Sudan University of Science and Technology

College of Graduate Studies

Evaluation of Lipids Profile among Sudanese Patients with Hypothyroidism in Khartoum State

تقييم مستوى الدهون في السودانيين المرضى بقصور الغدة الدرقية في ولاية الخرطوم

A Dissertation submitted for partial fulfillment of the requirement
Of M.Sc. degree in Medical Laboratory Sciences (Clinical Chemistry)

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بسم الله الرحمن الرحيم

قال تعالى:

وَاتَّقُوا اللَّهَ ۖ وَيُعَلِّمُكُمُ اللَّهُ ۗ وَاللَّهُ بِكُلِّ شَيْءٍ عَلِيمٌ ﴿٢٨٢﴾

سورة البقرة –الاية (282)

DEDICATION

To

"Who taught me how I could be human "

My mother

To

"Who worked hardly for us "

My father

To

My beloved brothers and **best friends** for their continuous support

To

My sister

ACKNOWLEDGMENTS

First of all thank to **my God**, who gave me the ability to completion of this study. With all the respect, appreciation and thanks to Dr. for good guidance, valuable direction and generous advice that has kept me on the right track.

Thanks to **Saad Rashwan Medical Center** staff and all teachers of clinical chemistry department, thanks to my best friend who helped me in this research, also thanks to any person helped me in this research.

It is a pleasure to express my respect, since thanks and gratitude to all subject groups for their agreement to participate in this study.

Abstract

Background: Hypothyroidism has a great impact on lipids as well as a number of other cardiovascular risk factors. Hypothyroidism is relatively common and is associated with an unfavorable effect on lipids..

Objectives: This study is done to assess the levels of lipid parameter in patients with hypothyroidism and to study the relation between hypothyroidism and lipid profile.

Material and methods: Astudy was carried out at Khartoum state (asia hospital) , during the period of April to July 2018,including 100 study group **,** All of them were clinically diagnosed with hypothyroidism . The plasma level of lipid profile were analyzed in fresh samples among volunteers by digital colorimeter instrument and data were analyzed used (SPSS) in computer program.

Results: There were significant increase in plasma level of (TC and LDL) and insignificant different in plasma lvel of (HDL) between patiens with hypothyroidism compare with the normal range.

Conclusion: From this study shows significant increase in(TC and LDL) (Mean±SD = 235.7±44.9, 154.3±43.1,$P \leq 0.05$). and in significant different in (HDL) (Mean±SD = 23.9±8.1 , $P \geq 0.05$). between hypothyroidism patients compare to normal range . Also showed the Prevalence of the hypothyroidism is more in elder female than in elder male . And The duration of disease per years affected the level of lipid profile .Finally in the result observed the age of the patient correlates positively with the level of lipid profile .

ملخص البحث

المقدمة: مرض قصور الغدة الدرقية لها تأثير كبير على الدهون ,فضلا عن انها احد عوامل الخطر القلبية الوعائية .قصور الغدة الدرقية شائع نسبيا ويرتبط مع تأثير غير معروف على الدهون.

الأهداف : هذّه الدراسة اجريت بغرض تقييم مستوى الدهون في المرضى الّذين يعانون من اختلال وظيفي في الغدة الدرقية, ودراسة العلاقة بين الخلل الوظيفي للغدة الدرقية والدهون.

المواد والأساليب : اجريت الدراسة في مدينة الخرطوم(مستشفى اسيا) ,خلال الفترة من ابريل حتى يوليو 2018 ,تم اختيار مجموعة الدراسة وعددهم 100, وتم تشخيص جميعهم سريريا بقصور الغدة الدرقية . تم تحليل مستوى الدهون في البلازما في عينة المتطوعين باستخدام اداة قياس كلورومیترية رقمية وتم تحليل البيانات

بواسطة استخدام برنامج التحليل الاحصائي .

النتائج : تشير نتائج هّذه الدراسة الي زيادة ذو دلالة احصائية في مستوى الكولسترول الكلي والبروتين الدهني منخفض الكثافة وايضا تغير في مستوى البروتين الدهني عالي الكثافة ليس ذي دلالة احصائية في مستوى بين المرضى الذين يعانون من قصور الغدة الدرقية مقارنة بالمعدل الطبيعي.

الخلاصة : من خلال هذه الدراسة تبين ان هناك زيادة معنوية (ذات دلالة احصائية) في مستوى الكوليسترول

الكلي والبروتين منخفض الكثافة (المتوسط الانحراف المعياري = 235.7 44.9 , 144.3 43.1 القيمة الاحتمالية اقل من او تساوي 0.05)واختلاف طفيف في مستوى البروتين عالي الكثافة(المتوسط الانحراف المعياري = 23.9 8.1 , القيمة الاحتمالية اكبر من او تساوي 0.05)بين مرضى قصور الغدة الدرقية مقارنة بالنطاق الطبيعي, واظهرت ايضا ان انتشار مرض قصور الغدة الدرقية هو اكثر في الاناث الاكبر سنا من الذكور الاكبر سنا, وفترة المرض بالسنين تؤثر على مستوى الدهون في الدم ,كما يلاحظ في النتائج ان عمر المريض يتناسب تناسب ايجابي وطردي مع مستوى الدهون في الدم.

Contents

List of tables

List of figures

Abbreviation

- **ADH** Alcohol Dehydrogenase
- **CVD** Cardio vascular disease
- **DIT** Di Iodo tyrosine
- **HDL** high Density Lipoprotein
- **LDL** Low Density Lipoprotein
- **MID** Mono Iodo tyrosine
- **Overt H** Overt hypothyroidism
- **RIA** Radio Imuno Assay
- **RXR** Retinoid X Recepter
- **Sub H** Sub clinical hypothyroidism
- **T3** Triiodothyronine
- **T4** Thyroxine
- **TBG** Total Bindig Golobulin
- **TC** Total cholesterol
- **TG** triglycerid
- **TRH** Thyroid relasing hormone
- **TSH** Thyroid stimulation hormone
- **WHO** World Health Organiza

Chapter One

Introduction, Rationale and Objectives

Chapter one
Introduction , Rationale and Objectives

1.1.Introduction

The thyroid gland is important in the human body because of its ability to produce the hormones triiodothyronine (T3) and tetraiodothyronine (T4), necessaries for appropriate energy levels and an active life. It has long been known that thyroid hormones are of vital importance in maintaining the initial level of phospholipids in cell membranes and fatty acids composition of the lipids (Tseng *etal*.,2012). T3 plays a critical role in lipid metabolism by regulating genes involved in lipogenesis and lipolysis (Tourner 2008). The underlying mechanisms, however, have only begun to be unraveled in recent years. Hypothyroidism, characterized by low serum thyroid hormone levels, is associated with reduced metabolism, reduced lipolysis, weight gain, reduced cholesterol clearance,and elevated serum cholesterol. It is known that thyroid hormone has genomic and nongenomic effects (Hueston 2004).
Hypercholesterolemia is favored due to the hormone deficitand to the decreased activity of the lipoprotein lipase (Mansourian *et al*., 2008).
Subclinical hypothyroidism (SCH), also called mild thyroid failure, is characterized by elevated levels of serum thyroid stimulating hormone (TSH) in the presence of normal thyroxine (T4) and triiodothyronine (T3) levels(Efstathiadou *etal*.,2001) . This condition is one of the most common endocrine disorders that occur in 4 to 20 percent of the general population (Tseng *etal*.,2012). The prevalence increases with age and is higher in women (Fatourechi.2009). SCH has clinical significance because of its high prevalence, the risk of progression to overt hypothyroidism (OH), poor quality of life related to nonspecific symptoms and potential consequences including neurobehavioral and cardiovascular disorders (Cooper and Biondi 2008). Cardiovascular outcome in these patients is partly due to its association with unfavorable lipid profile. Thyroid

hormones have varied effects on lipid metabolism, because thyroid function regulates lipids synthesis and degradation and mediates the activity of key enzymes in these pathways (Rizos and Pucci 2000). The association between OH and dyslipidemia is well known (pucci 2000), which may predispose to the development of cardiovascular disease (CVD), however it is uncertain whether SCH is also associated with lipid abnormalities (Altonsi 2004). Substantial studies on the association between SCH and lipid abnormalities have been conducted but results from these studies are not consistent (Pearce 2012). In this respect, it has been reported that SCH is associated with increased levels of total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and triglyceride (TG) (Tourner 2008).and decreased levels of high density lipoprotein- cholesterol (HDL-C) (Karthick 2013). However, some of the literature has reported no difference in the lipid parameters between SCH and healthy subject (Parle 1992). The decision about whether to screen patients for this disorder is clouded by inconsistent evidence of association of lipid abnormalities or other risk factors of CVD with SCH. Hypothyroidism may be associated with increased risk of coronary artery disease, peripheral vascular disease, and various biochemical abnormalities, including increased low-density lipoprotein-cholesterol levels and increased total cholesterol and serum triglyceride values(Hueston 2004).

Hypothyroidism, like obesity is one of the pathological conditions most frequently associated with disorders of lipid metabolism4 and finally dyslipidemia which is one of the major risk factors of coronary disease.(Limbu *etal*.,2008) Overt hypothyroidism is characterized by hypercholesterolemia and a marked increase in LDL because of a decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver. However the controversy persists regarding the lipids level in subclinical hypothyroidism and its clinical significance. Moreover it is likely to be a risk factor for atherosclerosis and coronary diseases.(Jeskra 2007).

1.2.Rationale

Hypothyroidism is the most common Thyroid disorder in both in the developed and less developed world . clinical features of Hypothyroidism are not specific and many of these symptoms are often confused with other health conditions. Symptoms of hypothyroidism usually appear slowly over several months or years but this disease is a slow killer which may further develop many other physical and mental problems.

If not detected earlier sometimes hypothyroidism may lead to thyroid carcinomas and may cause death.

In Sudan there is no recent study and review from this study.

1.3. Objective

1.3.1General Objectives

To evaluate lipids profile among patients with hypothyroidism in Khartoum states.

1.3.2 SPECIFIC OBJECTIVES

-To estimate the effect of thyroid dysfunction on lipid profile (TC, LDL-C and HDL-C).

