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Research Article

Lipid profile alterations and fasting blood glucose levels in primary hypothyroidism

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ABSTRACT

Background: Hypothyroidism has become a highly prevalent condition worldwide as well as in India. Females are affected more than men and dyslipidemia has been associated with hypothyroidism. This study was conducted to study the prevalence and pattern of dyslipidemia in hypothyroid patients and to justify the screening of lipid profile in hypothyroid patients.
Methods: This was a case control study which included 50 newly diagnosed and untreated hypothyroid patients and 50 healthy individuals in the age group of 20-40years. Free Triiodothyronine (FT3), free thyroxine (FT4), Thyroid Stimulating Hormone (TSH) were estimated by chemiluminiscence immunoassay. Serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), blood glucose were done in all the subjects by enzymatic colorimetric method. Low density lipoprotein cholesterol (LDL-C) was calculated using Friedwalds formula. Very Low density lipoprotein cholesterol (VLDL-C) was calculated from the triglyceride value.
Results: Lipid profile alterations were seen in hypothyroid patients. The mean (standard deviation)values of Total cholesterol, high density lipoprotein cholesterol (HDL-C), Low density lipoprotein cholesterol (LDL-C), Very Low density lipoprotein cholesterol (VLDL-C), triglycerides (TG), Fasting blood glucose were 183.7 (32.9), 38.12 (7.59), 104.4 (29.42), 31.66 (13.09), 158.44 (65.61), 95.9(9.9) mg/dl respectively. The statistical analysis showed that the difference in the above values between cases and controls was significant and all the mean values except HDL-C were increased in cases.
Conclusions: Hypothyroid patients demonstrate significant increase in serum lipids as compared to healthy individuals. More females are diagnosed with hypothyroidism and dyslipidemia is associated with primary hypothyroidism.

Keywords: Hypothyroidism, Dyslipidemia, TSH, Cholesterol, Fasting blood sugar

INTRODUCTION

Hypothyroidism is defined as a deficiency of thyroid activity, which results from reduced secretion of both T3 and T4 irrespective of the cause.[1] It is the most common pathologic hormone deficiency among the endocrine disorders. Hypothyroidism may be due to primary disease of the thyroid gland itself or lack of pituitary TSH.[2] Biochemically decrease in T4 and T3 concentrations lead to hypersecretion of pituitary TSH and an amplified increase in serum TSH levels. This is a key laboratory finding, particularly in the early detection of primary hypothyroidism. Auto immune etiology has been suggested as the most common cause for primary hypothyroidism.

Clinically hypothyroidism may present with variety of symptoms and signs involving major systems of the body like endocrine, cardio vascular, central nervous system, musculoskeletal, haematological, reproductive, gastrointestinal and dermatological.[3] There is a broad clinical spectrum ranging from an overt end organ failure to an asymptomatic or sub clinical condition with normal levels of T3 and T4 and mildly elevated levels of TSH.

Thyroid hormones have significant effects on synthesis, mobilization and metabolism of lipids. Overt hypothyroidism is associated with significant increase in circulating concentrations of total LDL-Cholesterol leading to coronary artery disease. Hypercholesterolemia is favoured due to the hormone deficit and to the decreased activity of lipoprotein lipase.[4,5] Dyslipidaemia is a well-recognized association of hypothyroidism and typically consists of raised levels of total cholesterol, apolipoprotein B, triglycerides, low density lipoprotein (LDL) cholesterol, and reduced levels of high density lipoprotein (HDL) cholesterol. Hypothyroidism particularly is associated with dyslipidemia which increases the risk of hypertension, endothelial dysfunction, and cardiovascular diseases.[6]

Early recognition and treatment of dyslipidemia in patients with hypothyroidism will attenuate cardiovascular risk and improve general wellbeing. The study was undertaken to estimate the relationship between serum lipids and hypothyroid status.

METHODS

This was a case control study conducted over a period of one year. The study included patients attending Medical Endocrinology OPD at Narayana General Hospital, Nellore. The study included a total of 50 hypothyroid subjects. All of them were in the age group of 20-40 years. Both males and females included. Oral consent was taken from all the individuals. 50 healthy individuals in the age group of 20-40 years were included in control group.

