AL-Nahrain University college of Medicine

2018- 2019

Hyperlipedimia in hypothyroidisim patient

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Abbreviation

TSH…….thyroid stimulating hormones

T4…….thyroxine

T3…….Triiodothyronine

LDL…….Low density lipoprotein

IDL…….Intermediate density lipoprotein

VLDL…….Very low density lipoprotein

HDL…….High density lipoprotein

CHO…….Cholesterol

TRIG…….Triglycerides

APO-B…….Apolipoprotein B

CHM…….Chylomicrons

LPL…….Lipoprotein lipase

HL…….Hepatic lipase

CETP…….Cholesteryl ester transfer protein

ACAT…….acyl-CoA:cholesterol acyltransferase

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Abstract

Hypothyroidism is a condition in which thyroid gland doesn't make enough thyroid hormone(1)

Abnormalities in plasma lipids are most frequently the result of the interaction between the individual and the environment; therefore, it is essential to look for secondary causes in all patients with dyslipidemia.
-To describe the pathogenesis of dyslipidemia and in particular the role of hypothyroidism as a secondary cause of dyslipidemia.

This study is an effort to identify association between the hypothyroidism and hyperlipidemia , done in Al-Imamain Al-kadhumain teaching hospital from the period of 15th of November ,2018 to 18th of February ,2019 .

We did cross sectional study and collect randomly 25 patients , did for them an investigation which are listed as thyroid function test (TSH, T4, T3) and lipid profile (Cho , trig, LDL, HDL) , we had chosen only primary , neither iatrogenic , nor subclinical causes of hypothyroidism and not associated with DM of all ages and both sexes.

hypothyroidism is associated to impairment of the lipid profile both quantitatively and qualitatively. Moreover, the association between low thyroid function and lipid plasma levels has been also found to extend into the normal range of TSH. However, confounders such as age, gender, may modify this association. The effects of treatment with levothyroxine for cholesterol reduction are warranted in Hypothyroidism .(2)
Conclusion: Hypothyroidism should always be considered in the evaluation of patients with dyslipidemia.

CHAPTER ONE :

INTRODUCTION

The aim of this review is to provide an update on lipid metabolism and to focus on its regulation by thyroid hormones. This paper includes an introduction to the physiopathology of dyslipidemias to provide a better understanding of lipid disorders in general. However, with the aim of discussing secondary dyslipidemia due to hypothyroidism, the consequent alterations of the lipid profile in hypothyroid patients are summarized according to updated literature. While evidence of an impaired lipid profile in overt hypothyroidism (OH) is quite consistent, lipid alterations in subclinical hypothyroidism (SCH) remain a matter of controversy in both adult and pediatric populations, particularly in the latter where evidence is lacking. In addition, the possible reversion of lipid changes in hypothyroid patients in response to levothyroxine is also discussed.

Definition of hypothyroidism

The thyroid gland is located in front of neck just below the voice box (larynx) it release hormones that control metabolism .

Hypothyroidism is condition in which the thyroid gland does not make enough thyroid hormone.

Symptoms :

Early symptoms :

- **Sensitive to cold**
- **Constipation**
- **Depression fatigue.**
- **Heavy menstruation.**
- **Joint and muscle pain.**
- **Pale or dry skin .**
- **Thin brittle hair.**

- **Weakness .**
- **Weight gain .**

Late symptoms :

- **Decreased taste and smell.**
- **Hoarseness.**
- **Puffy face, hand and feet**
- **Slow speech**
- **Thickening of the skin**
- **Thinning of eyebrows**

Signs:

A physical examination may reveal a smaller than normal thyroid gland , although sometimes the gland normal size or even enlarged (goiter). The examination may also reveal :

- **Brittle nails**
- **Coarse facial features**
- **Pale or dry skin, cool to touch**
- **Swelling of arms and legs.**
- **Thin and brittle hair .**

Laboratory tests to determine thyroid function :

- **TSH test**
- **T4 test**

Causes of – non iatrogenic – primary hypothyroidism ((in which the only involved causes in our study samples)) :

- **Primary atrophic hypothyroidism:**
  - ♦ **Primary idiopathic hypothyroidism**
  - ♦ **Sporadic athyreotic hypothyroidism (dysplasia or agenesis)**
  - ♦ **Endemic cretinism**
- **Goitrous hypothyroidism :**
  - ♦ **Hashiomotos thyroiditis**

- ♦ Riedell's Struma
- ♦ Inherited defects of hormone synthesis

Treatment[4] :

The purpose of treatment is to replace the thyroid hormone that is lacking .