-To compare between the lipid profile (TC ,LDL-C and HDL-C) in patients with subclinical Hypothyrodism and overt hypothyroidism .

-To correlate between the lipid profile and variable(age , duration of disease ,treatment status and type of disease).

Chapter two

Literature review

Chapter Two

Literatures Review

2.1.Thyroid gland

The thyroid gland is butterfly shaped and sits on the trachea, in the anterior neck. It is comprised of two lobes, which are 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 tissues. The thyroid is the largest exclusively endocrine gland in the body. The endocrine system is the body‘s communication hub, controlling cell, and therefore organ, function. A primary goal of the endocrine system is to maintain homeostasis within the organism, despite external fluctuations of any sort. Hormones, which act as chemical messengers, are the mechanism for this communication. The hormones secreted by the thyroid gland are essential in this process, targeting almost every cell in the body (only the adult brain, spleen, testes, and uterus are immune to their effects.) Inside cells, thyroid hormone stimulates enzymes involved with glucose oxidation, thereby controlling cellular temperature and metabolism of proteins, carbohydrates, and lipids. Through these actions, the thyroid regulates the body‘s metabolic rate and heat production. Thyroid hormone also raises the number of adrenergic receptors in blood vessels, thus playing a major role in the regulation of blood pressure. In addition, it promotes tissue growth, and is particularly vital in skeletal, nervous system, and reproductive development (American Thyroid Association, 2014). The two major thyroid hormones (TH) are unique in that, unlike most hormones, they are neither protein nor cholesterol based. Instead, they incorporate iodine as an active constituent; the amount of iodine differentiates

between thyroxine (also known as tetraiodothyronine or T4) with four iodine molecules and triiodothyronine (T3) with, predictably, three iodine molecules. While T4 exists in greater abundance than T3 in the body- thought to be at a fifty to one ratio, T3 is considered to be ten times more active. There is much debate about the physiological difference between the two hormones. It is currently thought that T4 may act as the reserve form, having a more direct role in the hypothalamus/pituitary negative feedback loop, while T3 has a more dynamic physiological effect in the body. Others suggest that both have a critical part in physiological activity (American Thyroid Association, 2014).

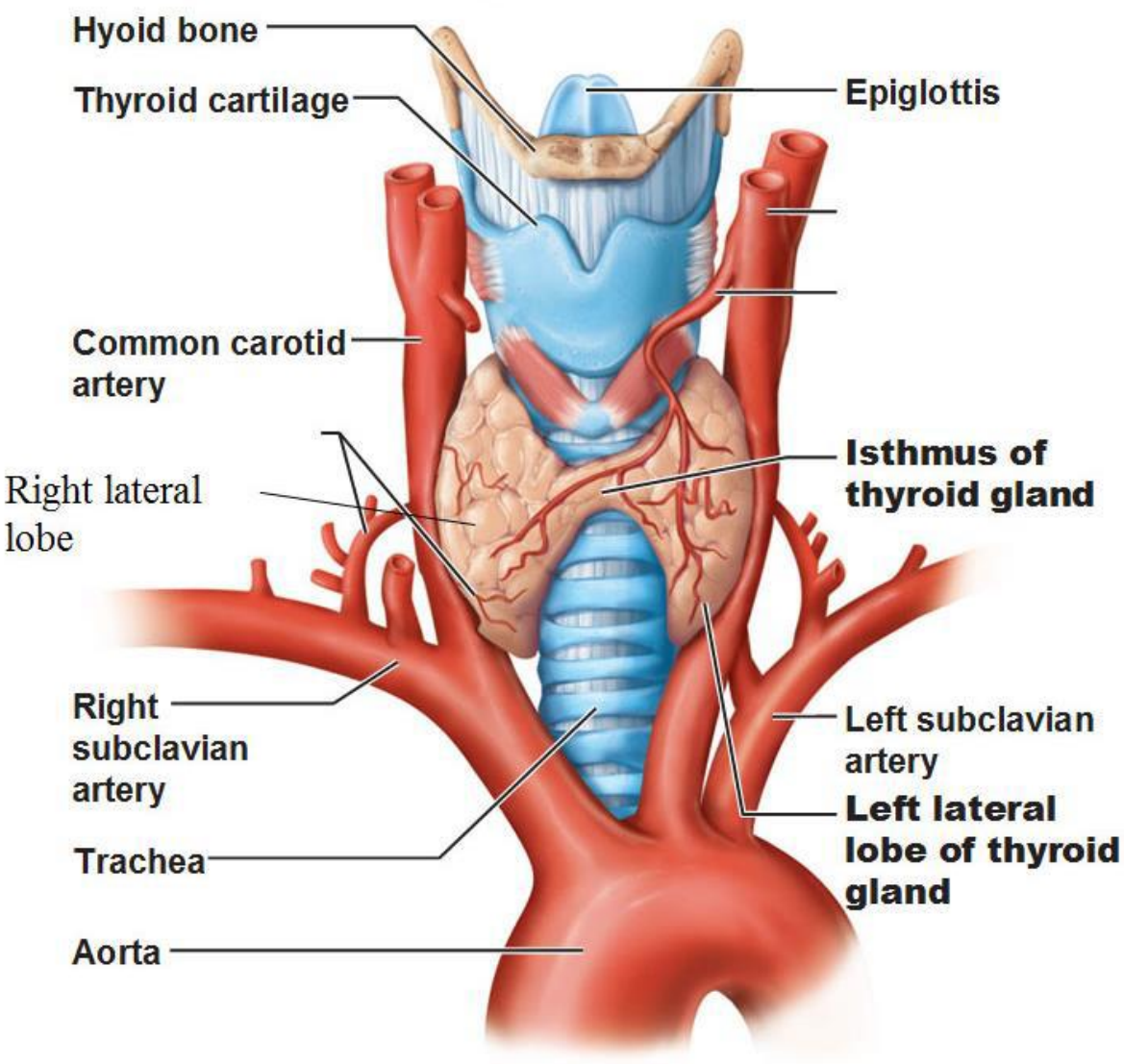

Figure 1.1: The thyroid gland

1.2. Hormones of thyroid gland

The thyroid gland produces

1. **Thyroxine (T4):** 80% of the total thyroid hormone which is a relatively inactive prohormone.

2. **Triiodothyronine (T3):** Lower amount of the active hormone, triiodothyronine (T3).Collectively, T3 and T4 are referred to as the thyroid hormones. Twenty percent of the body‘s triiodothyronine is made by the thyroid gland.

3. **Calcitonin:** The thyroid gland also produces calcitonin from cells called C-cells. Calcitonin is understood to play a role in regulating calcium levels in the body, but its exact function in humans remains unclear (Society for endocrinology, 2015).

1.2.1 Thyroid hormone synthesis

TH (particularly T4) is synthesized in the gland‘s colloid filled lumen from the combination of the glycoprotein thyroglobulin and stored iodine atoms. This process involves six interrelated steps that are initiated when thyroid stimulating hormone (TSH), released by the pituitary gland, binds to follicle cell receptors (yumpu.com, 2015).

1.2.1.1 Thyroglobulin synthesis

Tyrosine is converted into the glycoprotein thyroglobulin, which contains approximately 110 tyrosine residues and discharged into the lumen where it becomes part of the colloid mass (yumpu.com, 2015). The processing of iodine involves two stages as plasma iodine concentrations are very low (American Thyroid Association, 2014).

1.2.1.2 Iodine trapping

Plasma iodide ions (I-) are actively transported from the plasma into the follicular cells against a steep concentration gradient by the Na/I symporter (NIS). This is a rate-limiting step (yumpu.com, 2015).

1.2.1.3 Iodide oxidation

I- is rapidly oxidized into iodine (I2) by thyroid peroxidase (TPO) anchored on the luminal surface of the follicular cell membrane. The two components are then combined in the colloidal lumen (yumpu.com, 2015).

1.2.1.4 Iodination of thyroglobulin

Reactive iodine rapidly attaches to the tyrosine molecules within the extracellular thyroglobulin in a process that is catalysed by TPO. Monoiodotyrosine (MIT or T1) and diiodotyrosine (DIT or T2) are formed (yumpu.com, 2015).

1.2.1.5 Coupling

Tyrosine molecules within thyroglobulin are then coupled together. Combinations of T1 and T2 can form thyroid hormones (yumpu.com, 2015).

1.2.1.6 Secretion

Under the direction of thyroid stimulating hormone (TSH or thyrotrophin), iodinated thyroglobulin is taken into the follicular cells by pinocytosis and degraded by lysosomal enzymes. Coupled tyrosine molecules are released, including some T3 and T4. Some T4 is converted to T3 in the follicular cell cytoplasm by the enzyme type 1,5‘deiodinase. Whilst the secreted ratio of T4:T3 is usually 20:1 conversion to T3 is promoted by TSH stimulation and can result in the so-called T3 thyrotoxicosis. MIT and DIT are also released, but they are deiodinated by iodotyrosine deholgenase to recycle iodine (yumpu.com, 2015).

1.2.2 Regulation of thyroid hormone (T3 & T4) in the body

As well as stimulating the release of thyroid-stimulating hormone (TSH) from

thyrotrophs in the anterior pituitary gland Hypothalamic thyrotrophin-releasing hormone (TRH) also causes up regulation of TSH gene transcription. TSH acts on extracellular receptors (TSH-R) on the surface of thyroid follicle cells, activating the Gprotein–adenylcyclase– cAMP and phosphatidylinositol (PIP2) pathways. Ultimately, TSH stimulates the following processes in the thyroid gland:

• Iodine uptake.

• Transcription of thyroglobulin and thyroid peroxidase.

• Iodination.

• Coupling.

• Type 1 5‘deiodinase conversion of T4 to T3.

• Pinocytosis and secretion of thyroid hormones (yumpu.com, 2015).

As a result, T3 and T4 are synthesized and secreted more rapidly TSH also has long-term actions on the thyroid gland by increasing its size and vascularity to improve hormone synthesis. TSH forms part of a negative feedback loop, as its release is inhibited by increased serum T3 and T4 and also by somatostatin, glucocorticoids and chronic illness (yumpu.com, 2015).

