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A Study Of Thyroid Peroxidase And Creatine Kinase With Thyroid Patients

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Summary

Thyroid gland is the most common endocrine glands, and thyroid dysfunction isThe most common problem of endocrine system. Thyroid disorder can be divided in two main group hypothyroidism and hyperthyroidism. In hypothyroidism the level of TSH (thyroid stimulate hormone) becomes higher than control, while T3 (triiodothyronine), T4 (thyroxine) decrease than the control group .In hyperthyroidism the level of TSH (thyroid stimulate hormone) becomes lower than control, while T3 (triiodothyronine) T4 (thyroxine) increase than the control group.

In this study, creatine kinase (ck-mb) was used as a new marker to confirm its relationship with thyroid dysfunction.

The aim of this study is to find the distribution of Creatine Kinase ,Thyroid peroxidase ,lipid profile (HDL (high density lipoprotein),LDL(low density lipoprotein), Cholesterol ,T.G (triglycerides),VLDL (very low density lipoprotein) in three group hypothyroidism ,hyperthyroidism ,healthy people and the relationship between them with other parameters (gender and age) in some Iraqi patients.

This study had concluded (105) patients diagnosed by specialist, (35) patients Hypothyroidism, (35) hyperthyroidism, (35) healthy subjects as control group. The age range between (16-55) year's .The samples were examined and diagnosed at The National Diabetic Center /AlMustansuriya University in Baghdad /Iraq From the period (Dec. 2020 to Apr. 2021).

The distribution of hypothyroidism in was significantly higher in female (88.57%) than males and in hyperthyroidism also female was higher with (68.57%).The results of age and BMI found that the higher rate of hypothyroidism in age (37.97+_2.35) and in hyperthyroidism in age (40.83+_1.98).

The thyroid function tests were used in this study, including T4 (Thyroxine), T3 (Triiodothyronine), TSH (Thyroid stimulating hormone).There is no significant difference between T3and thyroid disorders with (1.441+_0.12b) in hypothyroidism and (3.232+_0.27b), while T4, TSH, TPO were highly

significant. In hypothyroidism patient T4was (81.68+_7.07b) while TSH was (26.25+_4.70a) and TPO was (10.14+_0.17b). And in hyperthyroidism patients T4was (155.95+_10.47a) while TSH was (0.164+_10.47a) and TPO was (10.73+_0.34b).

The activity of CK (creatine kinase) was found to be elevated in the samples of hypothyroidism contrast to control group with values (2.305+_ 0.17) and (1.834+_0.15) respectively.

While the Ck (creatine kinase) activity in hyperthyroidism showed values (2.386+_0.18).

The lipid profile biomarkers was determined of both patients groups and compared with control group .the results of that showed cholesterol was elevated in hypo and hyperthyroidism contrast with control group with values (169.74+_5.19),(150.17+_5.72),(115.93+_3.90) respectively while the values of Triglycerides was showed this values

hypo(140.08+_5.19),hyper(134.91+_11.80),control(90.32+_4.20).

The very low density lipoprotein levels were remains within normal values for the three groups.The HDL (high density lipoprotein) values showed non-significant results in both groups compared with control group.The LDL (low density lipoprotein) was found to be higher in all groups with values hypo (102.48+_4.63), hyper (94.25+_5.47), control (119.47+_5.27)

Introduction

The thyroid gland is located on the fore part of the neck below the thyroid gristle (Adam's apple). Thyroid is an endocrine gland, located directly below the larynx on either side of or advance to the trachea. The essential hormones of thyroid gland are: Thyroxine (T4) and Triiodothyronine (T3) and their concentrations are 93% and 7% respectively.

Hyperthyroidism causes the body to run out energy more quickly than it should be, and the chemical activity (like metabolism) in the cells speeds up. An underactive thyroid construct too little thyroid hormone, resulting in hypothyroidism.

Hypothyroidism ("Hypo" means "under" or "below.") When the amount of hormone liberated into the bloodstream is below normal, the body run out energy more slowly, and chemical activity (metabolism) in the cells slows down (1).

Hyperthyroidism is the term used to denote the overproduction of thyroid hormones from the thyroid gland. Hyperthyroidism is possible with hyperactive thyroid gland due to multi nodular thyroid disease or Grave's disease. (2)

Hyperthyroidism is the result of several diseases that may be located in the thyroid gland (primary), as well as in other locations (secondary), or be the product of an overeating of

high-iodinated foods or being an undesirable effect of some drugs (amiodarone, antitussives) (3).