Levothyroxine is the most commonly used medication . Doctors will prescribe the

Lowest dose possible that effectively relieves symptoms and brings TSH level to a normal range . If patients have heart disease or you are older,doctor may start with a very small dose .Life long therapy is require unless patients have a condition called transient viral thyroiditis .they must continue taking your medication even when your symptoms go away .When starting medication ,doctor may check your hormone levels every 2-3 months .After that , thyroid hormone levels should be monitored at least every year.

Complications [9,11]

Myxedema coma ,the most severe form of hypothyroidism , is rare. It may be caused by an infection , illness , exposure to cold , or certain medicatios in people with untreated hypothyroidism .

Symptoms and signs of myxedema coma include:

- **Below normal temperature**
- **Dyspnea**
- **Low blood pressure**
- **Low blood sugar**
- **Unresponsiveness**

Other complications:

- **Heart disease**
- **Increased risk of infection**
- **Infertility**
- **Miscarriage**

Physiopathology of Dyslipidemias

In general, dyslipidemias are the result of an increase in the synthesis of lipoproteins or more commonly, of defects in its metabolism and clearance in plasma. In fact, most hyperlipidemias are the result of the accumulation of lipoproteins in the blood, caused by one or more alterations in their metabolic pathways towards its disappearance.

Physiologically, the primary mechanisms responsible for the effectiveness of lipids metabolism include: the system of isoenzymes, lipoprotein lipase/ hepatic lipase (LPL/HL), liver receptors that interact with the apolipoprotein B (APO-B) and a lipoprotein-transfer system.

LPL and HL are enzymes that transform chylomicrons (CHM) and very low density lipoproteins (VLDL) in remnants through hydrolysis of triglycerides contained in the core of these lipoproteins. The lipolytic enzymes act in tune with apolipoproteins (Apo) that play a role of enzymatic co-factors (the Apo system c). This is the first step in the metabolism of both dietary or "exogenous" lipoproteins (CHM) and "endogenous" lipoproteins that are synthesized in the liver (VLDL).

The system that interacts with lipoproteins containing Apo B includes a group of hepatic receptors that play a key role in the internalization and plasmatic cleareance of endogenous and exogenous esterified cholesterol. Cholesterol esters are contained in the core of LDL, intermediate density lipoproteins (IDL), some subclasses of VLDL and the remnants of VLDL and CHM . Dyslipidemias characterized by increase in cholesterol in the blood are the result of dysfunction of these receptors or any of its co-factors.

Finally, the lipoprotein transfer system comprises a group of proteins that are actively involved in lipoproteins function and its remodeling in plasma. Two of these proteins, cholesteryl ester transfer protein (CETP) and acyl-CoA: cholesterol acyltransferase (ACAT) induce the exchange of lipids among different lipoproteins and the incorporation of cholesterol to their lipid core, fulfilling a crucial role in the reorganization of lipoproteic structures. Furthermore they exert an antiatherogenic effect by activating the reverse transport of cholesterol from the peripheral tissues to the liver.