1.2.3 Synthesis and regulation of TSH

Messages from the anterior pituitary gland are the main stimulus for the action of the thyroid gland. The pituitary gland, in turn, is triggered from above by the hypothalamus. The three organs are connected in a negative feedback loop that involves their vigilant monitoring of and response to the levels of Thyroid Hormone in the blood, as well as other internal and external stimuli; this relationship is sometimes referred to as the hypothalamic-pituitary-thyroid axis (American Thyroid Association, 2014). The hypothalamus secretes protein hormone thyrotropin releasing hormone (TRH), which heads directly to the pituitary gland via the hypophysial portal blood system, stimulating the release of TSH. TSH then moves through the bloodstream, binding with receptors in the

thyroid gland, prompting the secretion of TH into the blood. Both T4 and T3 then exert a negative feedback effect on the hypothalamus and pituitary-an increase in their blood levels lowers the amount of TRH and TSH secreted and a decrease in their levels causes a rise in the TRH and TSH (American Thyroid Association, 2014). Stimuli to the higher brain including temperature and stress can also effect TRH production in the hypothalamus; for instance, cold temperatures can increase the body‘s requirements for TH as more internal heat will be need to maintain homeostasis and the hypothalamus reacts accordingly (American Thyroid Association, 2014). Stress affects the thyroid gland not only through the hypothalamus, but also directly via the sympathetic nervous system. There are sympathetic nerves that connect with the gland; during their stimulation in times of stress, they trigger increased TH release. In addition, it appears that epinephrine from the adrenal gland can also act directly on the Diet can effect thyroid function, as a high calorie/high carbohydrate diet can lead to increased conversion of T4 to T3- a mechanism that likely assists in keeping an organism‘s weight stable. Meanwhile, prolonged fasting can result in a decrease in T3 production- which may be adaptive for conditions of food scarcity, slowing down the body‘s metabolism and energy (American Thyroid Association, 2014).

1.2.4 Transport of thyroid hormones in the body

In its behavior, Thyroid hormone (TH) functions somewhat similarly to steroid hormones. As it is not water soluble, it requires a protein-based molecule for transport throughout the blood stream. T3 and T4 will generally pair with thyroxine binding globulin (TBG) for this purpose, though they can also use albumin and prealbumin (American Thyroid Association, 2014). 70% are bound to thyroid-binding globulin (TBG), 30% are bound to albumin. While circulating in the blood in bound form, binding protein protects thyroid hormone from enzymatic attack (yumpu.com 2015). At any given moment, the vast majority of Thyroid

hormone in the body is in this bound, and essentially inactive, state, either in route or awaiting transport. The small percentage (Only 0.1% of T4 and 1% of T3) of unbound, physiologically active hormone is called ―free‖ T3 or T4(American Thyroid Association, 2014). It appears that TBG and albumin have higher affinity for T4, which could explain T4‘s higher levels in blood and its slower metabolism, and perhaps account for free T3 being the more physiologically active substance (American Thyroid Association, 2014).

Both T3 and T4 can cross cell membranes, though a carrier transport may be involved. The concentration of circulating T4 is much higher than that of T3 (50:1). There are two reasons for this:

The thyroid secretes more T4 than T3.

T4 has a longer half-life (7 days vs 1 day) (yumpu.com 2015).

1.2.5 Mechanism of thyroid hormone

The general effect of thyroid hormone is to activate nuclear transcription of large numbers of genes. Therefore, in virtually all cells of the body, great numbers of protein enzymes, structural proteins, transport proteins, and other substances are synthesized. The thyroid hormone receptor usually forms a heterodimer with retinoid X receptor (RXR) and binds at specific thyroid hormone response elements on the DNA This hormone receptor complex then initiates the transcription of many genes(yumpu.com 2015).

1.2.6 Physiological Effects of Thyroid Hormones:

1.2.6.1 Metabolism

Thyroid hormones, especially T3, enter tissue cells by diffusion or specific transport where they bind to two different receptors nuclear receptors designated as hTR-α1 and hTR-β1. The T3 receptor complex then binds DNA via ―zinc fingers‖ and this produces a change in the expression of a variety of genes that encode enzymes that control cellular metabolism and function (Torio, 2012). T3 and T4

stimulate metabolic activities in most tissues in the body resulting in an increase in basal metabolic rate. This causes an increase in body heat production due to increased oxygen consumption and energy expenditure. Increased thyroid hormone levels stimulate fat mobilization, which results in increased fatty acid concentration in the plasma. Carbohydrate metabolism is also stimulated, causing enhanced activity of glucose entering the cells and increased gluconeogenesis and glyogenolysis which generate free glucose (Torio, 2012).

1.2.6.2 Growth and Development

Other hormones, including Growth Hormone (GH) and Prolactin, also depend on the presence of TH to exert their own effects on cells; the absence of TH inhibits their activity (American Thyroid Association, 2014).

1.2.6.3 Calcium metabolism

Calcitonin is secreted by the C cells of parafollicular cells of the thyroid gland. It inhibits calcium absorption, thus lowering serum calcium levels. Secretion of calcitonin can be stimulated by increased levels of serum calcium, pentagastrin, and alcohol (Torio, 2012).

1.2.7 Degradation of Thyroid Hormone

The main site of TH degradation is in the liver and its primary elimination is via kidneys. Thyroxine (T4) and triiodothyronine (T3) are rapidly degraded by a purified preparation of myeloperoxidase (MPO) and H2O2 with the formation of iodide. T3 can be detected as a minor product of T4 degradation (Torio, 2012).

1.2.3 Thyroid diseases:

A thyroid disease is a medical condition impairing the function of the thyroid creating and using energy). These diseases frequently have wide-ranging systemic effects as thyroid gland manufactures hormones that regulate the body's metabolism. Thyroid gland diseases can result in either an overproduction or underproduction of thyroid hormones (National Library of Medicine,2014).

The main categories of disease are

 Hyperthyroidism - when thyroid gland makes more thyroid hormones than the body needs

 Hypothyroidism - when thyroid gland does not make enough thyroid hormones

 Thyroid cancer or carcinoma

 Thyroid nodules - lumps in the thyroid gland

 Thyroiditis

 Goitres (National Library of Medicine, 2014).

1.3.1 Hyperthyroidism

Hyperthyroidism is a hyper metabolic state caused by excess in the synthesis and secretion of thyroid hormone by the thyroid gland, which can be due to thyrotropic stimulus or autonomous function of thyroid (Karnath and Hussain, 2006).

tissue On the other hand, thyrotoxicosis is the clinical condition which is associated with elevated levels of free T4 and/ or free T3. The terms hyperthyroidism and thyrotoxicosis are oftentimes used interchangeably; however, hyperthyroidism pertains to the excess

synthesis and release of thyroid hormone, while thyrotoxicosis is the clinical presentation resulting from it. Its prevalence is 1 in every 2000 adults. Graves‘ disease is mostly account for hyperthyroidism (Torio, 2012). his is an autoimmune disease caused by an antibody that binds to and activates the TSH

receptor and stimulates the gland to synthesize and secrete excess thyroid hormone. Autonomous production of thyroid hormone occurs when thyrocytes function independently of TSH receptor activation, which could result from a benign thyroid adenoma or nodules from a toxic multinodular goitre. Toxic adenomas are common in younger patients and in iodine-deficient areas. Toxic multinodular goitre (also known as Plummer disease) accounts for about 15 to 20

percent of hyperthyroidism cases and can be 10-fold more common in areas where there is iodine deficiency. This also occurs more commonly among elderly patients with a long-standing goitre (Reid &Wheeler, 2005).

1.3.1.1 The causes of hyperthyroidism

The thyroid is a gland in the neck that produces two thyroid hormones, thyroxine (T4) and triiodothyronine (T3). Thyroxine is inactive and is converted by the tissues and organsnthat need it into triiodothyronine. The role of thyroid hormones, put simply, is to regulate the metabolism of virtually all cells in the body. In health, the production of these thyroid hormones is tightly regulated by the secretion of thyroid stimulating hormone (TSH; also known as thyrotropin) from the pituitary gland in the brain. When the thyroid gland becomes affected by disease, sometimes the production or release of thyroxine and triiodothyronine can be abnormally high, leading to increased levels in the blood; a state of thyroid overactivity known as hyperthyroidism or thyrotoxicosis. If this happens, the body‘s metabolism speeds up and this can be manifest by changes in various, and seemingly unrelated tissues, that are listed below. In this state of hyperthyroidism, a blood test will show an elevated amount of these thyroid hormones circulating. Conversely, the TSH level in the blood almost always becomes suppressed, because the pituitary gland senses the abnormally high levels of thyroid hormones, which are more than is needed by the brain (Karnath and Hussain, 2006).

1.3.2 Goitre

Goitre is a swelling in the neck caused by an enlarged thyroid gland. It is a common finding, and it is usually asymptomatic; however, large goitres can compress the oesophagus and trachea. If goitre is associated with hyperthyroidism it is described as toxic. Non-toxic goitres secrete normal or reduced levels of thyroid hormones. Non-toxic goitres are usually the result of excessive TSH

stimulation in the presence of hypothyroidism. Goitre is treated by correcting the underlying pathology or by surgical removal for cosmetic reasons or to prevent compression of surrounding structures (yumpu.com 2015).

2.3.2.1 Causes of Goiter

Goiters can occur when the thyroid gland produces either too much thyroid hormone (hyperthyroidism) or not enough (hypothyroidism). Much more rarely, the problem may arise when the pituitary gland stimulates thyroid growth to boost production of the hormone. Enlargement could also occur with normal production of thyroid hormone, such as a nontoxic multinodular gland (yumpu.com 2015).

1.3.3 Thyroid cancer

Thyroid carcinoma is relatively rare (ca. 16,000 cases annually), but is the most common endocrine malignancy. While the causes of this form of cancer are not precisely understood, it is known that iodine deficiency, long-term use of goitrogenic drugs and exposure to ionizing radiation are risk factors for thyroid hyperplasia and ultimately malignancy. Thyroid carcinoma may be discovered as a small thyroid nodule or a metastatic tumor arising from lung, brain or bone cancer (Deruiter, 2002). This cancer is detected by changes in the voice or swallowing due to tumor growth impinging on the trachea or esophagus. Treatment for thyroid carcinoma remains controversial but may involve partial or total thyroidectomy, TSH suppression therapy with levothyroxine, or radioactive iodine therapy (iodine concentrating tumors). Postoperative radiation therapy and chemotherapy also may be employed (Deruiter, 2002).