Hypothyroidism is ten times more common in women than in men, and it is more common among the elderly, accounting for 2 to 5% of the population. Hypothyroidism affects 1 to 2% of people in iodine-sufficient locations, although it can affect up to 3–4% of people in iodine-deficient areas. Hypothyroidism is a condition caused by a lack of thyroid hormone that can range from asymptomatic to life-threatening. Hypothyroidism can be caused by a decrease in thyroid hormone production in the thyroid gland, a secondary problem caused by a TSH deficiency in the pituitary, or a tertiary problem caused by a TRH deficiency in the hypothalamus.(4).

Thyroid peroxidase (TPO) is the commonest autoantigen for mankind, anti-TPO antibodies are practically universal in individuals withal clinical forms of autoimmune thyroid disease (AITD).TPO functions as a cell-surface enzyme and is predicted to have four modular domains .(5)

Thyroid function controls a wide range of metabolic parameters. Thyroid function has a significant impact on lipoprotein metabolism as well as some CVD risk factors, influencing overall CDV risk. Indeed, even within the normal range of thyroid-stimulating hormone (TSH) levels, there is a linear increase in total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TGs) and a linear decrease in high-density lipoprotein cholesterol (HDL-C)(6)Thyroid peroxidase belongs to the family of human peroxidases together with lacto peroxidase (LPO), myeloperoxidase (MPO) and eosinophil peroxidase (EPO). Its key physiological function is biosynthesis of thyroid hormones. The human TPO gene encodes a 933-amino acid protein with a molecular weight of approximately 100 kDa. (7)

Creatine kinase (CK)is an enzyme that catalyzes the reversible transfer of a high energy phosphate bond from adenosine triphosphate (ATP) to creatine. As a result, it is also referred to as creatine phosphokinase. Is found in high concentrations in skeletal muscles, the heart, the urinary bladder, the intestinal tract, the brain, and the uterus, and in lower concentrations in the lung, liver, kidney, and prostate. It is a dimer composed of two subunits, either M (Muscle) or B (Brain) (Brain). As a result, the three distinct cytosolic isoenzymes formed in the cytosol by various combinations of M (muscle) and B (brain) subunits are CK-MM, CK-MB, and CK-BB. The cardio-specific creatinine kinase isoenzyme

CKMB is widely regarded as the most sensitive and specific indicator of myocardial cell necrosis (8).

Lipid, any of a diverse group of organic compounds that includes fats, oils, hormones, and certain membrane components and is grouped together because they do not interact significantly with water. Triglycerides are a type of lipid that is stored as fat in adipose cells, which serve as an energy storage depot for organisms as well as thermal insulation. Lipid, any of a diverse group of organic compounds that includes fats, oils, hormones, and certain membrane components and is grouped together because they do not interact significantly with water (9).

1.2 Aim of Study:

To study the role of (CK) Creatine Kinase and Thyroid peroxidase (TPO)

And its relation in patients (Hyper and Hypothyroidisim) by the following steps:

1- Determination of Body mass index (B.M.I) in patient and healthy control.

2 - Assessment the CK- MB in studies groups.

3_ Assessment of (TPO) in studies groups

4 _Determination of Lipid profile (Cholesterol, Triglyceride, High density lipoproteins (HDL), Low density lipoproteins (LDL).

5_Study the statistical relationship among the above parameters in studies groups.

Materials and Methods;

All the information has been obtained from all patients by interview .Detailed chemical examination with a special questions formula that filled for all subjects both patients and controls contain :

1- patient name

2-Age

3- Gender

4- Length

5-Weight

6- family history of thyroid gland dieses

7- past medical history

Collection of blood samples ;

Blood samples were drawn from patients and control using a 5-10mL syringe and placed in the gel tube ,after that separated in centrifuged at 3500-4000rpm for 10 min and then emptied .The serum was separated

And placed in the deep freeze in the eppendrof tube at- 20 C until work time .