Lipid Changes in Patients with Hypothyroidism

Hypothyroidism is characterized by a decrease in both synthesis and catabolism of lipoproteins . In most patients with myxedema , the relative greater decrease in catabolism and the resulting preponderance of synthesis results in high cholesterol concentration . primary hypothyroidism is believed to play an important role in the development of atherosclerosis , which is the mediated by the presence of hypercholesterolemia , the latter of which is the consequence of thyroid hormone deficiency . This deficiency causes a reduction in the activity of lipoprotein lipase . which may finally lead to cardiovascular disease via an increase in serum LDL level .[12,13,14]

Thyroid hormone is known to play a role in regulating the synthesis , metabolism and mobilization of lipids . In patients with primary hypothyroidism there is an increase in serum total cholesterol , low- density lipoprotein , cholesterol , apolipoprotein B , lipoprotein(a) levels , and possibly triglyceride levels . Most lipid abnormalities in patients with primary hypothyroidism with resolve with thyroid hormone replacement therapy . The lipid –altering effects of thyroid hormone make it an appealing target for drug development . The development of specifically targeted thyroid hormone analogues that could potentially treat hyperlipidemia without causing systemic thyrotoxicosis is currently ongoing[15]

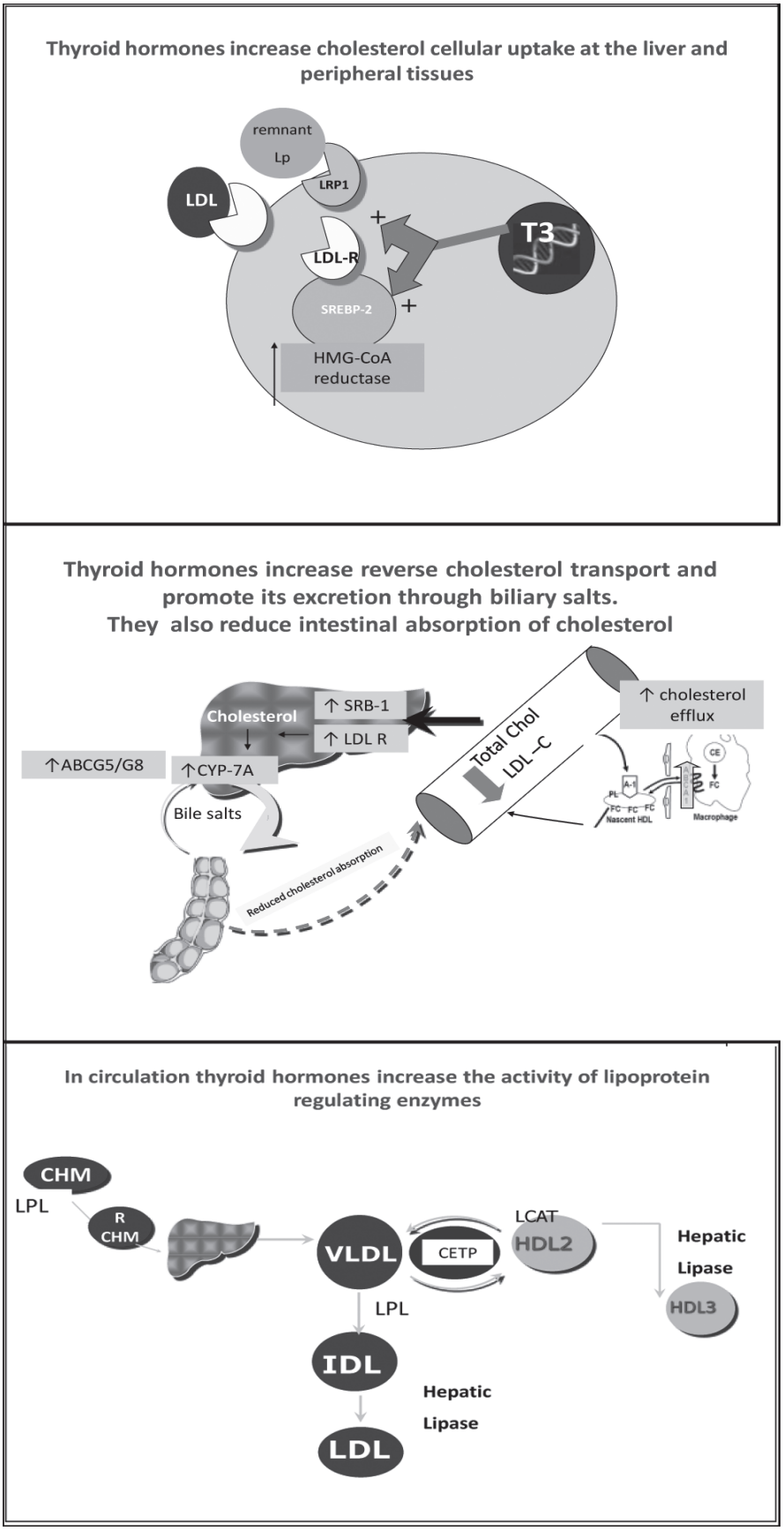

Figure 1: *Regulation of lipoprotein metabolism by thyroid hormones*
Footnote: ABCG5/G8: ATP-binding cassette sub-family G members;
LRP1: LDL receptor-related protein 1; SREBP2: Sterol regulatory element binding protein 2; HMG-CoA reductase: 3-hydroxy-3-methyl-glutaryl-CoA reductase
SRB1: Scavenger receptor class B member 1; CYP7A: cholesterol 7 alpha-hydroxylase; ABCA1: ATP-binding cassette transporter; CHM: Chylomicron
