

Contents lists available at BioMedSciDirect Publications

International Journal of Biological & Medical Research

Journal homepage: www.biomedscidirect.com



Original article

COMPARATIVE STUDY OF LIPID PROFILE IN HYPOTHYROIDISM, HYPOTHYROID PATIENTS TAKING TREATMENT FOR MORE THAN 5 YEARS AND CONTROL GROUP.

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ARTICLEINFO

Kevwords: Cholesterol HDL-C Hypothyroidism LDL-C Triglycerides

ABSTRACT

Objective: Hypothyroidism the most common functional disorder of the thyroid gland characterised by a cluster of clinical manifestations resulting from deficiency of thyroid hormones. 01% to 10% of the global population has some evidence of abnormally low thyroid hormones. Present study was undertaken to compare lipid profile in newly diagnosed hypothyroid subjects and hypothyroid subjects who were already receiving treatment for more than 5 years and to find out if there was any improvement in these parameters with thyroxine supplementation therapy. STUDY DESIGN: Cross-sectional case-control study. STUDY SAMPLE: 90 adults (Males & Females) of age group more than 30 years, divided into three equal groups of 30 subjects (28 female and 2 males) each belonging to the same socioeconomic status. Exclusion criteria: Individual with diabetes, hypertension cardiovascular, pulmonary, renal or liver diseases, pregnancy, other endocrine and dyslipidaemic disorders. Statistics applied: Statistically significant variation in three Groups determined by one way ANNOVA test and multiple comparisons between Group I vs. Group II, Group I vs. Group III, and Group II vs. Group III done by Tukey test. Results: It was found that mean value of serum Total cholesterol, Triglycerides, LDL-C, VLDL-C was significantly increased in Group II as compared to Group I and the mean value of serum HDL-C was decreased in Group II as compared to Group I. There were no significant difference found in serum Total cholesterol, Triglycerides, HDL-C, LDC-C and VLDL-C in Group I and group III. Serum Total cholesterol, Triglycerides, LDL-C, VLDL-C were significantly low in Group III as in comparison with Group II and the mean value of HDL-C was significantly high in Group III as compared with Group II.

Conclusions: Thyroid hormones have significant effect on synthesis, mobilization and metabolism of lipids. Substitution therapy with levo-thyroxine significantly improves lipid metabolism abnormalities.

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1. Introduction

Lymphatic filariasis (LF) is a globally distributed disease recognized by the World Health Organization (WHO) as one of the most disabling diseases [1]. LF caused by Wuchereria (W.) bancrofti and Brugia (B.) malayi is a major public health and socioeconomic problem in tropical and subtropical countries include central Africa, the Nile delta [2, 3]. An estimated 120 million people in 73 countries are infected with LF, and an estimated 1.4 billion live in areas where the disease is endemic [4, 5]. A series of studies revealed that incidence of microfilaria (mf), increased in different governorates in Egypt [6]. Approximately

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The Indian Thyroid society (ITS) has identified thyroid disorders as the 'Next Diabetes'. Hypothyroidism is the most prevalent disorder affecting one in every eight women, women being five to eight times more susceptible to the disease [1].

The thyroid gland is one of the larger endocrine glands secretes the thyroid hormones, which maintains the level of metabolism in the tissues that is optimal for their normal function. Thyroid hormones stimulate O2 consumption by most of the cells in the body, helps to regulate lipid and carbohydrate metabolism.

The most common functional disorder of the thyroid gland is hypothyroidism. Hypothyroidism is a cluster of clinical manifestations resulting from thyroid hormone deficiency or more rarely, from their impaired activity at tissue level [2].

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Consequences of thyroid gland dysfunction depend on the life stage at which they occur. Absence or hypo-function of thyroid gland during foetal and neonatal life results in severe mental retardation and dwarfism. In adults, hypothyroidism is accompanied by mental and physical slowing and poor resistance to cold [3].

It is observed that between 01% and 10% of the global population has some evidence of abnormally low thyroid hormones. Mild thyroid failure occurs eventually in 04% to 21% of women and 03% to 16% of men, with the risk increasing with age. Women In all age groups have a higher risk than men. For example, one out of every 4,000 infants is born with congenital hypothyroidism; female infants are at higher risk than males [4]. Thyroid Problems are on the rise among Indians: Over 4.2 crores of people in the country are estimated to suffer from such disorders making it increasingly important for people to pay attention to this often overlooked health problem [5]. The prevalence of hypothyroidism as evident by demographic studies in India, shows a considerable figure of 3.9% overall, with higher fraction in women than men [6].

Thyroid hormones have significant effects on synthesis, mobilization and metabolism of lipids. Hypothyroidism is associated with significant increase in circulating concentrations of total LDL-Cholesterol leading to coronary artery disease. Hypercholesterolemia is due to the hormone deficit and to the decreased activity of lipoprotein lipase [7].

Aims and Objectives

- 1) To study lipid profile in newly diagnosed hypothyroid patients, hypothyroid patients taking treatment for more than 5 years and control group.
- 2) To compare the effect of levothyroxine therapy on lipid profile and metabolism in newly diagnosed hypothyroid patients, patients who were already getting treatment for more than 5 years with that of euthyroid control group.