Results and Discussion

Comparison between difference groups in Hormones level

As the findings in Table (3-2) which showed the results of the levels of hormones (ng/dL) with difference study groups, there was a high significant differences between T3 **(**Figure.3) and T4 (Figure.4) hormone levels with hyperthyroidism patients and the result was (3.232 ±0.27) and (155.95 ±10.47) respectively .While TSH hormone levels (Figure.5) was a highly significant in patients suffering from hypothyroidism (26.25 ±4.70), the P-value of all study groups was (0.0001).

Table (3-2): Statistical distribution of hormones in serum samples of thyroid dysfunction patients and controls.

Group	Mean ± SE		
	T3(ng/dL)	T4 (µg/dL)	TSH (µIU/ml)
Hypo	1.441 ±0.12 b	81.68 ±7.07 b	26.25 ±4.70 a
Hyper	3.232 ±0.27 a	155.95 ±10.47 a	0.164 ±0.08 b
Control	1.830 ±0.12 b	98.93 ±2.77 b	2.164 ±0.23 b
LSD value	0.530 **	20.964 **	7.628 **
P-value	0.0001	0.0001	0.0001
Means having with the different letters in same column differed significantly. ** (P≤0.01).			

Findings of this study is in agreement withBlick et al.,2021 andMathew and Prashanth,2020 who cleared that both T3 and T4 levels are increased and TSH levels tend to decrease due to negative feedback inhibition exerted on the anterior pituitary by T3 and T4 (95,20).

The current study's findings were consistent with those of many others who found an inverse relationship between TSH and thyroid hormones (96) and (97).

Some clinical studies have found that both T3 and TSH levels can decline at the same time, particularly in obese individuals that lose weight (98) and (99). The results of Huber et al., 2002 showed positive effects as a significant increase (P≤0.0001) in thyroid stimulating hormone and Thyroid hormones T4 and T3 in rabbit's serum that drenched 6ml pomegranate juice /Kg body (101).