RCHM: remnant chylomicron; VLDL: Very-low-density lipoprotein
HDL: High-density lipoprotein; LDL: Low-density lipoprotein; IDL: Intermediate-density lipoprotein; LPL: Lipoprotein lipase; CETP: Cholesteryl ester transfer protein; LCAT: Lecithin—cholesterol acyltransferase

CHAPTER TWO:

THE STUDY

AIM

The study done to estimate the relationship between hyperlipidemia in patient with primary hypothyroidism .

Patients and methods

In this cross sectional study, 25 patients who attended the endocrinology clinic in Al-Imamain Al-Kadhumain teaching hospital where interviewed between the period of 15th of November ,2018 and 18th of February ,2019 .

All The patients were documented cases of primary hypothyroidism. They consulted the endocrinology clinic in the hospital for follow up of their condition. A thyroid function test and a lipid profile were ordered from the patients to monitor their health condition and the changes in the lipid profile that may occur in hypothyroidism.

They did lipid profile to monitor their lipid changes and to correlate their result with their general health and the duration of hypothyroidism and to detect the complication of hyperlipidemia.

After completing data collection, the data (name, age, gender, thyroid function test, and lipid profile) were allocated in the form of a questionnaire (see the next page) and grouped according to age and gender to simplify the insertion and calculation.

Al-Imamain Al-Kadhumain teaching hospital

Department of Medicine

Research Questionnaire

Patient name:

Gender:

M ☐ F ☐

Age:

Lipid profile:

- LDL:
- HDL:
- TOTAL CHOLESTROL :
- TRIGLYCERIDES :
- TG / HDL

Thyroid function test:

- ♦ TSH:
- ♦ F T3 :
- ♦ F T4:

Result

From total 25 patients that have been counsel the endocrinology clinic during the mentioned period .

Figure 1 shows the gender distribution of the patients in the study sample. 28% were males and 72% were females.