Subjects in the age group of 20 to 40 years, newly diagnosed and untreated cases of hypothyroidism were included in the case group.

Subjects having diabetes mellitus, PCOD, tuberculosis, other systemic illness, liver disorders, renal disorders, congestive cardiac failure, those taking oral contraceptive pills, statins and other medications that alter thyroid functions and lipid levels, pregnant and menopausal women, known cases of overt hypothyroidism or hyperthyroidism were excluded from the study.

Sample collection and analysis: The name, age and sex of the subjects were noted and about 5ml of venous blood sample was collected in the morning after 12 hours of an overnight fast after taking informed consent under aseptic conditions. Blood is allowed to clot; samples centrifuged at 2000 rpm(revolution per minute) for 10 minute at room temperature. Serum is separated and stored at -20°C until the analysis, to minimize non-specific variability of all parameters. Plain tubes for serum, sodium fluoride, heparin for plasma were used.

Haemolysed and lipemic samples were avoided. Turbid samples were centrifuged before testing. For adequate quality control both normal, abnormal reference control serum solutions and calibrators were run before each testing.

FT3, FT4, TSH (sandwich assay) were estimated in the serum samples by chemiluminescence immunoassay using Beckman Coulter Access 2. Based on serum TSH values, hypothyroid cases were selected. Patients having TSH value greater than 5µIU/ml were selected as cases. Thirty age matched controls were taken and the same exclusion criteria were applied. Thyroid function tests were done and normal TSH values were noted.

Simultaneously lipid profile and blood glucose was estimated in all the subjects.

Total cholesterol was estimated by CHOD-POD method, trigycerides by GPO-PAP method and HDL-C fraction determined after precipitating other lipoproteins using precipitating reagents and is measured in supernatant by homogenous enzymatic assay.

LDL-cholesterol was calculated using Friedwald's formula.

LDL = total cholesterol –(HDL cholesterol – Triglyceride)/5.

VLDL-C was calculated by dividing the triacylglycerol concentration by 5.

Plasma glucose was determined by the glucose oxidase and peroxidase method (GOD-POD) using a commercially available kit Human (gmbh Germany) using Humastar 300 chemistry analyzer (Human gmbh Germany).

Statistical Analysis

The statistical analysis was performed using IBM SPSS Version-20. Continuous data were expressed as Mean(SD). For statistical significance, a two tailed probability value of less than 0.05 was considered.

RESULTS

The study group included 50 hypothyroid cases and 50 normal controls. Table 1 shows the thyroid profile values expressed as mean (standard deviation). The mean TSH in cases and controls was 19.6 (14.59) mIU/ml and 2.08 (1.13) mIU/ml, P<0.0001 respectively. Mean FT4 was decreased in cases compared to controls [0.51(0.28) vs 0.88(0.14), P<0.0001]. FT3 in cases was significantly decreased as compared to controls (2.58(0.71) vs 2.94(0.29) pg/ml, P=0.001).

Table 1: Thyroid profile in cases and controls.

Parameters	Cases n=50	Controls n=50	P value
TSH(mIU/ml)	19.6(14.59)	2.08(1.13)	<0.0001
FT3(pg/ml)	2.58(0.71)	2.94(0.29)	0.001
FT4(ng/dl)	0.51(0.28)	0.88(0.14)	<0.0001

Data is expressed as mean (standard deviation). P <0.05 is considered significant.

Table 2 gives the mean values of TC, HDL, LDL, VLDL, TG and FBS in cases and controls. All the parameters of lipid profile (except HDL) and fasting blood glucose are significantly increased in hypothyroid subjects.

Table 2: Lipid profile and fasting blood glucose in hypothyroid cases and controls.

Parameters	Cases n=50	Controls n=50	P value
Total cholesterol (mg/dl)	183.7(32.9)	160.5(7.6)	0.001
HDL-C (mg/dl)	38.12(7.9)	48.44(9.28)	<0.0001
Triglycerides (mg/dl)	158.44(65.61)	64.68(17.74)	<0.0001
LDL-C (mg/dl)	104.4(29.42)	86.64(11.45)	0.003
VLDL-C (mg/dl)	31.66(13.09)	12.9(3.48)	<0.0001
Fasting blood glucose (mg/dl)	99.5(9.9)	83.4(10)	<0.0001

Data is expressed as mean (standard deviation). P <0.05 is considered significant.