1.3.4 Thyroiditis

Thyroiditis is the medical term for inflammation (swelling) of the thyroid gland, which can either cause abnormally high or low levels of thyroid hormones in the blood (National Library of Medicine, 2014). There are several different types of thyroiditis. The common types are:

1.3.4.1. Hashimoto's thyroiditis (the most common)

Hashimoto's thyroiditis is an autoimmune condition. This means immune system mistakenly attacks thyroid gland, causing it to gradually swell and become damaged (NHS, 2014).

1.3.4.2 De Quervain's or subacute thyroiditis

De Quervain's thyroiditis (sometimes called subacute thyroiditis) is a painful swelling of the thyroid gland that is thought to be triggered by a viral infection, such as mumps or the flu. It's most commonly seen in females aged 20 to 50 (NHS, 2014).

1.3.4.3 Post-partum thyroiditis (triggered after giving birth)

Like Hashimoto's thyroiditis, post-partum thyroiditis is an autoimmune condition, but it only happens in women who have recently given birth. In post-partum thyroiditis, immune system attacks thyroid gland within around six months of giving birth, causing a temporary rise in thyroid hormone levels (thyrotoxicosis) and symptoms of an overactive thyroid gland (NHS, 2014). Then, after a few weeks, thyroid gland becomes depleted of thyroid hormone, leading to low levels of thyroid hormone and symptoms of an underactive thyroid gland. However, not every woman with post-partum thyroiditis will go through both these phases (NHS, 2014).

1.3.4.4 Silent or painless thyroiditis

Silent thyroiditis is very similar to post-partum thyroiditis. It is also an autoimmune condition, but is not related to giving birth and can occur in both men and women. Like postpartum thyroiditis, there may be a phase of high thyroid hormone levels (thyrotoxicosis), causing symptoms of an overactive thyroid gland. This may then be followed by a phase of symptoms of an underactive thyroid gland, before the symptoms eventually go away within around 12 to 18 months (NHS, 2014). If low thyroid hormone levels are causing severe symptoms, patients

need to take thyroid hormone replacement until the condition gets better. In a few cases, the low thyroid levels can be permanent (NHS, 2014).

1.3.4.5 Drug-induced thyroiditis

Thyroiditis can also be triggered by medications including interferon, amiodarone, lithium and a class of drugs to treat certain cancers (which include sunitinib), if these medicines damage the thyroid gland (NHS, 2014).

2.3.4.6 Radiation-induced thyroiditis

Radioactive iodine treatment for an overactive thyroid gland or radiotherapy for certain cancers can also damage the thyroid gland, leading to symptoms of an overactive thyroid gland or symptoms of an underactive thyroid gland (NHS, 2014).

1.3.4.7 Acute or infectious thyroiditis

Acute or infectious thyroiditis is usually triggered by a bacterial infection. It is rare and is associated with either a weakened immune system or, in children, with a problem in the development of the thyroid (NHS, 2014).

1.3.5 Thyroid Nodules

Thyroid disorders can also occur because of thyroid nodules, which are growths on the gland. These small growths are usually harmless and can go unnoticed for years. At times, thyroid nodules can be cancerous (Wartofsky *et al*, 2013).

1.4 Hypothyroidism

Hypothyroidism is a common endocrine disorder mainly characterized by a deficiency of thyroid hormone due to insufficient amounts produced by the thyroid gland. It could also be due to inadequate secretion of either TRH from the hypothalamus or TSH from the pituitary, affecting the feedback loop, and therefore causing hypothyroidism. Normally, the thyroid gland releases 100 to 125 nmol of T4 and small amounts of T3 daily. T4, with a half-life of 7 to 10 days, is converted in the peripheral tissues to T3, which is the active form of thyroid hormone. Early

on in the disease, compensatory mechanisms are at work in order to maintain adequate T3 levels. When there is a decreased production of T4, the pituitary gland compensates by increasing the secretion of TSH, which stimulates thyroid hypertrophy and hyperplasia and more T3 release (Torio, 2012).

1.4.1 Types of Hypothyroidism

1.4.1.1 Subclinical hypothyroidism

Subclinical hypothyroidism is defined biochemically as a normal serum free thyroxine (T4) concentration in the presence of an elevated serum thyroid-stimulating hormone (TSH) concentration. Some patients with subclinical hypothyroidism may have vague, non-specific symptoms suggestive of hypothyroidism, but attempts to identify patients clinically have not been successful. Thus, this disorder can only be diagnosed on the basis of laboratory test results (Gavrila, 2012).

1.4.1.2 Overt Hypothyroidism

Overt hypothyroidism is characterized by an increased TSH and a decreased T4 level. All patients with overt hypothyroidism are usually treated with thyroid hormone pills (Gavrila, 2012).

1.4.2 Symptoms and Signs of hypothyroidism

General Fatigue, weight gain, anemia, coldintoleranceDermatologic Dry coarse skin, brittle hair, hairloss, nonpitting peripheral edemaEars, eyes, throat Hearing loss, hoarse voice,periorbital edema, facial puffinessNeck GoiterPulmonary Dyspnea, pleural effusions,hypoventilation, sleep apneaCardiac Bradycardia, congestive heartfailure, pericardial effusions Gastrointestinal Anorexia, constipation Genitourinary Menstrual disorders, decreasedlibido, impotence, infertility Neuromuscular Muscle weakness, delayed ankle jerk relaxation phase

Psychiatric Depression, psychomotor retardation, coma. (Karnath and Hussain, 2006).

1.4.3 Causes of hypothyroidism

There can be many reasons why the cells in the thyroid gland can‘t make enough thyroid hormone. Here are the major causes, from the most to the least common.

1.4.3.1 Autoimmune disease

In some people‘s bodies, the immune system that protects the body from invading infections can mistake thyroid gland cells and their enzymes for invaders and can attack them. Then there aren‘t enough thyroid cells and enzymes left to make enough thyroid hormone. This is more common in women than men. Autoimmune thyroiditis can begin suddenly or it can develop slowly over years. The most common forms are Hashimoto‘s thyroiditis and atrophic thyroiditis (Karnath and Hussain, 2006).

1.4.3.2 Surgical removal of part or all of the thyroid gland

Some people with thyroid nodules, thyroid cancer, or graves‘ disease need to have part or all of their thyroid removed. If the whole thyroid is removed, people will definitely become hypothyroid. If part of the gland is left, it may be able to make enough thyroid hormone to keep blood levels normal (Karnath and Hussain, 2006).

1.4.3.3 Radiation treatment

Some people with graves‘ disease, nodular goiter, or thyroid cancer are treated with radioactive iodine (i-131) for the purpose of destroying their thyroid gland. Patients with Hodgkin‘s disease, lymphoma, or cancers of the head or neck are treated with radiation. All these patients can lose part or all of their thyroid function (Karnath and Hussain, 2006).

1.4.3.4 Congenital hypothyroidism (hypothyroidism that a baby is born with)

A few babies are born without a thyroid or with only a partly formed one. A few have part or all of their thyroids in the wrong place (ectopic thyroid). In some babies, the thyroid cells or their enzymes do not work right (Karnath and Hussain, 2006).

1.4.3.5 Thyroiditis

Thyroiditis can make the thyroid dump its whole supply of stored thyroid hormone into the blood at once, causing brief hyperthyroidism (too much thyroid activity); then the thyroid becomes underactive (Karnath and Hussain, 2006).

1.4.3.6 Medicines

Medicines such as amiodarone, lithium, interferon alpha, and interleukin-2 can prevent the thyroid gland from being able to make hormone normally. These drugs are most likely to trigger hypothyroidism in patients who have a genetic tendency to autoimmune thyroid disease (Karnath and Hussain, 2006).

1.4.3.7 Too much or too little iodine

The thyroid gland must have iodine to make thyroid hormone. Iodine comes into the body in food and travels through the blood to the thyroid. Keeping thyroid hormone production in balance requires the right amount of iodine. Taking in too much iodine can cause or worsen hypothyroidism (Karnath and Hussain, 2006).

1.4.3.8 Damage to the pituitary gland

The pituitary, the ―master gland,‖ tells the thyroid how much hormone to make. When the pituitary is damaged by a tumor, radiation, or surgery, it may no longer be able to give the thyroid instructions, and the thyroid may stop making enough hormones (Karnath and Hussain, 2006).

1.4.3.9 Rare disorders that infiltrate the thyroid

In a few people, diseases deposit abnormal substances in the thyroid and impair its ability to function, for example, amyloidosis can deposit amyloid protein,

sarcoidosis can deposit granulomas, and hemochromatosis can deposit iron (British thyroid association, 2014).

1.4.4 Thyroid Function Testing for Hypothyroidism

The majority of hypothyroidism cases result from primary thyroid failure. The pituitary gland responds to that failure by secreting more TSH, raising serum TSH levels to 10 to 15 μU/mL well before there is a detectable decline in circulating thyroid hormones T4 and tri-iodothyronine (T3). Thus, elevated TSH level is the earliest and most definitive indicator of hypothyroidism (Deruiter, 2002). As thyroid failure progresses, T4 and T3 levels eventually become very low or even undetectable, and the TSH level increases to100 μU/mL or more. If the patient has obvious thyroid dysfunction, the free T4 level should be measured in addition to the TSH level. Measuring the total T4 level may not be necessary since its results are difficult to interpret; for example total T4 consists largely of hormone that is bound to serum proteins or whose levels can be altered by drugs or nonthyroidal illness (Deruiter, 2002). Measurements of serum T3 levels likewise have little diagnostic value because they can be lowered by so many other conditions, including aging, other illnesses, weight loss, and a number of drugs. Low or normal TSH and free T4 levels rule out hypothyroidism unless the patient has symptoms consistent with diminished pituitary function, in which case testing for hypopituitarism is indicated (Deruiter, 2002). If the TSH level is elevated, free T4 levels should be determined. A low level T4 indicates hypothyroidism. A high TSH and normal T4 indicate subclinical hypothyroidism and mandates testing for antithyroid antibodies; these patients may have no clinical signs of hypothyroidism. A TSH level greater than about 15 μU/mL or an antithyroid antibody titer greater than 1:1,500 (or a recent history of exposure to radioactive iodine or thyroid surgery) points to impending overt hypothyroidism. A TSH level of less than 15 μU/mL and an antibody titer of less than 1:1,500 in an

asymptomatic patient is inconclusive. The TSH level should be measured again after six months, although one can opt for treatment if the patient has begun to experience symptoms (Deruiter, 2002).

