

Lipid Profile in 'Newly Diagnosed' and 'On Treatment' Hypothyroid

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ABSTRACT

Introduction: Primary hypothyroidism is a common disorder affecting a large group of population and is a cause of the secondary hyperlipidemia. The aim of the present study was to assess the relation between the lipid profile and thyroid profile in newly diagnosed hypothyroid, subjects on treatment for hypothyroidism and controls.

Materials and Methods: The present study was performed on 150 subjects of both sexes between 11–78 years of age. The subjects were divided into three groups. First group was Controls (n = 50), second group was 'Newly Diagnosed' hypothyroid (n = 50) and the third group was hypothyroid patients

'On Treatment' (n = 50). T₃, T₄, TSH, Total Cholesterol, High Density Lipoproteins (HDL), Low Density Lipoproteins (LDL) and Triglycerides were estimated.

Results: ANOVA was calculated among the three groups. TSH, Total Cholesterol and LDL levels were decreased in "On treatment" group when compared to "Newly diagnosed" group. T₄ was found to be elevated, but T₃ remained low in "On treatment" group.

Conclusion: Cholesterol and LDL levels are elevated in hypothyroidism and their levels decreases with treatment but not to the level of euthyroid state.

Key Words: Hypothyroidism, Hypercholesterolemia, LDL

INTRODUCTION

Thyroid dysfunction is relatively a common disease which affects people, irrespective of their age and gender. Hypothyroidism is a clinical syndrome which is caused due to the deficiency of thyroid hormones, resulting in a generalized slowing down of the metabolic process. The incidence of hypothyroidism varies, depending on geographical and the environmental factors such as dietary iodide, goitrogen intake, the genetic characteristic of the population and the age distribution of the population. Hypothyroidism affects the cardiovascular, pulmonary, renal, neuromuscular, nervous and the reproductive systems. A majority of the cardiovascular signs and symptoms are associated with a derangement in the lipid metabolism [1]. Thyroid hormones stimulate the utilization of the lipid substrates, owing to an increased mobilization of the triglycerides which are stored in the adipose tissue [2]. Hypothyroidism is associated with dyslipidaemia, thus contributing to the development of atherosclerosis. Its signs and symptoms are reversible on treatment with levothyroxine (T₄). The aim of the present study was to identify the relationship between the thyroid profile and the total cholesterol and the low density lipoprotein (LDL) levels among newly diagnosed hypothyroid subjects who were on treatment for hypothyroidism and in the controls.

MATERIALS AND METHODS

This cross sectional study was performed on 150 subjects, whose ages ranged from 11 to 78 years, who attended the NRI General Hospital, Chinakakani, in the Guntur district. The study was performed after getting approval from the institutional ethics committee. Informed consent was taken from all the individuals who were included into the study groups.

The inclusion criteria was subjects attending the hospital with complaints of weight gain, muscle cramps, thyroid swelling, generalized

weakness and easy fatigability, primary infertility and menorrhagia. The exclusion criteria was subjects with coronary heart disease, acute illness, pregnancy or disorders which affected the lipid metabolism (diabetes mellitus, renal failure or pancreatitis).

The subjects were categorized into three groups. The subjects without any disease and those who were not on any medication were taken as the controls. The subjects with symptoms and investigations which were suggestive of hypothyroidism and those who were not on any medication were considered as the 'newly diagnosed hypothyroid' group. The subjects who were on medication for hypothyroidism without any complications were taken as the 'on treatment' group.

Venous blood samples were drawn after 12 hrs of overnight fasting. The blood samples were allowed to clot and they were centrifuged by using a Remi centrifuge (R-8C) to separate the serum. The serum which was obtained was divided into two parts. The first part was analyzed on immuno-analyzer Centaur CP by using an analyzer specific kit from Siemens for Triiodothyronine (T₃), Thyroxine(T₄)and Thyroid Stimulating Hormone(TSH) by the chemiluminescence method. The normal reference range of T₃, T₄ and TSH is from 0.6 to 1.81 ng/ml, 4.5 to 10.9 µg/dl and 0.35 to 5.5 µg/ml respectively.

The second part of the serum was estimated on chemistry analyzer Dade Behring Dimensions Rx Max by using the Siemens Kit for total cholesterol, triglycerides and HDL cholesterol. LDL cholesterol was calculated by using Friedewald's formula. The lipid concentration was considered to be altered when the total cholesterol was ≥ 200 mg/dl, the triglycerides were ≥ 150 mg/dl, HDL cholesterol was ≤ 35 mg/dl and LDL cholesterol was ≥ 130 mg/dl.

$$LDL = TC - (HDL + TG/5)$$

Parameter	Controls	Newly Diagnosed	On Treatment	F (df)	p
T ₃	1.16±0.34	0.96±0.46	0.98±0.35	3.88 (2,147)	<0.05
T ₄	8.48 ± 1.52	6.19±2.84	8.98±3.58	14.24 (2,147)	<0.001
TSH	2.63±1.15	22.41±30.07	3.68±3.55	20.22 (2,147)	<0.001
Total Cholesterol	139.02±22.59	233.8±32.96	163.24±34.73	129.7 (2,147)	<0.001
LDL	84.2±18.14	152.04±34.32	94.56±34.20	74.83 (2,147)	<0.001
Age	45.32±14.72	49.34±13.7	44.6±14.65	1.58 (2,147)	<0.05

[Table/Fig 1]: ANOVA among Control, Newly Diagnosed and On Treatment group

The Bio-Rad internal and external quality control was performed to confirm the accuracy of the values which were obtained. The values were reconfirmed by a repetitive assessment of the study samples.