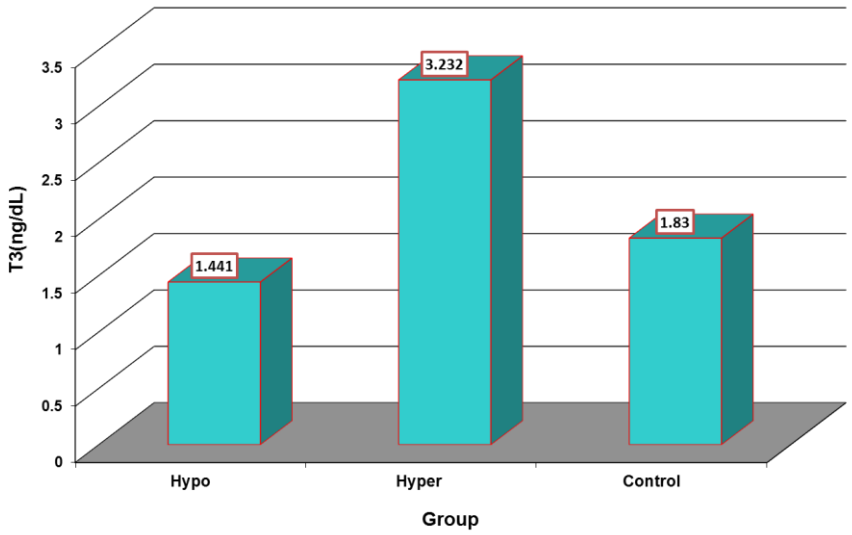

Figure 3. Comparison between difference groups in T3

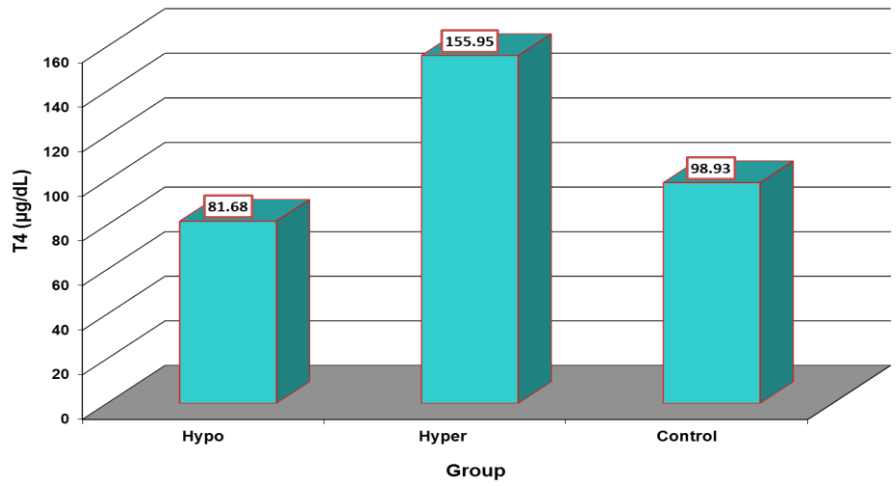

Figure 4. Comparison between difference groups in T4

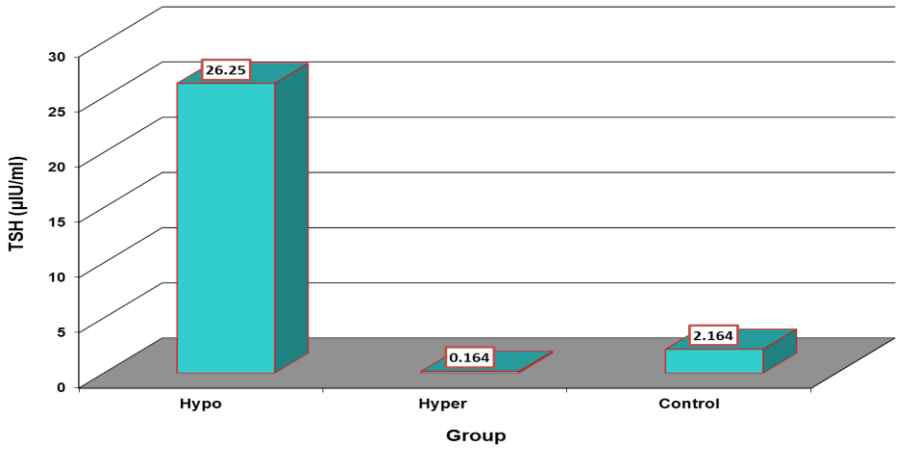

Figure 5. Comparison between difference groups in TSH

Comparison between difference groups in TPO and CK

Thyroperoxidase (TPO) enzyme results showed a high significant differences in present study, the highest results were among control group (12.45 ±0.55) and P-value was (0.0002); (P≤0.01). As it shown in Table (3-3) and (Figure.6).

Creatine kinase (CK) levels that shown in Table (3-3) and (Figure.7) gave no significant differences; but the highest level was among patients with hyperthyroidism (2.386 ±0.18), LSD value was (0.475) and P-value was (0.0497).

Table (3-3): Comparison between difference groups in TPO and CK.

Group	Mean ± SE	
	TPO (ng/dL)	CK (mcg/L)
Hypo	10.14 ±0.17 b	2.305 ±0.17 ab
Hyper	10.73 ±0.34 b	2.386 ±0.18 a
Control	12.45 ±0.55 a	1.834 ±0.15 b
LSD value	1.087 **	0.475
P-value	0.0002	0.0497
Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01).		

Thyroperoxidase (TPO) results of this study which was significatlly high diffrences in control group and gave nealy close results of thyroid dysfunction , agreed with (100) who said that TPO-Ab is found in 5–20% of the general population. TPO-Ab may play a role in the management of subclinical hypothyroidism (101).

Although the previous study confirmed that anti-TPO antibodies are predominately exist in subjects with abnormal TSH, it was difficult to prove a direct relationship between serum levels of these biological markers (102).

A study done bySiriwardhane et al.,2019 got the results 73% of hypothyroid subjects and 68.6% of hyperthyroid subjects had anti-TPO 252 (±33) and 277 (±151) days prior to the onset of the thyroid dysfunction, respectively (103). Both subclinical/overt hypothyroidism and hyperthyroidism showed a significantly higher percentage of subjects who had anti-TPO prior to the onset of thyroid dysfunction compared to the combined control group.

Other study done by Fadhil et al.,2019 said there is no significant differences have been found between hypothyroid and hyperthyroid patients in the level of Anti-TPO (104).

The increasing of autoantibodies that increased the likelihood of patients having an autoimmune disease (Graves' disease and Hashimoto's Thyroiditis) because patients produced high levels of thyroid autoantibody and had lymphoid tissue that resembled secondary lymphoid follicles (105).