Figure 1 shows fasting blood glucose level comparison between cases and controls. Hypothyroid patients had blood glucose levels ranging from 76 -120 [mean 95.9(9.9)] mg/dl significantly higher than the control group(mean 83.4(10)mg/dl, P<0.0001).

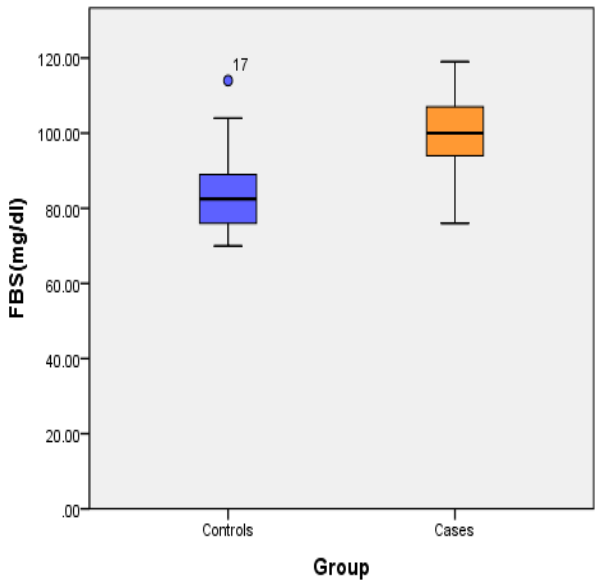

Figure 1: Fasting Blood Glucose in hypothyroid cases and controls.

Figure 2 demonstrates the comparison of various lipid profile factors between cases and controls. There is significant difference between the case and control groups.

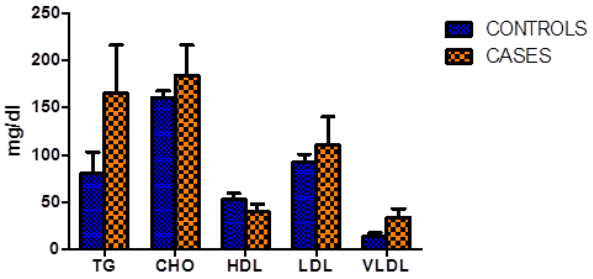

Figure 2: Lipid Profile comparison between hypothyroid cases and controls.

DISCUSSION

The present study was conducted at Narayana Medical College and Hospital, Nellore with the objective to study changes in lipoprotein levels and fasting blood glucose levels in hypothyroid patients and compare it with matched healthy controls in population. Only patients of overt hypothyroidism were included as cases. Majority of the cases were females in the 20-40 year age group. This is in accordance with other studies showing a higher prevalence of hypothyroid status in females as compared to males.[7,8,9]

The higher prevalence of hypothyroidism among middle aged women, associated with an increase in total plasma cholesterol.[10] This is in agreement with our findings showing that hyperlipidemia is associated with hypothyroidism. Hypothyroidism results in a small increase in low density lipoprotein (LDL)-C, total serum cholesterol and decrease in high density lipoprotein (HDL)-C that enhance the risk for development of atherosclerosis and coronary artery disease, there is no clear evidence to date that hypothyroidism causes clinical heart disease.[11] Hypothyroidism increases the oxidation of plasma cholesterol mainly because of (i) an altered pattern of binding and (ii) due to the increased levels of cholesterol, which presents substrate for oxidative stress. Serum total cholesterol and LDL-C levels are increased by approximately 30% in patients with overt hypothyroidism and over 90% of overtly hypothyroid patients have hyperlipidemia.[12,13] In our study it was observed that total cholesterol and LDL-C were significantly greater in cases than in controls (P=0.001&0.003) respectively. Triglyceride levels and VLDL may be normal or increased in overt hypothyroidism. [13]Although the effects of overt hypothyroidism on HDL-C have been variable across studies, the preponderance of evidence suggests that HDL-C levels are normal to slightly elevated in overt hypothyroidism, resulting in an unfavorable ratio of LDL-C to HDL-C. Despite the reduced activity of HMG-CoA reductase, there is often an increase in the serum total cholesterol concentration in hypothyroid patients

