputer in the differential diagnosis between hypothyroid and obese women. Arch Hell Med ; 4:30–33.
- Goroll AH and Mulley AG . (2000). Primary care medicine: office evaluation and Management of the adult patient. 4th ed. Philadelphia: Lippincott Williams & Wilkins:60-63.
- Grogan A, Seaman HE, Wright JW and Vries CS. (2008).The incidence of autoimmune thyroid disease: a systematic review of the literature. Clin Endocrinol; 69:687-696.
- Heuck CC, Kallner A, Kanagasabapathy AS and Riesen W . (2000) . Diagnosis and monitoring of the disease of the thyroid. WHO Document : 8-9.
- Howard BV, Cowan LD ,Welty TK ,Robbins DC and Lee ET. (1998). Adverse effects of diabetes on multiple cardiovascular disease risk factors in women. The Strong Heart Study. Diabetes Care. Aug; 21(8):1258-1265.
- Hollowell JG, Staehling NW and Flanders WD. (1994). Serum TSH, T4, and thyroid antibodies in the United States population .National Health and Nutrition Examination Survey (NHANES III) Journal of Clinical Endocrinology and Metabolism; 2002. 87(2):489–499.
- Jack Detroiter. (2002). Thyroid pathology. Endocrine Module (PYPP 5260), Thyroid Section, spring;1-30.
- Kelly M, Rehan, Robert M, Sargis J,Larry Janeson and Anthony P. (2010). in:An over view of thyroid :Amajor player in regulating your metabolism.
- Kim B. (2008). Thyroid hormone as a determinant of energy expenditure and the basal metabolic rate. Thyroid ; 18 (2):141–144.

- Kussi T, Sacrinen P and Nikkila EA.(1980). Evidence for the role of hepatic endothelial lipase in the metabolism of plasma high density lipoprotein 2 in man. Atherosclerosis; 36: 589-593.
- Kuus T, Saarinen P and Nikkila EA. (1980). Evidence for the role of hepatic endothelial li-pase in the metabolism of plasma high density lipoprotein in man. Atheroscle;36(4):589-93.
- Knudson PB. (1995). Hyperthyroidism in adults: variable clinical presentations And approaches to diagnosis. J Am Board FAM Pract; 8:109-13.
- Lagrost L.(1994). Regulation of cholesteryl ester transfer protein (CETP) activity: Review of in vitro and in vivo studies. Biochem Biophys Acta; 1215: 209-236.
- Levy EG.(1991). Thyroid disease in the elderly. Med Clin North Am;75: 151-67.
- Mareib Elain N and Hoehn K .(2007). Human Anatomy & Physiology; Seventh Ad. Pearson Education, Inc. San Francisco, CA:110-112.
- Mercado G, Adelstein DJ, Saxton JP, Secic M, Larto MA and Lavertu P. (2001). Hypothyroidism: a frequent event after radiotherapy and after radiotherapy with chemotherapy for patients with head and neck carcinoma. Cancer; 92:2892–2897.
- Miller VT. (1990). Dyslipoproteinemia in women. Special considerat ions. Endocrinol Metab Clin North Am;19(2):381-98.
- Ness GC, Dugan RE, Lakshmanan MR, Nepokroeff CM and Porter JW. (1973). Stimulation of hepatic ™-hydroxy-methyl-glutaryl Coenzyme A reductase in hypophysectomized rats by L-triiodothyronine. Proc Natl Acad Sci USA; 70: 3839-3842.

- Rousset BA and Dunn JT.(2004). Thyroid hormone synthesis and secretion. In Thyroid disease manager (chap. 2):111-113.
- Ridgway EC. (1980). Modern concepts of primary thyroid gland failure. Atheroscle; 36(4):589-93.
- Rizos CV, Elisaf MS and Liberopoulos EN. (2011). Effects of thyroid dysfunction on lipid profile. Open Cardiovasc Med ; 5:76-84.
- Stryer L.(1988).Biochemistry.W.H.Freeman and Company. New York; 284-7.
- Tabas I.(2002). Cholesterol in health and disease. J Clin Invest; 110:583-90.
- Tietz N, Burtis C and Ashwood ER.(2010).Textbook of Clinical chemistry, 3rd edition. Wb Saunders Co:220-223.
- Turnbridge WM, Evered DC, Hall R, Appleton D, Brewis M and Clark F . (1977).The spectrum of thyroid disease in a community: the Whickham survey. Clin Endocrinol (Oxf); 7:481-93.
- Trivalle C, Doucet J, Chassagne P, Landrin I, Kadri N and Menard JF. (1996). Differences in the signs and symptoms of hyperthyroidism in older and Younger patients. J Am Geriatr Soc; 44:50-3.
- Vanderpump MPJ.(2005). The epidemiology of thyroid diseases.In: Braverman LE, Utiger RD, eds. Werner and Ingbar's The Thyroid: A Fundamental and Clinical Text; 9th edn: 398-406.
- Vetter ML and Kaul S .(2008).Tyrosine kinase inhibitors and the thyroid as both an unintended and an intented target. Endocr Pract; 14:618–624.

- Wartofsky L.(1994). Diseases of the thyroid. In Isselbacher KJ, Braunwald E, Wilson JD, Martin JB, Fauci AS, Kasper DL. Harrison's principles of internal medicine, 17th ed. New York: McGraw-Hill, Inc;1930-1953.
- Weetman AP. (2000). Graves' disease. N Engl J Med; 343:1236-48.
- Yeh HC, Futterweit W and Gilbert P.(1996). Micronodulation: ultrasonographic sign of Hashimoto thyroiditis. J Ultrasound Med; 15:813–819.

Appendices

Sudan University of Science and Technology

College of Graduated Studies

Questionnaire

Master Degree

TOPIC: the assessment of plasma lipid profile (total cholesterol, triglycerides, HDL and LDL) among sudanese with thyroid disorders.

A: general information:

1-name…….. 2-age……

3-sex……..

B: type of thyroid disorders:

1-hyperthyroidism 2-hypothyroidism

C: present history of disease:

1-Liver disease 2-heart disease

3-diabetes 4-others

D: past history of disease:

1-hypertention 2-liver disease

3-renal disease 4-diabetes

E: investigation:

1-plasma Total cholesterol…….mg/dl

2-plasma Triglycerides…….mg/dl

3-plasma HDL……mg/dl

4-plasma LDL…….mg/dl