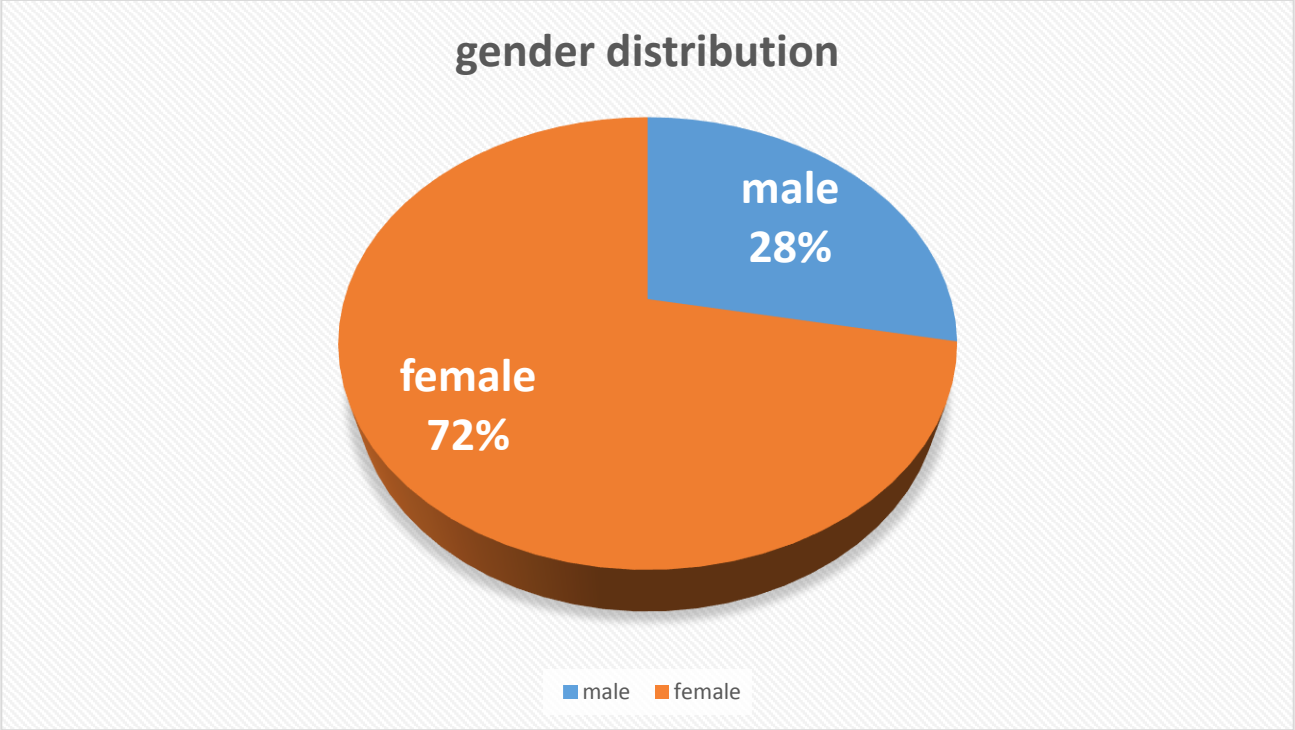

Figure 1: the gender distribution in the study sample

The age of the patients in the study sample ranged between 17-49 years with the mean age being 37 years. Figure 2 shows the age distribution of the study sample. The most common age group was 41-50 (44%), followed by the age group 21-30 (28%), the age group 31-40 (24%), and the age group 11-20 (4%).