$Materials\, and\, Methods$

The present study was carried out in the department of Physiology in collaboration with Medicine and Biochemistry department of Indira Gandhi Govt. Medical College and Mayo Hospital, Nagpur during the period from February 2013 to October 2014.

The study protocol was approved by the Institutional Ethics Committee and informed written consent was obtained from all the study subjects enrolled in the study.

METHODOLOGY:

The present study is cross-sectional case-control study.

Definition and Selection of Study Subjects:

Sample size of 90 Adults (Males & Females) having age more than 30 years were divided into three equal groups of 30 subjects each.

Group I: Euthyroid subjects (Control group)

Group II : Newly diagnosed and untreated hypothyroid patients.

Group III: Hypothyroid patients taking synthetic thyroid hormone for more than 5 years.

Group I: This group of 30 subjects (28 females and 2 males) were selected randomly from healthy volunteers from general population. These subjects were not having any known or diagnosed illness and their thyroid profiles were within normal range.

Group II: This group included 30 (28 female and 2 males) patients recently diagnosed as having hypothyroidism (either raised TSH above normal with total T4 and T3 within normal range or raised TSH with below normal total T4 and T3) and were not started with hormone replacement therapy.

Group III: This group included 30 (28 females and 2 males) hypothyroid patients who were already taking synthetic thyroid hormone replacement therapy for more than 5 years.

All the study subjects were selected from the outpatient department of Indira Gandhi Government Medical College and Mayo Hospital, Nagpur which were having same socio-economic status. While those patients having diabetes, hypertension cardiovascular, pulmonary, renal or liver diseases, pregnancy, dyslipidaemic and other endocrine disorders were strictly excluded from the study.

PROCEDURE:

Before starting the study work all participants were given detailed information about the study and every effort was taken to solve their queries. This was an attempt to establish a good rapport with the participants and relieve their anxiety.

After taking detailed history with set of screening questions referring to the principal sign and symptoms of thyroid disease thorough general and systemic examination were done and recorded in Case Report form.

BLOOD INVESTIGATIONS:

About 5ml of blood sample was collected from each subject in early morning after strict 12 hours of fasting. Venous blood sample was withdrawn from the ante-cubital vein of each participant after taking all aseptic precautions using sterile needles and syringes without the aid of a tourniquet. Haemolysed samples were excluded from the study. The blood samples were immediately transferred to a clean dry sterile plain bulb. It was allowed to coagulate for 30 minutes and centrifuged to separate the serum. Serum thyroid and lipid profile were analyzed from the blood sample collected.

LIPID PROFILE ESTIMATION: [8].

Equipments and facility for lipid profile analysis:

TRANSASIA ERBA CHEM-5 PLUS Semi-Automatic Analyzer:

- 1). Estimation of serum cholesterol (Enzymatic method-Cholesterol esterase Oxidase and Peroxidase-End point):
 - 2) Estimation of serum triglycerides:

(Glycerol phosphate oxidase and peroxidase; End point method)

- 3) Estimation of serum high density lipoprotein cholesterol: (Precipitation method- End point):
- 4) Estimation of low density lipoprotein cholesterol (LDL-cholesterol) and very low density lipoprotein cholesterol (VLDL-cholesterol): (Indirect Method-Friedewald Equation)

STATISTICAL METHODS:

Statistically significant variation in three Groups determined by one way ANNOVA test and multiple comparisons between Group I vs. Group II, Group I vs. Group III, and Group II vs. Group III done by Tukey test.

The software used in the analysis was SPSS 17.0 and Graph Pad Prism 5.0 version. Significant level was set as p > 0.05 was no significant, p < 0.05 as significant, p < 0.01 as highly significant and p < 0.001 as very highly significant.

Observations and Results

In the present study it was found that mean values of serum Total cholesterol, triglycerides, LDL-C, VLDL-C were significantly increased in Group II as compared to Group I and the mean value of serum HDL-C was decreased in Group II as compared to Group I. There were no significant difference found in serum Total cholesterol, triglycerides, HDL-C, LDL-C and VLDL-C in Group I and group III. From the table no 2 it was observed that values of serum total cholesterol, triglycerides, LDL-C, VLDL-C were significantly low in Group III as in comparison with Group II and the mean value of HDL-C was significantly high in Group III as compared with Group II.

Table 1: Lipid profile in three groups

Lipid Profile	Group I	Group II	Group III	F- value	p-value
TC (mg/dl)	182.06±12.11	210.56±13.75	181.43±10.63	55.48	0.006 **
TG (mg/dl)	98.76±7.20	158.56±14.94	100.70±6.79	323.40	0.0006***
HDL-C (mg/dl)	48.66±5.31	37.73±5.23	48.73±3.30	54.26	0.0007***
LDL-C (mg/dl)	113.64±12.98	141.12±14.19	112.56±11.65	46.60	0.0008***
VLDL-C (mg/dl)	19.75±1.44	31.71±2.98	20.14±1.35	323.40	0.0006***

^{*} p<0.05 significant, **p<0.01 highly significant, ***p<0.001very highly significant, p>0.05 non significant.