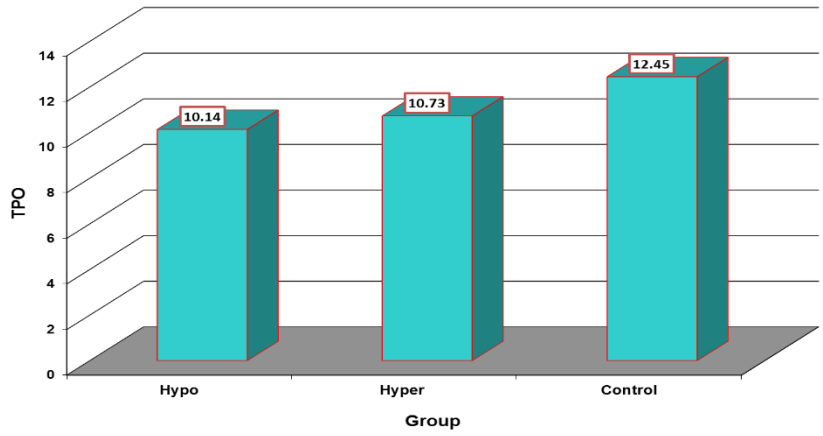

Figure 6. Comparison between difference groups in TPO

Serum creatine kinase levels in present studty agreed with Mavaiet al.,2018 who said there is no significant differences were observed in CK levels among the three groups (hypothyroidsm, hyperthyroidsm and control group) (106).

A study done by Baqir et al.,2003 said that the creatine kinase activity in patients with hypothyroidism was on the average significantly higher than controls ($p<0.005$). In hyperthyroid patients, although the serum activity of creatine kinase was significantly lower as compared with controls, however, it is within the normal range (107).

Other studies observed significantly differences higher creatine kinase activity in hypothyroid patients than controls (108), (109) and (110).

Increased CK levels in the blood indicate muscle damage because muscle breakdown releases its contents into the blood. Others have found elevated CK levels in thyroid dysfunction patients (111).

The creatine kinase activity, according to a study ofGiampietro et al.,1984 , said that CK is one of the best indications of hypothyroid myopathy. Because it is sensitive for early diagnosis of muscle involvement owing to metabolic illnesses and is closely related to the patients' metabolic problems. Several theories have been proposed as probable causes for the increased activity of creatine kinase in hypothyroidism. Increased membrane permeability in relation to fluctuations in high energy phosphate levels, increased muscle bulk, and reduced clearance were indicated as the most likely causes by some, while others suggested that the cause has not been determined (112).

The serum creatine kinase activity in hyperthyroidism tends to be towards the lower end of the reference interval. Muscle wasting has been blamed for the reduced level of creatine kinase activity in hyperthyroidism, rather than a direct inhibitory action of thyroid hormones on the enzyme..Hypothyroidism can produce considerable increases in creatine kinase activity, according to the findings.Because hypothyroidism can cause symptoms that resemble cardiovascular disease (113).

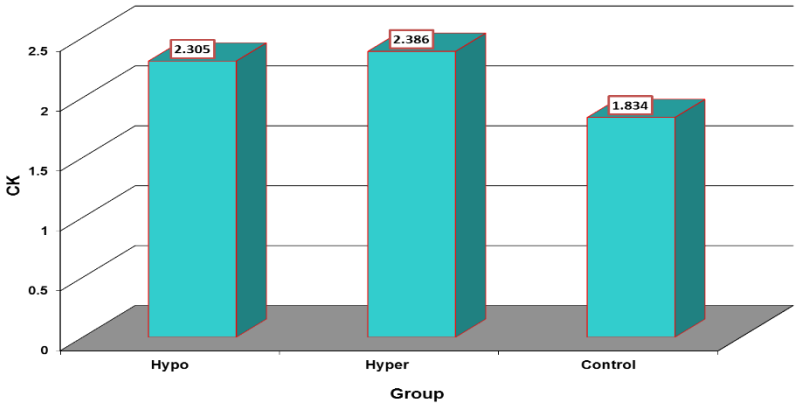

Figure 7. Comparison between difference groups in CK

Comparison between difference groups in Lipid profile

The findings of lipid profile analysis presented in Table (3-4). Cholesterol showed a high significant differences with hypothyroidism patients (169.74 ±5.19), and P-value (0.0001). **(**Figure .8) showed the results.