1.4.5 Test used to identify Hypothyroidism:

1.4.5.1 Measurement of Serum Thyroid Hormones: T4 by RIA

T4 by RIA (radioimmunoassay) is the most used thyroid test of all. It is frequently referred to asa T7 which means that a resin T3 uptake (RT3u) has been done to correct for certain medications such as birth control pills, other hormones, seizure medication, cardiac drugs, or even aspirin that may alter the routine T4 test. The T4 reflects the amount of thyroxine in the blood. If the patient does not take any type of thyroid medication, this test is usually a good measure of thyroid function (Norman, 2016).

1.4.5.2 Measurement of Serum Thyroid Hormones: T3 by RIA

As stated on our thyroid hormone production page, thyroxine (T4) represents 80% of the thyroid hormone produced by the normal gland and generally represents the overall function of the gland. The other 20% is triiodothyronine measured as T3 by RIA. Sometimes the diseased thyroid gland will start producing very high levels of T3 but still produce normal levels of T4. Therefore measurement of both hormones provides an even more accurate evaluation of thyroid function (Norman, 2016).

1.4.5.3 Measurement of Pituitary Production of TSH

Pituitary production of TSH is measured by a method referred to as IRMA (immunoradiometric assay). Normally, low levels (less than 5 units) of TSH are sufficient to keep the normal thyroid gland functioning properly. When the thyroid gland becomes inefficient, such as in early hypothyroidism, the TSH becomes elevated even though the T4 and T3 may still be within the "normal" range. This rise in TSH represents the pituitary gland's response to a drop in circulating thyroid hormone; it is usually the first indication of thyroid gland failure. Since TSH is

normally low when the thyroid gland is functioning properly, the failure of TSH to rise when circulating thyroid hormones are low is an indication of impaired pituitary function. The new "sensitive" TSH test will show very low levels of TSH when the thyroid is overactive (as a normal response of the pituitary to try to decrease thyroid stimulation).Interpretations of the TSH level depends upon the level of thyroid hormone; therefore, the TSH is usually used in combination with other thyroid tests such as the T4 RIA and T3 RIA (Norman, 2016).

1.4.5.4 Thyroid Scan

Taking a "picture" of how well the thyroid gland is functioning requires giving a radioisotope to the patient and letting the thyroid gland concentrate the isotope (just like the iodine uptake scan above). Therefore, it is usually done at the same time that the iodine uptake test is performed. Although other isotopes, such as technetium, will be concentrated by the thyroid gland; these isotopes will not measure iodine uptake which is what we really want to know because the production of thyroid hormone is dependent upon absorbing iodine. It has also been found that thyroid nodules that concentrate iodine are rarely cancerous; this is not true if the scan is done with technetium. Therefore, all scans are now done with radioactive iodine (Norman, 2016). Thyroid scan is used for following reasons:

- Identifying nodules and determining if they are "hot" or "cold"
- Measuring the size of the goiter prior to treatment
- Follow-up of thyroid cancer patients after surgery
- Locating thyroid tissue outside the neck, i.e. base of the tongue or in the chest (Norman, 2016).

1.4.5.5 Thyroid Antibodies

The body normally produces antibodies to foreign substances such as bacteria; however, some people are found to have antibodies against their own thyroid tissue. A condition known as Hashimoto's Thyroiditisis associated with a high

level of these thyroid antibodies in the blood. Whether the antibodies cause the disease or whether the disease causes the antibodies is not known; however, the finding of a high level of thyroid antibodies is strong evidence of this disease. Occasionally, low levels of thyroid antibodies are found with other types of thyroid disease. When Hashimoto's thyroiditis presents as a thyroid nodule rather than a diffuse goiter, the thyroid antibodies may not be present (Norman, 2016).

2 Lipid profile

2.1. Cholesterol

Cholesterol is a soft, waxy substance found in the blood stream and the body's cells, it is consist of four linked hydrocarbon rings forming the bulky steroid structure**.** There is a hydrocarbon tail linked to one end of the steroid and a hydroxyl group linked to the other end. Cholesterol is known as a "sterol" because it is made out of alcohol and steroid (Berg, 2002). It is carried by two types of lipoprotein; low-density lipoprotein (LDL) carried bad cholesterol and high-density lipoprotein (HDL) carried good cholesterol. Cholesterol is an extremely important biological molecule that has roles in contributes to the structure of cell walls, makes up digestive bile acids in the intestine, allows the body to produce vitamin D and enables the body to make certain hormones(Lewis and Rader, 2005).Synthesis of cholesterol, like that of most biological lipids, begins from the two-carbon acetate group of acetyl-CoA. The acetyl-CoA utilized for cholesterol biosynthesis is derived from an oxidation reaction (e.g.,fatty acids or pyruvate) in the mitochondria and is transported to the cytoplasm by the same process as that described for fatty acid synthesis. Acetyl-CoA can also be synthesized from cytosolic acetate derived from cytoplasmic oxidation of ethanol which is initiated by cytoplasmic alcohol dehydrogenase (ADH). All the reduction reactions of cholesterol biosynthesis use NADPH as a cofactor.The process of cholesterol synthesis can be considered to be composed of five major steps:

2.1.1. Acetyl-CoAs are converted to 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA)

2.1.2. HMG-CoA is converted to mevalonate

2.1.3. Mevalonate is converted to the isoprene based molecule, isopentenyl pyrophosphate (IPP) with the concomitant loss of CO2

2.1.4. IPP is converted to squalene

2.1.5. Squalene is converted to cholesterol.

Hypercholesterolemia is a condition when there is an extremely high level of cholesterol in the body. Usually this means that there is a high concentration of LDL and low concentration of HDL. When too much LDL circulates the blood cell, it can built up the inner walls of arteries that feed the heart and brain, therefore, cause the clogging of the arteries. The health significance is that they are prone to cardiovascular diseases. If clot forms and blocks the narrowed artery, a series of cardiovascular diseases such as hypertension, arteriosclerosis, heart attack or stroke can result. High levels of cholesterol are also closely associated to diabetes (Lecerf and Lorgenl ,2011).

2.2. Triglycerides

A triglyceride is an ester derived from glycerol and three fatty acids. Triglycerides are the main constituent of body fat in humans and animals. There are also present in the blood to enable the bidirectional transference of adipose fat and blood glucose from the liver, and are a major component of human skin oils (Nelson, 2000). There are many different types of triglyceride, with the main division being between saturated and unsaturated types. Saturated fat are "saturated" with hydrogen all available places where hydrogen atoms could be bonded to carbon atoms are occupied. These hare a higher melting point and are more likely to be solid at room temperature. Unsaturated fats have double bonds between some of the carbon atoms, reducing the number of places where hydrogen atoms can bond

to carbon atoms. These a lower melting point and are more likely to be liquid at room temperature (Alfred,2002). The overall process of triglyceride biosynthesis consists of four biochemical pathways: fatty acyl-CoA biosynthesis, conversion of fatty acyl-CoA to phosphatidic acid, conversion of phosphatidic acid to diacylglycerol, finally conversion of diacylglycerol to triglycerol (Hemat, 2003).

2.3. High density lipoprotein (HDL)

High density lipoprotein is the smallest of the lipoprotein particales , it is composed of 80-100 proteins/particle which transport all fat molecule (lipids) around the body within the water outside cells. The fat carried include cholesterol, phospholipids, and triglycerides (Betteridge et *al*., 2008). The liver synthesizes lipoproteins as complex of apolipoproteins and phospholipid, which resemble cholesterol-free flattened spherical lipoprotein particles, the complexes are capable of picking up cholesterol carried internally from cells by interaction with the ATPbinding cassette transported A1(ABC A1). A plasma enzyme called lecithincholesterol acyl transferase (LCAT) converts the free cholesterol into cholesterol ester (a more hydrophobic form of cholesterol), which is then sequestered into the core of the lipoprotein particle, eventually causing the newly synthesized HDL to assume a spherical shape. HDL particles increase in size as they circulate through the blood stream and incorporate more cholesterol and phospholipid molecules from cells and other lipoproteins (Huang and Zhang, 2013).

2.4. Low density lipoprotein (LDL)

Low density lipoprotein is one of the five major groups of lipoprotein, LDL has a highly hydrophobic core consisting of polyunsaturated fatty acid known as linoleate and hundreds to thousands esterified and unesterified cholesterol molecules. This core carries varying numbers of triglycerides and other fats and is surrounded by a shell of phospholipids and unesterified cholesterol (Segrest et *al.*,

2011). LDL particles are sometimes referred to as bad cholesterol because they can transport their content of fat molecules into artery walls, attract macrophages and thus atherosclerosis (Krauss, 2010).

Chapter Three

Materials and methods

Chapter Three

Materials And Methods

Material :

3.1. Study design

This is an cross sectional study was conducted in Khartoum state , in Hypothyrodism patient to determine TC, LDL, HDL .

3.2. Study area

Blood samples were collected from Hypothyrodism patient around Khartoum state.

3.3. Sample size

A hundred blood samples were collected from the subjects their age ranged between (35 to 80 years) .

3.4. Study period

This study was carried out during the period from April to July 2018

3.5. Sample

Heparin zed plasma sample was used in this study.

3.6. Sample collection

3ml of venous blood sample was collected from each participant ,the blood sample was drawn in heparin containers, then centrifuged at 4000 rpm for three minutes to get plasma. The plasma prepared was collected into 1.5 ml eppendorf tubes and kept frozen at (-20ċ) until analysis .

3.1.7 Inclusion criteria

Study group clinically diagnosed with hypothyroidism .