Table 2: Multiple Comparison of lipid profile: Tukey Test

Lipid Profile	Group		Mean Difference	Std. Error	p-value	95% Confidence Interval
(mg/dl)	Group I	Group II	-28.50	3.15	0.003 **	-36.03 - 20.96
		Group III	0.63	3.15	0.978	-6.89 - 8.16
	Group II	Group III	29.13	3.15	0.004 **	21.60 - 36.66
TG (mg/dl)	Group I	Group II	-59.80	2.67	0.000 ***	-66.17 - 53.42
		Group III	-1.93	2.67	0.750	-8.30 - 4.43
	Group II	Group III	57.86	2.67	0.000 ***	51.49 - 64.23
(mg/dl)	Group I	Group II	10.93	1.21	0.007 **	8.03 - 13.83
		Group III	-0.06	1.21	0.998	-2.96 - 2.83
	Group II	Group III	-11.00	1.21	0.005 **	-13.89 - 8.10

(mg/dl)	Group I	Group II	-27.47	3.35	0.000 ***	-35.46 - 19.47
		Group III	1.08	3.35	0.944	-6.90 - 9.08
	Group II	Group III	28.56	3.35	0.000 ***	20.56 - 36.55
(mg/dl)	Group I	Group II	-11.96	0.53	0.000 ***	-13.2310.68
		Group III	-0.38	0.53	0.750	-1.66- 0.88
	Group II	Group III	11.57	0.53	0.000 ***	10.29-12.84

a) *p<0.05 significant, **p<0.01 highly significant, ***p<0.001 very highly significant,

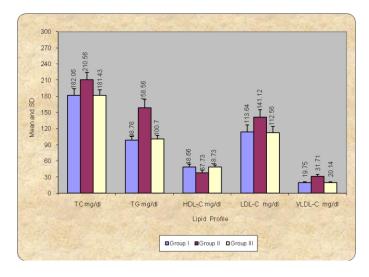
p>0.05 non significant.

b) Group I –Controls (Euthyroids), Group II – Newly diagnosed untreated hypothyroid

patients, Group III – Hypothyroid patients taking treatment for > 5 yrs.

c) TC- Total cholesterol, TG- Triglycerides, HDL-C High density lipoproteins cholesterol, LDL-C low density lipoproteins cholesterol, VLDL-C Very low density lipoprotein cholesterol.

Figure 1: Lipid profile in three groups



Discussion

Hypothyroidism is associated with dyslipidemia which is reversible with timely and regular levothyroxine therapy. Study was undertaken to evaluate whether there is effect of hypothyroidism on lipid profile and also see these changes in group III subjects who were already on levothyroxine therapy.

In the present study we found that mean value of serum TC, TG, LDL-C, VLDL-C were significantly high and HDL-C was significantly low in Group II as compared to Group I. Findings of our study were in agreement with Poyrazoglu O K et al [10], Shekhar R et al [11], Kumar A N et al [12] in which hypothyroid patients showed increased TC and LDL-C. Mittal A. et al [13] found increased mean concentration of TC and TG in hypothyroids was in accordance with our findings. Krishnaveni D V et al [14] observed significant increase in mean levels of TC,TG,LDL-C in agreement with our study but they found no

significant decrease of HDL-c which does not match with our findings, we found decreased level of HDL-c in our study may be due to increased CETP(cholesterol ester transport protein) activity in hypothyroids. Our study compares well with the studies of Sunanda V et al [7], Khan MAH et al [15], Shanmugapriya V [16], Shilpashree M K et al [17] and Tayal D et a l[18] in which hypothyroids showed increased level of TC, TG, LDL-C, VLDL-C and decreased HDL-C.

Significantly decreased values of TC, TG, LDL-C, VLDL-C and increased HDL-C were observed in Group III as compared to Group II. These findings were in accordance with Saxena A et al [19] who observed increased TC, TG, LDL-C and decreased HDL-C levels in hypothyroid patients and significant decrease in TC, TG, LDL-C levels and increased HDL-C level after levothyroxine treatment and in agreement with Poyrazoglu OK et al[10] , Shekhar R et al[11] , Kumar AN et al[12] as they also observed increased TC and LDL-C in hypothyroid patients which show decreased levels after levothyroxine therapy while no significant difference was found in values of above lipid parameters in Group Iand Group III in the present study.

Substitution therapy with levo-thyroxine significantly improves lipid metabolism abnormalities. A period of 4-6 weeks is usually needed to correct dyslipidaemia. The changes in serum lipoproteins are correlated with changes in free T4. [20].

Summary and Conclusions

- 1) Increased values of TC, TG, LDL-C, VLDL-C and decreased value of HDL-C was found in Group II as compared to group I.
- 2) Decreased values of TC, TG, LDL-C, VLDL-C and increased value of HDL-C was found in Group III as compared to Group II. Showing the effect of treatment they were getting.

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