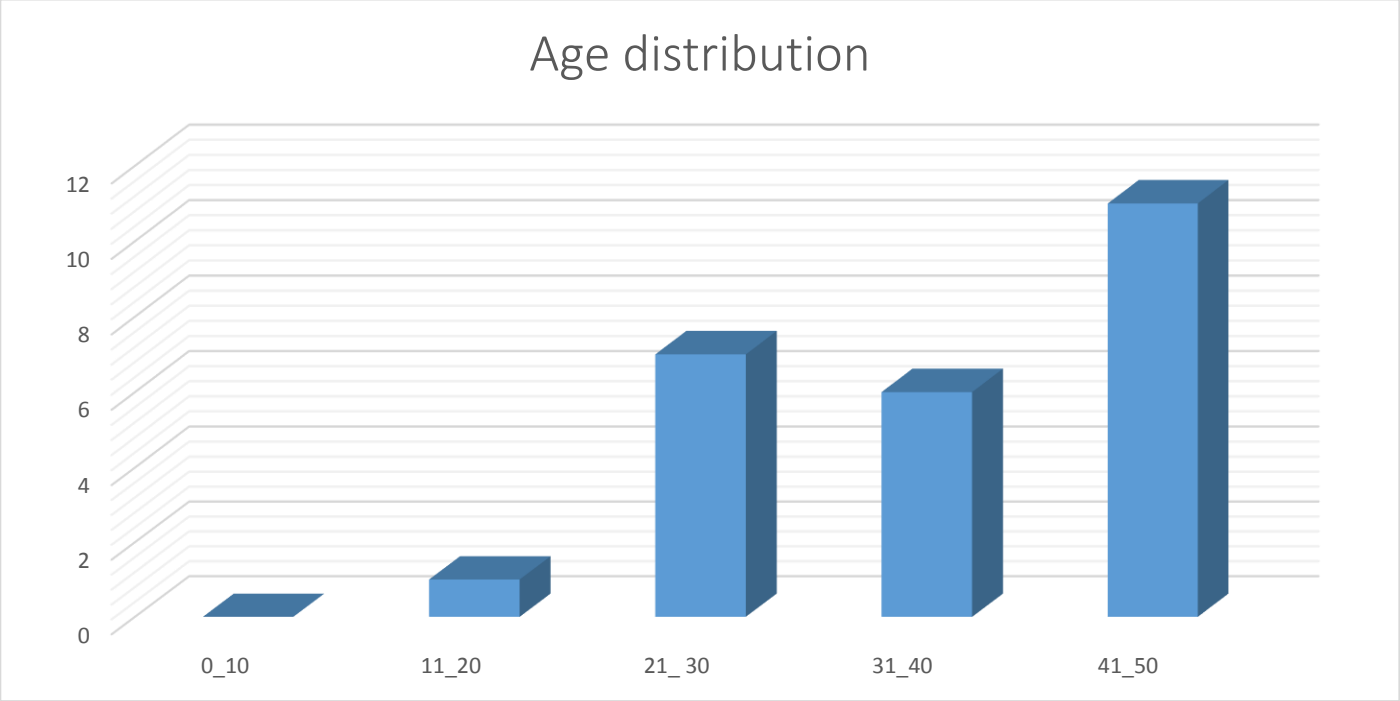

Figure 2: the age distribution in study sample

Thyroid function test was performed by all the patients in which normal TSH levels were considered to be in the range of 0.2-4.5 mu/L.

As shown in figure 3, 48% of the patients had normal TSH levels, 44% had high TSH levels and 8% had low TSH levels.