3.1.8 Exclusion criteria

Group with heart disease

3.2. Methodology:

2.2.1 Estimation of parameters

3.2.1.1 principle of method use for estimation of Cholesterol:

Cholesterol is measured enzymatically in serum or plasma in a series of coupled reactions that hydrolyze cholesteryl esters and oxidize the 3-OH group of cholesterol. One of the reaction byproducts, H_2O_2 is measured quantitatively in a peroxidase catalyzed reaction that produces a color. Absorbance is measured at 500 nm.

Reagents ,procedure and calculation appendix (3) page

3.2.1.2 principle of method use for estimation of Triglycerides :

Triglycerides are measured enzymatically in serum or plasma using a series of coupled reactions in which triglycerides are hydrolyzed to produce glycerol. Glycerol is then oxidized using glycerol oxidase, and H_2O_2, one of the reaction products, is measured as described above for cholesterol. Absorbance is measured at 500 nm.

Reagents ,procedure and calculation appendix (4) page

3.2.1.3. principle of method use for estimation of High density lipoprotein (HDL) cholesterol :

Direct HDL method. HDL is measured directly in serum. The basic principle of the method is as follows.

HDL-cholesteryl esters PEG-cholesteryl esterase > HDL-unesterified cholesterol + fatty acid

(3) Unesterified chol + O_2 PEG-cholesterol oxidase > cholestenone + H_2O_2

(4) H_2O_2 + 5-aminophenazone + N-ethyl-N-(3-methylphenyl)-N'_succinyl ethylene diamine + H2O + H^+ peroxidase > qunoneimine dye + H_2O

Absorbance is measured at 600 nm.

Reagents ,procedure and calculation appendix (5) page

3.2.1.4. principle of method use for estimation of LDL-cholesterol :

LDL-cholesterol is calculated from measured values of total cholesterol, triglycerides and HDL-cholesterol according to the relationship:

[LDL-chol] = [total chol] - [HDL-chol] - [TG]/5

where [TG]/5 is an estimate of VLDL-cholesterol and all values are expressed in mg/dL.

Reagents ,procedure and calculation appendix (6) page

3.3. Quality control method:

The precision and accuracy of all methods used in this study were checked each time by commercial prepared control sera.

3.4.Statisticalanalysis

The data obtained from all participantswere recorded and analyzed by using statistic package for social scie (SPSS) version on programmed computer

T-test was used to find out the difference between means of compared group. Person correlation was used to find out the relationship between some variables in the study**.**

3.9. Ethical consideration:

Permission of this study will be obtained from the local authorities in the area of the study. The objectives of the study will be explained to the local authorities in the area of the study and to all individual in the study. A written consent will be obtained from each participates in this study. (Appendix 2)

3.10. Data collection:

3.10.1. Interview and Questionnaire:

Questionnaire was designed to provide personal and medical information about the subjects (appendix I).

Chapter four

Results

Chapter four

RESULTS

The present study was conducted during the period from April to July 2018, it included 100 as study group clinicly diagnosed with hypothyroidism.

The samples were analyzed for plasma level of (TC , LDL and HDL) concentration.

The results obtained were illustrated as follow:

Table (4-1) shows significant increase in(TC and LDL) (Mean±SD = 235.7±44.9, 154.3±43.1 $P \leq 0.05$). and in significant different in (HDL) (Mean±SD = 23.9±8.1 , $P \geq 0.05$). between hypothyroidism patients compare to normal range .

Table (4-2) shows significant increase in (TC and LDL) (Mean±SD = 192.5±45.3, 128.3±46.7, $P \leq 0.05$) and no different in (HDL) (Mean±SD = 21.3±9.2 , $P \geq 0.05$) between female study group compare with that of the male of study group.

Table (4-3) shows significant increase in (TC and Ldl) (Mean±SD =259.5±32.2, 172.3±29.4, $P \leq 0.05$). and insignificant decrease in (Hdl) (Mean±SD = 22.0±8.6 , $P \geq 0.05$). between (duration les than 2 years) compare to the (duration more than 2 years) .

Table (4-4) shows significant increase in (TC and LDL) (Mean±SD = 241.8±45.8, 160.4±40.1, $P \leq 0.05$). and insignificant different in (HDL) (Mean±SD = 24.1±7.7 , $P \geq 0.05$). between treated group compare to untreated of study group.

Table (4-5) shows significant increase in (TC and LDL) (Mean±SD = 259.8±30.64, 172.6±30.87, $P \leq 0.05$). and insignificant different in (HDL) (Mean±SD = 26.73±6.83 , $P \geq 0.05$). between overt hypothyrodism group compare with subclinical hypothyrodism group.

Table (4-6) the result showed that 20 (20%) of the patients had desirrable TC, 27 (27%) had borderline TC and 53 (53%) had high TC. Also showed 16(16%) of the patien had optimal LDL , 33(33%) had disrable LDL , 34(34%) had high leve LDL

and 17 (17%) had very high LDL. And 96(96%) of the patien had high risk HDL and 4(4%) had low risk HDL.

Figure (4-1): Show the distribution of the study group according to gender.

Figure (4-2): Show the distribution of the study group according to type of disease.

Figure (4-3): shows significant posative correlation between the plasma level of cholesterol and the age of the study group per years(r =0.525**, P= 0.00).

Figure (4-4): shows significant posative correlation between the plasma level of Ldl and the age of the study group per years(r = o.321** , P= 0.001).

Figure (4-5): shows no correlation between the plasma level of (HDL) and the age of the study group per years (r = o.161 , P= 0.109).

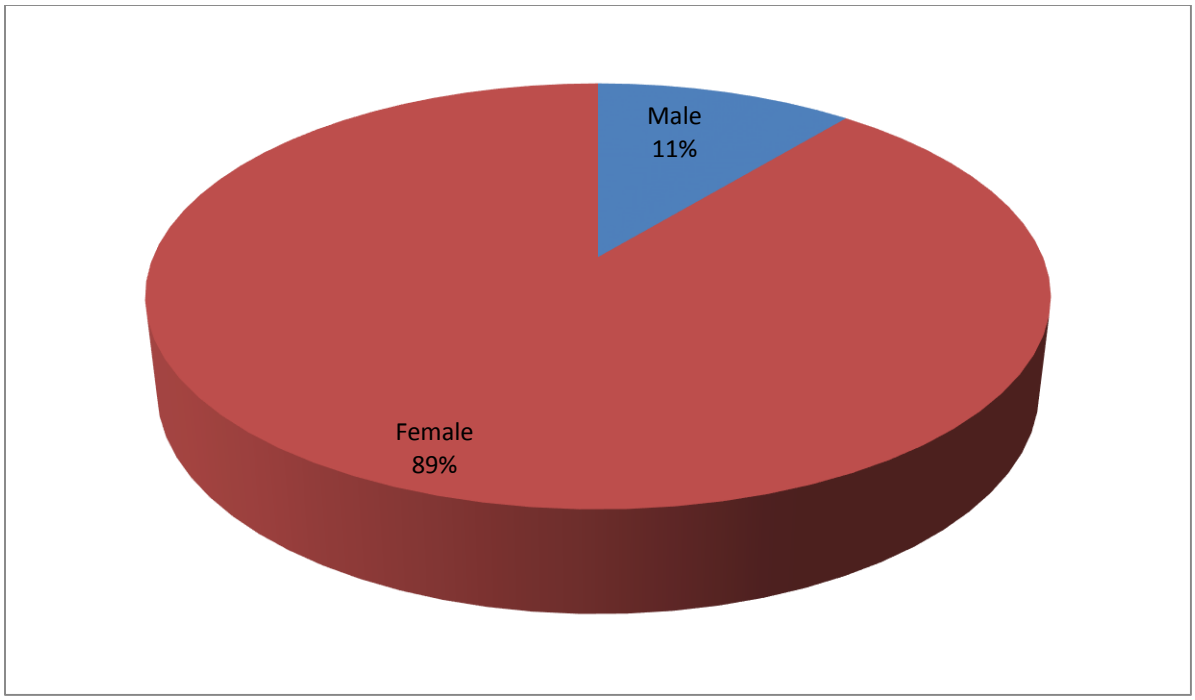

Figure (4-1) distribution of patients according to gender

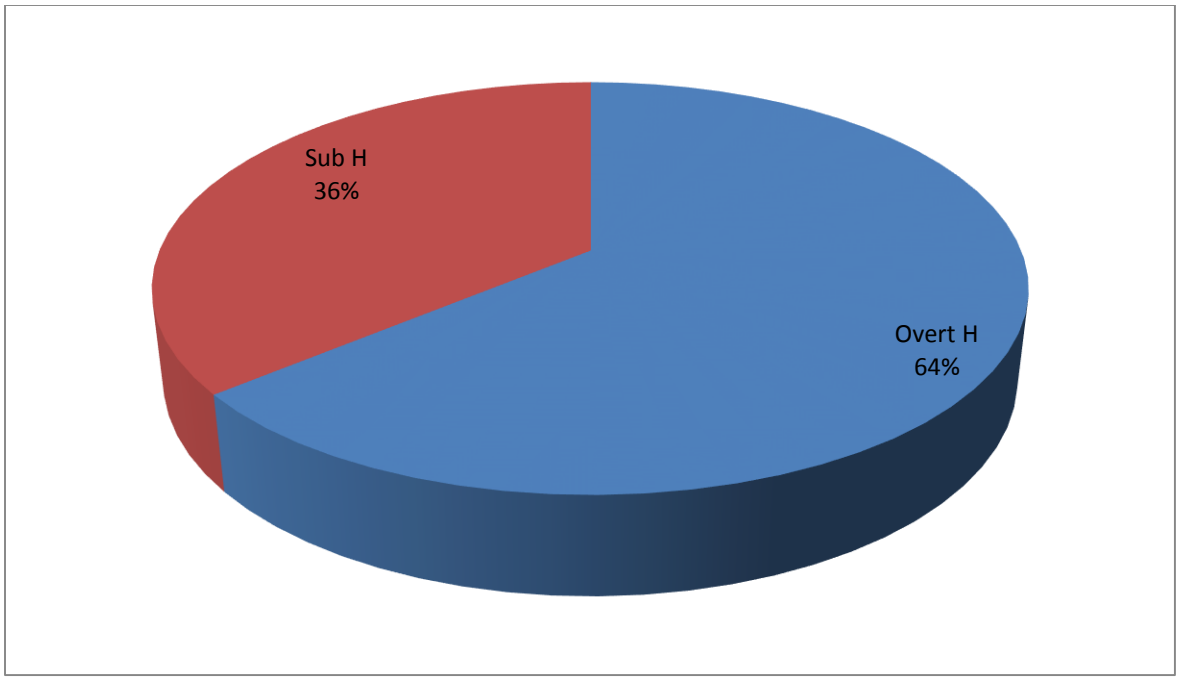

Figure (4-2) distribution of patients according type of disease

Table (4-1): Comparison of means of plasma level of (TC , LDL and HDL) in study group with WHO normal range.