Triglyceride also showed a high significant differences in both study groups (hyperthyroidism and hypothyroidism) with (140.08 ±14.45 a for hypothyroidism patients) and (134.91 ±11.80 for hypothyroidism patients) and P-value was (0.0030). (Figure.9) shown the results of TG and study groups.

High density lipoprotein was non-significant. But the highest level was in hypothyroidism patients. (Figure .10) showed the results, P-value was (0.108). Low density lipoprotein gave a high significant differences results, the highest level was among control group (119.47 ±5.27), P-value (0.0027) as shown in (Figure .11**)** which showed the levels.

Very low density lipoprotein in current study findings showed a high significant differences, the highest level was among both groups of patients. (28.02 ±2.89) for hyperthyroidism and (26.98 ±2.36), and P-value was (0.0030).

Table (3-4) : Comparison between difference groups in Lipid profile.

Group	Mean ± SE (mg/dl)				
	Cholesterol	Triglyceride	HDL	LDL	VLDL
Hypo	169.74 ±5.19 a	140.08 ±14.45 a	45.61 ±1.58	102.48 ±4.63 b	28.02 ±2.89 a
Hyper	150.17 ±5.72 b	134.91 ±11.80 a	41.57 ±1.66	94.25 ±5.47 b	26.98 ±2.36 a
Control	115.93 ±3.90 c	90.32 ±4.20 b	45.37 ±1.24	119.47 ±5.27 a	18.06 ±0.84 b
LSD value	14.03 **	30.98 **	4.225 NS	14.411 **	6.197 **
P-value	0.0001	0.0030	0.108	0.0027	0.0030
Means having with the different letters in same column differed significantly. ** (P≤0.01).					

As the results of currentstudy found that there is a statistical association between lipid profile as well as thyroid disease , this finding is in agreement with Al-Sharifia and Satar,2021 results showed significant increase in cholesterol, triglyceride and LDL-cholesterol in patients compared with control group(114).

Although hypothyroidism has long been linked to hypercholesterolemia, the link between subclinical hypothyroidism and hypercholesterolemia remains controversial. All lipid profile measures, including TC, HDL, LDL, and TG, were shown to be raised in subclinical hypothyroidism in this investigation, and the difference was statistically significant (115).

Studies ofKanaya et al.,2002 andAsvold et al.,2007 have demonstrated that lower thyroid function can be a risk factor for a worse lipid profile in elderly patients(116 and 68).

The 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase, which is the initial step in cholesterol production, is induced by thyroid hormones. Furthermore, triiodothyronine (T3) controls the activation of LDL receptor genes, which upregulates LDL receptors. The direct binding of T3 to certain thyroid hormone responsive elements (TREs) causes T3-mediated gene activation .T3 also affects the gene expression of the LDL receptor through the sterol regulatory element-binding protein-2 (SREBP-2) . T3 has also been linked to the protection of LDL against oxidation (71).

Thyroid hormones can affect HDL metabolism by increasing the activity of the cholesteryl ester transfer protein (CETP), which transfers cholesteryl esters from HDL2 to VLDL and TGs in the opposite way (8). Thyroid hormones also activate the enzymes lipoprotein lipase (LPL), which catabolizes TG-rich lipoproteins, and hepatic lipase (HL), which hydrolyzes HDL2 to HDL3 and contributes to the conversion of intermediate-density lipoproteins (IDL) to LDL, and then LDL to small dense LDL (sdLDL) . T3 also increases the expression of apolipoprotein AV (ApoAV), which is important for TG control (73).