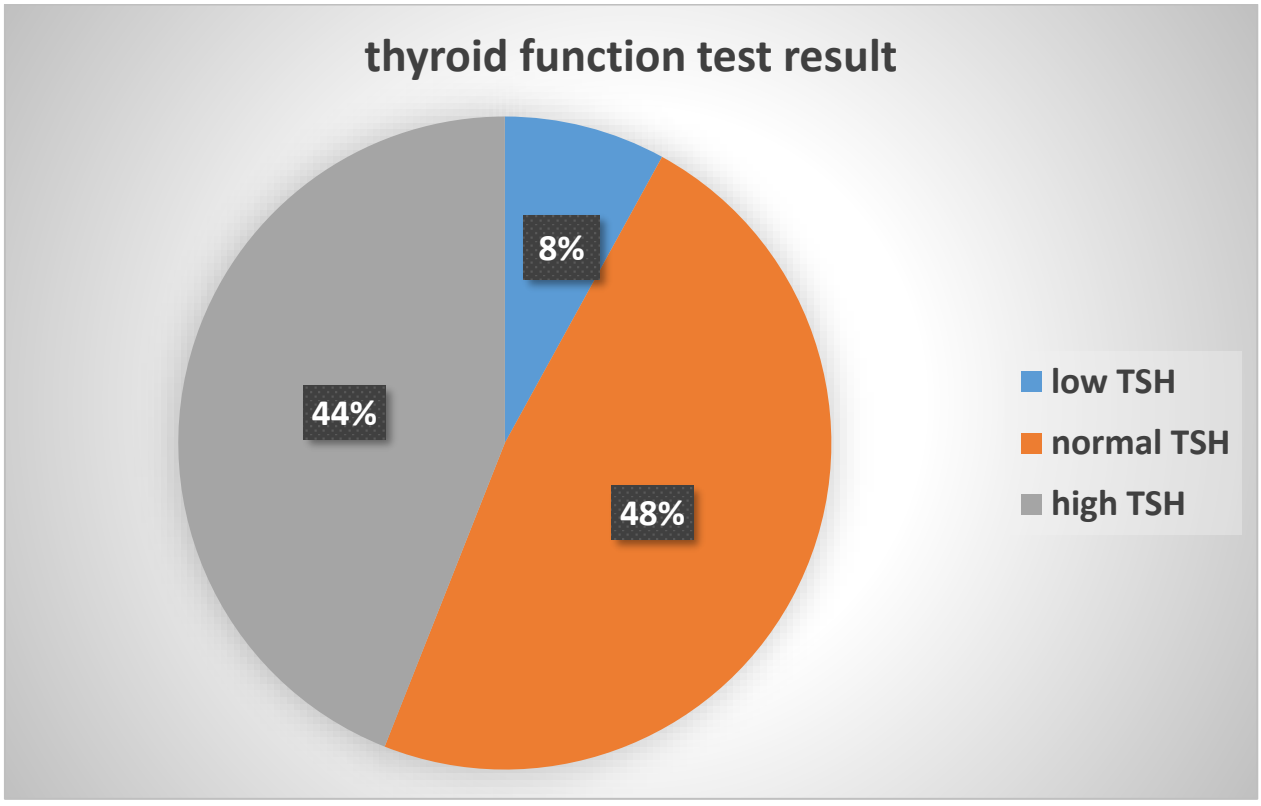

Figure 3: Thyroid function test results for the patients in the study sample

In figure 4, in the study sample there is different result according to lipid profile in term of

(Cholesterol, LDL , HDL , TG) that classified by desirable ,boarder line and high .