Table (4-1) mean of lipid profile in comparison with normal range

Parameters	**Mean±SD**	**(R.V)**	***P-value***
Cholesterol	235.7±44.9	Up 200	0.000
LDL	154.3±43.1	Up 130	0.000
HDL	23.9±8.1	Up 35	0.532

The tables shows the mean ±standard deviation and probability (P) .

Independent t-test was used for comparison.

P-vale ≤0.05 is considered significant

Table (4-2): Comparison of means of plasma level of (TC, LDL and HDL)between male study group r and female study group.

Table (4-2) mean of lipid profile across gender

Parameters	Male (Mean±SD)	Female (Mean±SD)	*P-value*
Cholesterol	192.5±45.3	241.1±42.3	0.001
LDL	123.6±35.1	158.1±42.6	0.010
HDL	21.3±9.2	24.23±7.9	0.410

The tables shows the mean ±standard deviation and probability (P) .

Independent t-test was used for comparison.

P-vale ≤0.05 is considered significant

Table (4-3): Comparison of means of plasma level of (TC , LDL and HDL) between duration <2Years and ≥ 2Years.

Table (4-3) mean of lipid profile according to duration of disease

Parameters	<2Years (Mean±SD)	≥2Years (Mean±SD)	*P-value*
Cholesterol	201.4±38.2	259.5±32.2	0.000
LDL	128.3±46.7	172.3±29.4	0.000
HDL	25.3±7.3	22.0±8.6	0.044

The tables shows the mean ±standard deviation and probability (P) .

Independent t-test was used for comparison.

P-vale ≤0.05 is considered significant

Table (4-4): Comparison of means of plasma level of (TC , LDL and HDL)between treated study group and untreated study group.

Table (4-4) mean of lipid profile according to treatment status

Parameters	Treated (Mean±SD)	Untreated (Mean±SD)	*P-value*
Cholesterol	203.7±20.7	241.8±45.8	0.001
LDL	121.9±45.4	160.4±40.1	0.002
HDL	23.1±9.7	24.1±7.7	0.652

The tables shows the mean ±standard deviation and probability (P) .

Independent t-test was used for comparison.

P-vale ≤0.05 is considered significant

Table (4-5) mean of lipid profile according to type of disease

Parameters	Overt Hypothyroidism (Mean±SD)	Sub clinical H ypothyroidism (Mean±SD)	*P-value*
Cholesterol	259.8±30.64	192.8±32.67	0.000
LDL	172.6±30.87	121.7±42.93	0.000
HDL	26.73±6.83	19.03±7.65	0.870

The tables shows the mean ±standard deviation and probability (P) .

Independent t-test was used for comparison.

P-vale ≤0.05 is considered significant

Table (4-6) distribution of patients according to lipid profile status

Parameters	**Frequency**	**Percentage (%)**
TC		
Desirable	20	20.0
Borderline	27	27.0
High	53	53.0
LDL		
Optimal	16	16.0
Borderline	33	33.0
High	34	34.0
Very high	17	17.0
HDL		
High risk	96	96.0
Low risk	4	4.0
Total	**100**	**100**

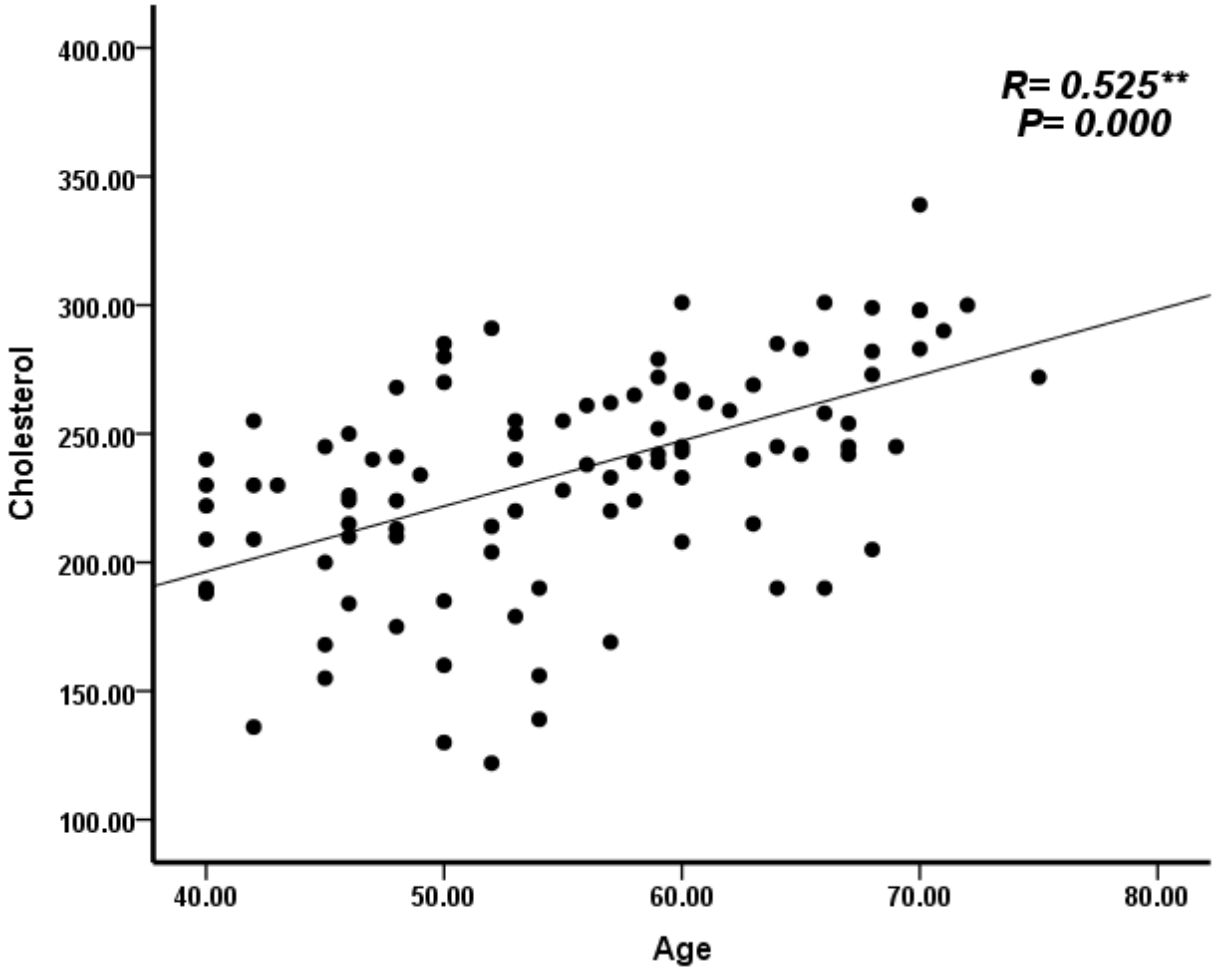

Figure (4-3) correlation between age and cholesterol level

A scattered plot show the positive correlation between the plasma level of cholesterol and age per years .

(r =0.525**, P= 0.00)

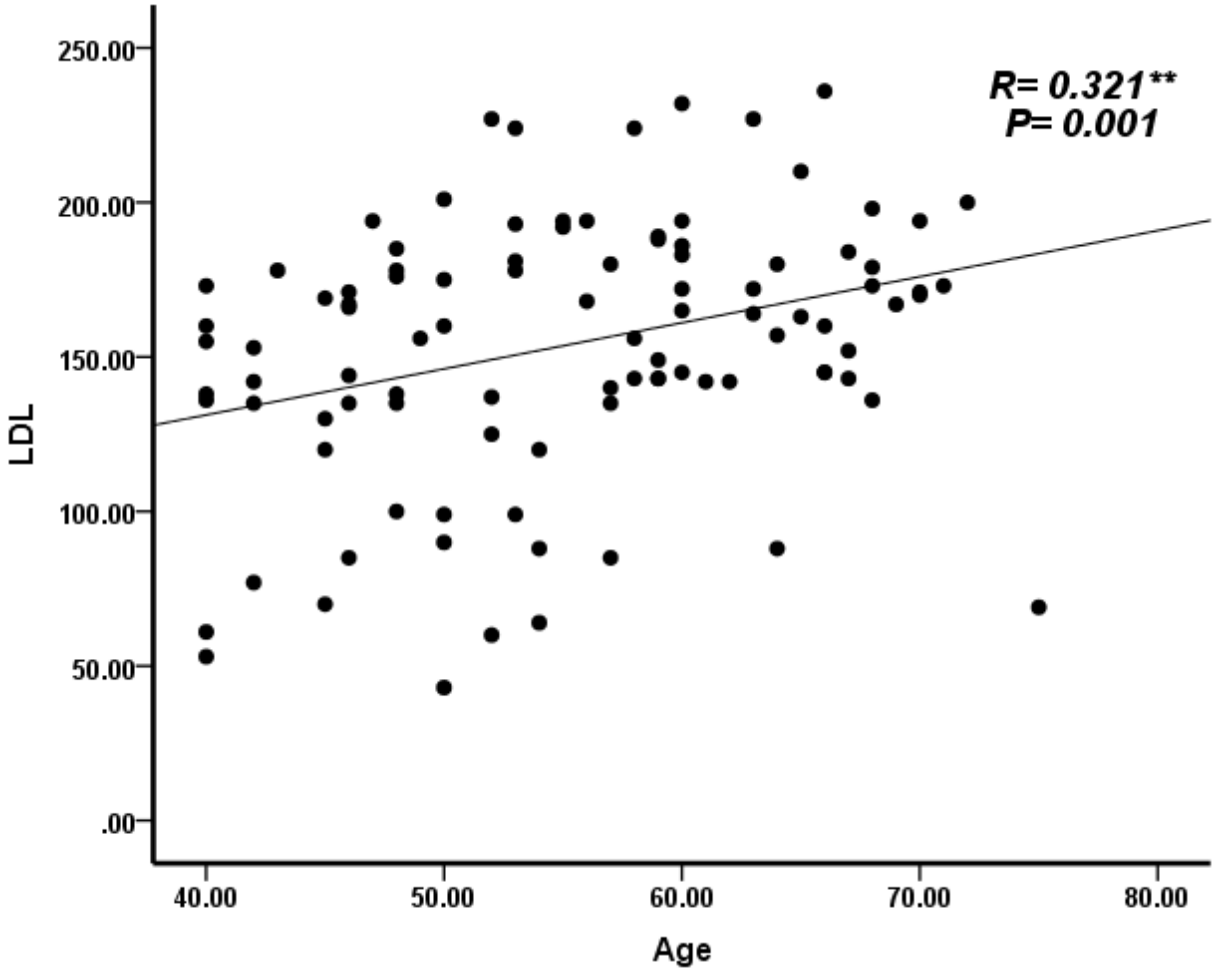

Figure (4-4) correlation between age and LDL level

A scattered plot show the positive correlation between the plasma level of LDL and age per years .