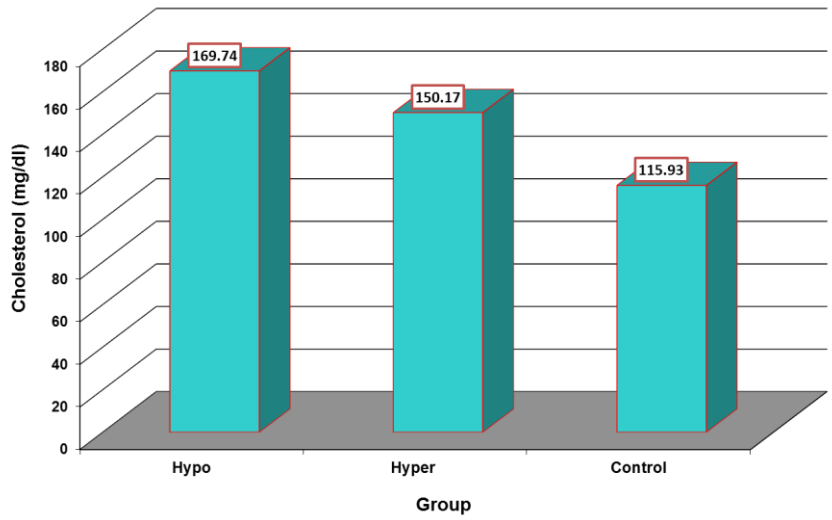

Figure 8. Comparison between difference groups in Cholesterol

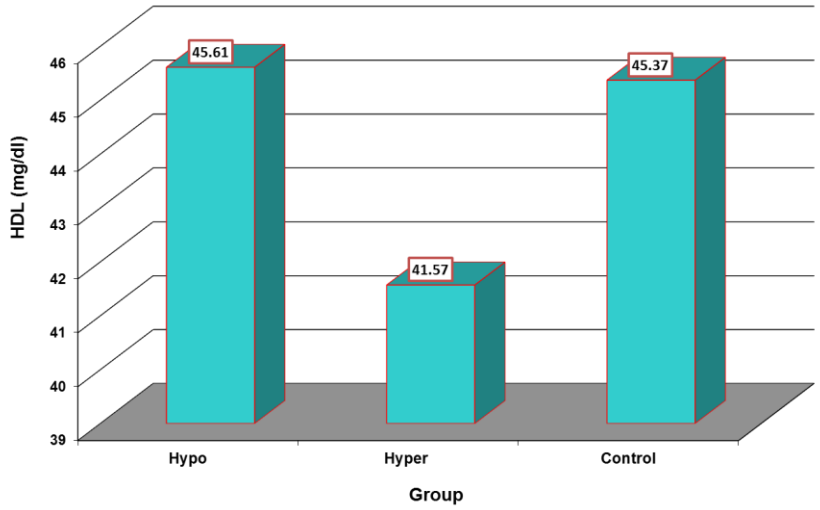

Figure 10: Comparison between difference groups in HDL

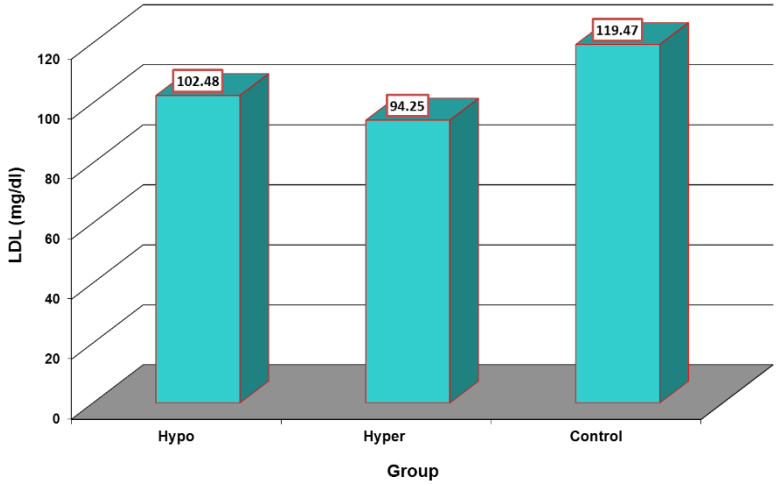

Figure 11: Comparison between difference groups in LDL

Conclusions:

From the present study, we concluded the followings:

1- Decrease in activity of Creatine kinase in sera in patients with hyperthyroidism while raise in activity in sera with thyroid patients with hypothyroidism contrast to control group.

2- A Height of a sample in the range of Cholesterol in both hypo and hyperthyroidism contrast to control group.

3- Keeping values of Triglycerides in normal in both patients hypo and hyperthyroidism contrast to control group.

4- The very low density lipoprotein(VLDL,HDL) levels were remains within normal values for the three groups

5- The LDL (low density lipoprotein) was found to be higher in all groups.
6- TPO were highly significant in in both hypo and hyperthyroidism contrast to control group.

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