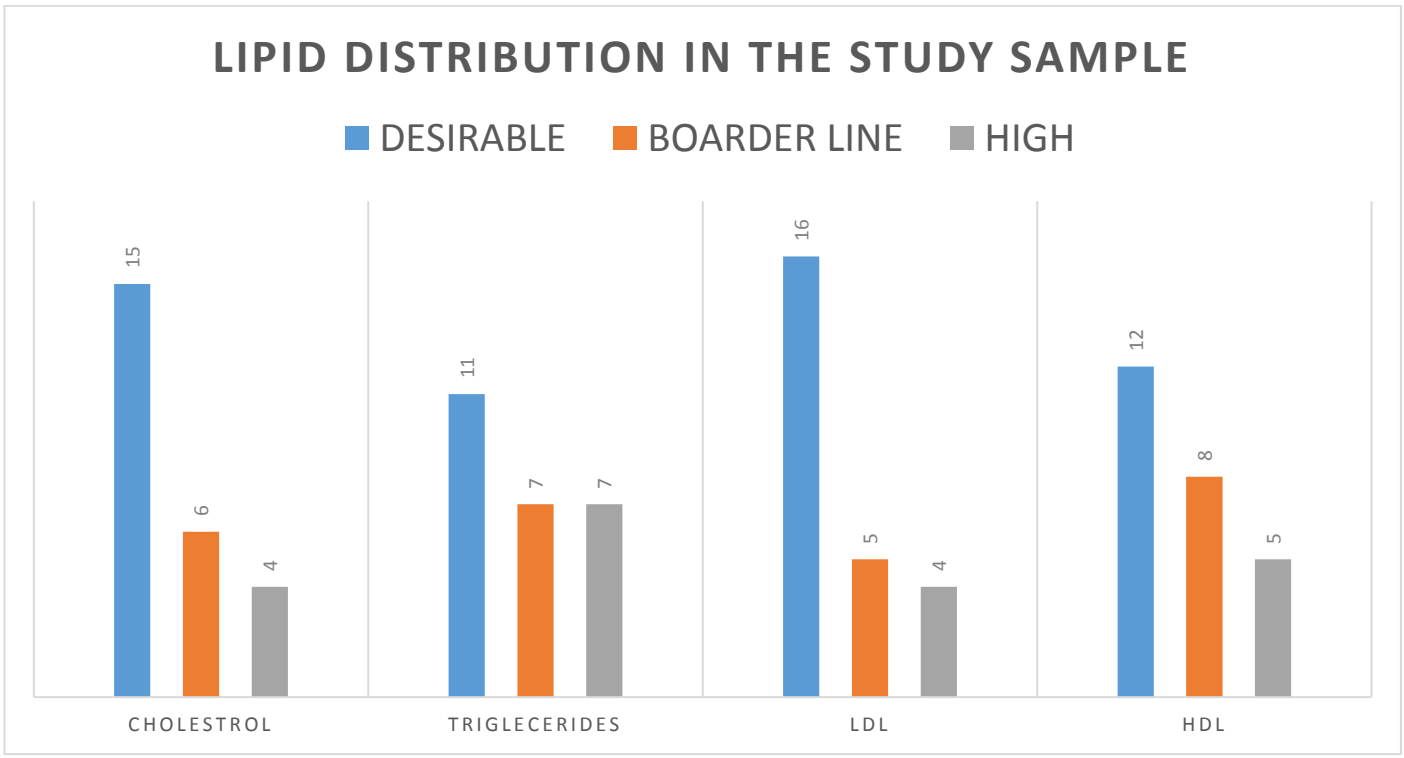

Figure 4: lipid distribution in study sample that revealed the numbers of patients with lipid profile

Changes	Frequency	Number of high TSH level
Cholesterol ↑	4	4
Triglycerides ↑	7	5
HDL ↓	5	3
LDL ↑	4	4

Table 1 : the relationship between numbers of hyperlipidemic patient and TSH level in study sample

Discussion

Hypothyroidism is a very common condition and seen more in women than in men. Our study also indicates that majority of our patients were women and in the age group of 41 to 50 years.

This current study show a correlation between hyperlipidemia and hypothyroidism in the patient that ordered in the study sample .

Thyroid hormones have a significant role to play in metabolism of lipids. Any deficiency of thyroid hormones tends to cause hyperlipidemia, which is a known risk factor for development of atherosclerotic disease. In this study, we discuss the role of thyroid hormones on the levels of cholesterol, LDL , HDL and triglycerides and the pathogenic mechanisms underlying the same.

From our study it was observed that total cholesterol and LDL are elevated in cases of overt hypothyroidism. This finding supports other studies such as the one done by Chan Hee Jung et al in Seoul, Korea (Jung CH et al, 2003)[18,19]**.** This is due to the fact that expression of LDL receptor is modulated by thyroid hormones.

We also observed the elevation of triglycerides in overt hypothyroidism. This is due to the fact that there is poor clearance of endogenous and exogenous triglycerides from circulation in hypothyroidism (Tulloch BR, 1973)[17]**.**

HDL level was found to be increased in hypothyroid cases when compared to controls.

Conclusion

This research highlight several aspect in which further study would clarify the correlation between hyperlipidemia and hypothyroidism patient .

It has been shown in our study that hypothyroid patients have elevated atherogenic parameters and are at high risk for developing cardiovascular disorders.

Normal Ranges[14]

Lipid Profile Test				
	Unit	Optimal	Intermediate	High
Total Cholesterol	mg/dL	<200	200 - 239	>239
	mmol/L	<5.2	5.3 - 6.2	>6.2
LDL Cholesterol (calculated)	mg/dL	<130	130 - 159	>159
	mmol/L	<3.36	3.36 - 4.11	>4.11
HDL Cholesterol	mg/dL	>60	40 - 60	<40
	mmol/L	>1.55	1.03 – 1.55	<1.03
Triglycerides	mg/dL	<150	150 - 199	>199
	mmol/L	<1.69	1.69 - 2.25	>2.25
Non-HDL-C (calculated)	mg/dL	<130	130 - 159	>159
	mmol/L	<3.3	3.4 - 4.1	>4.1
TG to HDL ratio (calculated)	mg/dL	<3	3.1 – 3.8	>3.8
	mmol/L	<1.33	1.34 – 1.68	>1.68

Test	(normal range in bracket)
TSH (μIU/ml)	(0.3-4.5)
T4 (μg/dl)	(4.5-12.5)
Free T4 (ng/dl)	(0.8-2.0)

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