(r = o.321** , P= 0.001)

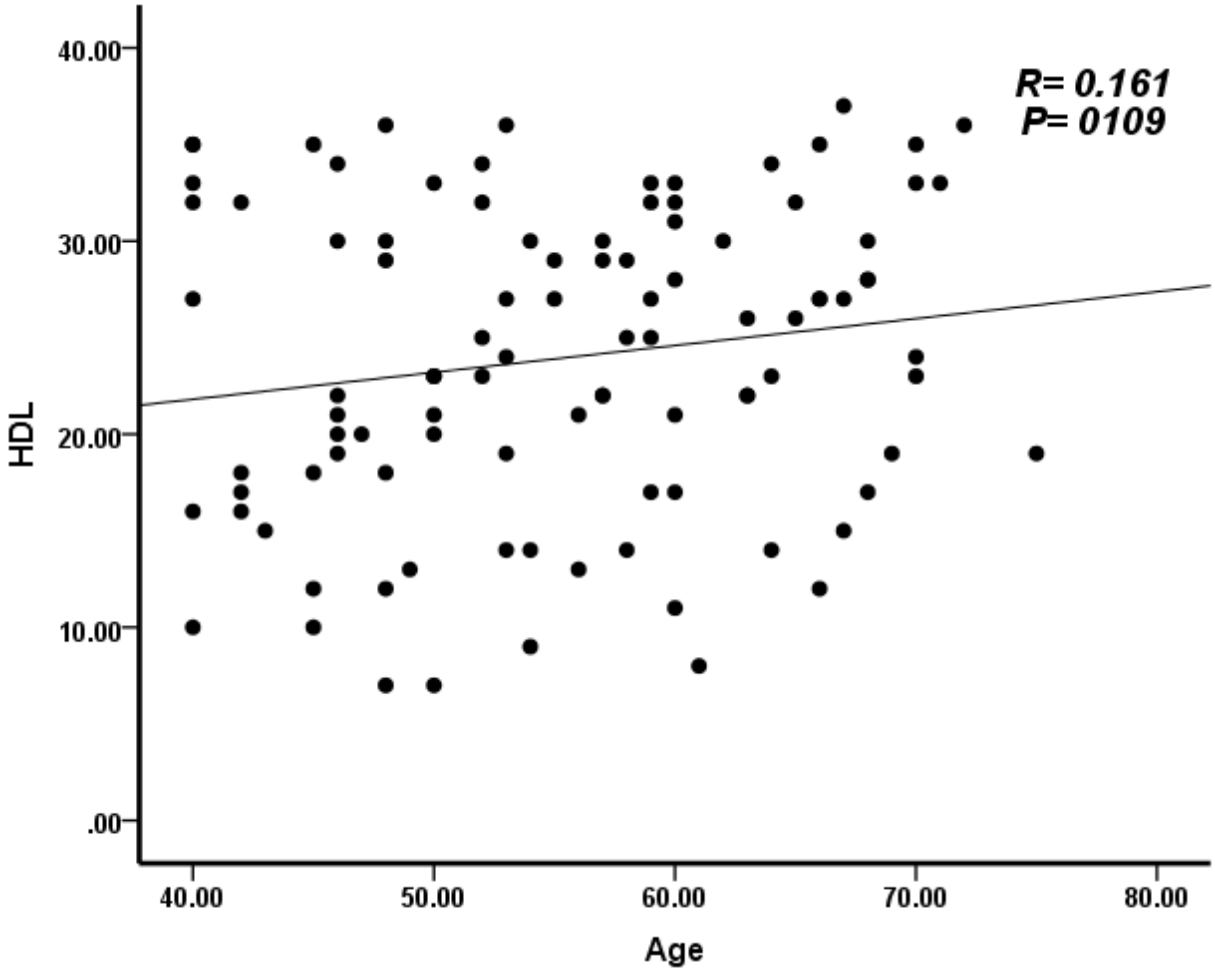

Figure (4-5) correlation between age and HDL level

A scattered plot show the no correlation between the plasma level of HDL and age per years .

(r = o.161 , P= 0.109).

Chapter Five

Discussion, Conclusion and Recommendation

Discussion, Conclusion and Recommendation

5.1 Discussion

About 200 million people in the world have some form of thyroid disease. Thyroid diseases for the most part are treatable; however, untreated thyroid disease can produce serious results sometimes in many other parts of the body (Norman, 2016).The diagnosis of thyroid disease can be particularly challenging. In particular, people may not associate the signs and symptoms with the disease process and thus may not bring them to the attention of themselves against thyroid disorder. For this reasons, if early detection of these disorders would be possible then, it would not become any life threatening problem.

The result show the hypothyroidism is more prevalence in elder female (89%) than in elder male (11%) . And this study agree with (Fatourechi.2009).

The study reported the prevalence of overt hypothyroidism (64%) is more than the prevalence of sub clinical hypothyroidism (36%) . But this result of study not agrees with (Cooper and Biondi 2008).

The current study agrees with (Mansourian *et al*., 2008), there was significant increase in total cholesterol levels and LDL among hypothyroidism compare with normal range .(P-value 0.000). And insignificant different of HDL in hypothyroidism patien compare with normal range .(P-value 0.532).

A cross-sectional study by (Pearce,2012) Suggested that the treatment of the hypothyroidism patien can affected on the lipid profile, the same was found in this study.

Also in our study show significant different in (TC and LDL) between patien with hypothyroidism <2years compare with ≥2Years .(Pvalue 0.000), but insignificant different in HDL between patien with hypothyroidism <2years compare with ≥2Years .(Pvalue 0.044) and this agree with (Liu and Prent 2010).

In this study there was significant different in TC level and LDL level in overt hypothyroidism patien compare with subclinical hypothyroidism patien .(Pvalue 0.000), respectively this agree with (Jeskra 2007) because of a decreased fractional clearance of LDL by a reduced number of LDL receptors in the liver .

Acording to WHO classification of the lipid profile the result showed that 20 (20%) of the patien had disrrable TC, 27 (27%) had borderline TC and 53 (53%) had high TC. Also showed 16(16%) 0f the patien had optimal LDL , 33(33%) had disrable LDL , 34(34%) had high leve LDL and 17 (17%) had very high LDL. And 96(96%) of the patients had high risk HDL and 4(4%) had low risk HDL.

The important observation of this study was that there are significant posative correlation between the level of (TC and LDL) with the age of hypothyroidism patien (r =0.525**, P= 0.00). (r = o.321** , P= 0.001), and this agree with (Fatourechi.2009).

This study shows no correlation between the level of HDL and the age of hypothyroidism patients (r = o.161 , P= 0.109).

5.2 Conclusion

-From this study it can be concluded Plasma (TC and LDL were significantly increase in hypothyroidism patients . And the Plasma (HDL) was insignificant different in hypothyroidism patients . Also showed the Prevalence of the hypothyroidism is more in elder female than in elder male . And The duration of disease per years affected the level of lipid profile .Finally in the result observed the age of the patient correlates positively with the level of lipid profile .

5.3 Recommendation

- Study the effect of the Levothyroxine on the lipid profile should be done.
- Further study with large sample size to investigate triglycerids and other lipoproteins.

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Appendices

Appendix (1)

Sudan University of Science and Technology

Evaluation of Lipids Profile among Sudanese Patients with Hypothyroidism in Khartoum State

Questionnaire

Date:…….

1. Gender : male () female ()

2. Telphone : ……

3. Age :……Yea

4. Type of disease

Overt hypothyroidism ( )

Sub clinical hypothyroidism ( )

5. Treatment status

Treated Yes ( ) NO ( )

6. The Investigation :

TC :…….

LDL:……..

HDL:……

Appendix "2"

Sudan University of Science and Technology

Evaluation of Lipids Profile among Sudanese Patients with Hypothyroidism in Khartoum State

Informed consent

إعلام موافقة

هذه دعوة منى: الباحث / مصعب صلاح النعيم محمد طالب ماجستير - مختبرات طبية – كيمياء سريرية – بجامعة السودان للعلوم والتكنولوجيا لمشاركتكم في برنامج بحث هدفه تقييم مستوى الدهون في الدم لمرضى قصور الغدة الدرقية بولاية الخرطوم .

إذا رغبتم في إنجاح هذا البرنامج فإني ساقوم :-

بأخذ عينة من الدم لقياس مستوى الدهون .

بملء إستمارة بمعلومات تخصكم لها علاقة بموضوع البحث.

أي معلومة تخصكم في الإستمارة سوف تكون سرية.

مشاركتكم في البرنامج تسعدنا وتساعد في إنجاح هدف البحث.

لكم كامل الحرية في إختيار عدم المشاركة, المشاركة أو الإنسحاب من برنامج البحث في أي وقت تشاءون.

يمكنكم الحصول علي إجابة لأي سؤال عن برنامج البحث.

التاريخ .....

توقيع المتبرع .....

توقيع الباحث .....