mainly due to raised levels of serum LDL cholesterol and intermediate density lipoprotein (IDL) cholesterol. Decreased activity of LDL-receptors resulting in decreased receptor-mediated catabolism of LDL and IDL is the main cause of the hypercholesterolemia observed in hypothyroidism. Hypertriglyceridemia associated with increased levels of VLDL is less commonly found in these patients. These changes are attributable to the decreased activity of Lipoprotein lipase (LPL),which results in a decreased clearance of triglyceride-rich lipoproteins. The VLDL and IDL particles in hypothyroidism are rich in cholesterol and apolipoprotein E. Compared to all other parameters the maximum increase was seen in serum triglyceride level between cases and controls. (P<0.0001) This can be due to the high TSH levels in our study group and autoimmunity also plays a role. Erem et al studied alterations in lipid profile in thyroid dysfunction.[14] They stated that thyroid hormone regulates lipid metabolism through various mechanisms. The key role is played by LDL receptor pathway. In the present study there was significantly increased LDL and total cholesterol values in overt hypothyroid patients.

Thyroid hormones regulate cholesterol and lipoprotein metabolism, whereas thyroid disorders, including overt and subclinical hypothyroidism (SCH), considerably alter lipid profile and promote cardiovascular disease. Hypercholesterolemia in hypothyroidism is caused by a reduction in low-density lipoprotein (LDL) receptors and the diminishing control by T3 over sterol regulatory element-binding protein 2 (SREBP- 2), crucial for the expression of LDL receptor. The action of thyroid hormone on bile acids has recently emerged as a discernible hypocholestrolemic effect. Increased flow of bile acids causes depletion of the hepatic cholesterol pool followed by an increase in the synthesis of cholesterol in the liver and the hepatic uptake of cholesterol from the circulation.[14]

Fasting blood glucose mean in controls and cases was 83.4(10) and 99.5(9.8) mg/dl respectively[significantly lower in controls, P<0.0001]. Thyroid hormones have a large impact on glucose metabolism. A direct regulation on thyroid responsive genes at the target organ has been described and more recently an indirect effect involving hypothalamic pathways that regulate glucose metabolism via control of the sympathetic nervous system has been reported. Furthermore, thyroid hormone effects can be insulin agonistic, such as demonstrated in muscle or antagonistic such as observed in the liver.

Dyslipidemia was observed in the patient group. Levels of total and LDL cholesterol tend to increase as the thyroid function declines. Therefore, hypothyroidism constitutes a significant cause of secondary dyslipidemia.[15]

From this study it is evident that hypothyroidism is associated with lipid disorders characterized by normal or slightly elevated cholesterol levels, increased LDL cholesterol and lowered HDL cholesterol. Early detection and treatment of dyslipidemia in hypothyroid patients will attenuate cardiovascular risk and improve general well being.

Our study clearly shows that lipid fractions are abnormal in hypothyroid patients. Because these individuals with thyroid dysfunction have a high probability of developing cardiovascular disease, it is essential that necessary medication alongwith dietary modifications be included in the management of primary hypothyroidism.[16,17] A small sample size and referral bias limit this study and larger studies are needed. This study indicates that monitoring of lipid level in patients with thyroid dysfunction would be helpful in preventing cardiovascular diseases.

Earlier studies have already established a clear association between thyroid disorders, diabetes mellitus and dyslipidemia.[18,19,20] Unrecognized dyslipidemia may increase cardiovascular risk. The increased frequency of dyslipidemia in thyroid hypofunction calls for a systematic approach to lipid profiling.

CONCLUSION

In the present study, an association between dyslipidemia, high fasting blood glucose levels and hypothyroidism is evident. Therefore regular screening strategy may be evolved to monitor the serum lipid profile in the hypothyroid patients. Larger epidemiological studies are required to find out the actual prevalence and incidence of dyslipidemia in primary hypothyroidism.

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