RESULTS

One hundred and fifty subjects within the age group of 11-78 years were included in the study, which comprised of 75 males and 75 females. The data which was obtained was analyzed statistically by using the Analysis of Variance (ANOVA) [Table/Fig-1].

The total T₃ levels were found to be low in subjects who were on treatment with levothyroxine than in the controls. The 'on treatment' group had increased total T₄ levels which were found to be higher than those in the control group. TSH was found to be normalized with replacement therapy, which was very high in the 'newly diagnosed' group. The cholesterol and LDL levels remained higher than those in the control group even after the treatment.

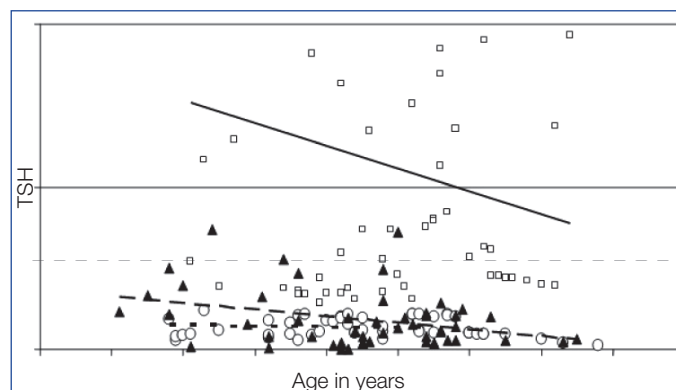
The TSH levels were found to decrease with increasing age [Table/Fig-2].

DISCUSSION

The thyroid hormone influences the metabolism of cholesterol and the triglycerides. The degradation of cholesterol is caused due to an increase in the hepatic LDL and in the number of receptors and an accelerated LDL clearance. Consequently, the total cholesterol and LDL levels are elevated in patients with hypothyroidism. The increase in LDL results in a decreased conversion of cholesterol to the bile acids and the down-regulation of the LDL receptor. Increased levels of very low density lipoprotein (VLDL) and chylomicrons are present due to the decreased activity of lipoprotein lipase, resulting in a decreased clearance of triglyceride rich lipoprotein, thus reflecting the decreased activity of hepatic lipase.

T₃ is formed from T₄ by peripheral deiodination in tissues outside the thyroid gland, particularly the liver, kidney and the skeletal muscle. Only a fraction of T₃ gets diffused outside the cell. Thus, the T₃ levels may be low in spite of the replacement therapy, as was observed in the present study.

A small fraction of T₄ is bound to the plasma lipoproteins. The T₄-LDL complex is recognized by the LDL receptor and this interaction provides an additional mode of T₄ entry into the cells. Thus, the lipoprotein bound T₄ could be involved in protecting LDL from oxidation. Vidya et al (1997) reported that the LDL is more susceptible to oxidation in hypothyroidism and that it is resistant to oxidation in euthyroidism. The risk for atherosclerosis in hypothyroidism is thought to be due to elevated cholesterol levels [3]. In a number of studies, total cholesterol and LDL were found to be elevated in hypothyroidism as compared to the controls and to be decreased after thyroxine substitution [4], which was similar to the findings of the present study. Hypercholesterolaemic subjects have high concentrations of LDL due to decreased LDL cellular receptor numbers and the consequently reduced removal of



[Table/Fig-2]: Correlation of age and TSH among Control (CONT), Newly diagnosed (ND) and On treatment (OT) group

LDL from plasma. The high levels of LDL cholesterol with increased age could contribute to the enhanced oxidizability of these particles [5]. Some studies have confirmed the presence of an inverse relationship between thyroxine and cholesterol. The increase in LDL and VLDL seems to depend on a decrease in the oxidative capacity of the fatty acids, which is reflected in a reduction of their catabolism [6].

Substitution therapy with levothyroxine improves the lipid metabolism. The lowering of total cholesterol and LDL cholesterol is observed, as there is an up-regulation of the LDL receptors, which results in the enhanced catabolism of the LDL particles. The HDL cholesterol levels also tend to decrease because levothyroxine stimulates the cholesterol ester transfer protein (CETP). Thyroid replacement also stimulates the hepatic lipase and the lipoprotein lipase (LPL). It inhibits LDL oxidation [7]. Substitution therapy restores euthyroidism and improves the lipid levels, thus preventing atherosclerosis [8].

In older people who are free from the thyroid disease, the thyroid function remains relatively normal, because the thyroidal uptake of iodine is decreased. Hence, the daily production of T₃ and T₄ also decreases. This change appears to be concomitant with a decreased rate of T₃ degradation. Thus, the overall concentrations of T₃ and T₄ do not appear to change with age. The TSH levels are lowered as age advances. But, the prevalence of the thyroidal disease increases with age [9, 10]. A similar effect was observed in the present study. Hypothyroidism in the elderly is often atypical and it lacks the classical symptoms which are seen in the younger patients. The treatment requires thyroid hormone replacement, but the elderly hypothyroids require a lower dose [11].

CONCLUSION

All the subjects who were on replacement therapy had decreased total cholesterol and LDL levels, but the levels were not normalized. This suggests that T₄ replacement does not make the subject euthyroid. The T₃ replacement therapy, in combination with T₄ replacement, can be tried for better results.

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