

Original Research Article

Evaluation of lipid profile status in nondiabetic and diabetic hypothyroidism patients

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Abstract: In the last few decades, abnormality in lipid profile is a serious concern in various diseases including diabetes mellitus. However, limited studies have been documented on lipid abnormality in hypothyroidism (HT) along with diabetes. The objective of present study was to determine the glycemic and lipid profile in nondiabetic and diabetic hypothyroidism patients and to determine their role in disease complexity. Fasting and post prandial blood glucose levels along with serum total cholesterol, triglycerides, HDL, LDL and VLDL levels were estimated by using standard methods in 100 patients of HT divided into two groups of 50 HT nondiabetic patients and 50 HT diabetic patients as Group II and Group III respectively, and compared it with 50 age matched healthy controls (Group I). The values were expressed as Mean \pm SD and data from patients and controls were compared using students't' test. Serum total cholesterol, triglycerides, LDL and VLDL levels along with fasting blood sugar were significantly high ($p < 0.001$) and serum HDL levels were significantly low ($p < 0.001$) in Group III patients as compared to control. However, serum total cholesterol, triglycerides, LDL and VLDL levels were altered significantly ($p < 0.05$) in Group II subjects. These finding suggest that diabetic HT patients are at enhanced risk to develop cardiovascular complication due to their altered glycemic and lipid profile with respect to nondiabetic HT patients. Therefore, maintenance of normal thyroid profile, regular monitoring of cardiac markers, control on blood sugar level along with proper treatment of dyslipidemia and diabetes in these patients can prove to be protective.

Keywords: Dyslipidemia, hyperglycemia, hypothyroidism, cardiovascular disease.

INTRODUCTION

Thyroid hormones have significant impact on diabetes, so it is important to consider the physiological association of thyroid dysfunction in relation to diabetes mellitus [1]. Hypothyroidism has been associated with disorders of glucose and insulin metabolism involving defective insulin secretion in response to glucose, hyperinsulinemia, altered peripheral glucose disposal and insulin resistance [2]. Moreover, thyroid hormones (TH) plays an important role not only in metabolism of glucose but also in that of lipids too. Alteration in thyroid levels in association with insulin resistance has a significant effect on lipid profile. Bakker et al. in their study also suggested that insulin resistance augments

the deleterious effect of hypothyroidism on the lipid profile [3]. Hypothyroidism is known to cause hypercholesterolemia, elevated low-density lipoprotein (LDL), and hypertriglyceridemia [4]. It was reported that high circulating thyroid stimulating hormone (TSH) levels were associated with abnormally elevated serum lipids, and triggered increased oxidation of the LDL particles [5]. Moreover, the increased cardiovascular risk in thyroid dysfunction has been found to be related to the deranged lipid profile, endothelial dysfunction, metabolic, hormonal, and hemodynamic changes and coagulation disturbances [6]. By virtue of this type of association of thyroid disorder with cardiac complications, hypothyroid patients are considered to

be at high risk of cardiovascular diseases. Interestingly, some studies have revealed normalized lipid profiles in hypothyroid patients when treated with thyroxine replacement therapy [7]. Therefore, the objectives of present study were to estimate glycemic and lipid profile in nondiabetic and diabetic hypothyroidism patients and to determine the relationship of these profiles with disease complexity which may confer us more rational approach to the treatments of such complicated conditions.

MATERIALS & METHODS

In the present study, 50 healthy subjects, 50 hypothyroidism patients with diabetes and 50 hypothyroidism patients without diabetes were taken in study group as Group I, Group II and Group III respectively. A general information or pre-experimental questionnaire regarding demographic information, family history and limited physical examination including blood pressure measurement was completed from all the subjects after taking their informed consent and approval of protocol by ethics committee of college.

Inclusion criteria: The inclusion criteria adopted were: age 30 to 60 years, newly diagnosed and untreated cases for hypothyroidism with and without diabetes. The American Diabetes Association criteria 2015 were used for diagnosis of diabetes mellitus.

Exclusion criteria: Patients suffering from cardiovascular disease, hepatic disease, tuberculosis, renal disease and taking drugs like steroid, amiodarone, lithium, antioxidant vitamin supplement or non-steroidal anti-inflammatory drugs, antihypertensive drugs and other medications that alter thyroid functions and lipid levels led to exclusion from the study. Pregnancy and menopause also accounted for exclusion from the study.

Estimation of serum thyroid profile (T3, T4 and TSH) was done in VITROS EciQ immunodiagnostic system using an immunometric assay technique. Fasting blood glucose was estimated by glucose oxidase method. Glucose oxidase converts glucose to gluconic acid. In addition, peroxidase (POD) produces hydrogen peroxide which oxidatively couples with 4-aminoantipyrine and phenol to produce red quinoneimine dye [8].

Serum total cholesterol was estimated by enzymatic kit method which involves the conversion of cholesterol ester into free cholesterol and fatty acid by cholesterol esterase. In the second reaction, cholesterol oxidase acts on cholesterol and produce cholest-4-ene-3-one and hydrogen peroxide. H₂O₂ oxidatively couples with 4-aminoantipyrine and phenol to produce red

quinoneimine dye. This dye had absorbance maximum at 510 nm [9].

Enzymatic kit method was also used in the estimation of serum triglyceride. Triglyceride was hydrolyzed by lipoprotein lipase to release glycerol which was converted into glycerol 3 phosphate by glycerol kinase. In addition, glycerol phosphate oxidase converts glycerol 3 phosphate into dihydroxy acetone phosphate and hydrogen peroxide. In presence of peroxidase, hydrogen peroxide oxidizes phenol chromogen to red color compound. The intensity of color was directly proportional to concentration of triglyceride and measured at 510 nm [10]. Serum high density lipoprotein (HDL) was estimated by using phosphotungstic acid/Mg²⁺ which precipitates chylomicrons, VLDL and LDL fraction whereas HDL fraction remains unaffected in supernatant. Cholesterol content of HDL fraction was assayed using Autozyme cholesterol [11].

Serum LDL-cholesterol and VLDL-cholesterol levels were calculated by Friedwald's formula [12].

$$\text{LDL-C} = \text{TC} - [(\text{TG}/5) + \text{HDL-C}]$$

$$\text{VLDL cholesterol} = \text{Total chol.} - (\text{HDL} + \text{LDL})$$

Values were expressed as Mean \pm SD. The significance of mean difference between groups was compared by using Student's t-test and distribution of probability (P).

RESULT:

Demographic profile of study group subjects is represented in Table 1. Out of the selected patients of each group, more patients of hypothyroidism without and with diabetes belonged to age group 40- 50 years i.e. 45.8 ± 8.4 and 46.4 ± 6.7 years in Group II and Group III respectively. In addition to diabetes Group III subjects were obese whereas Group II subjects were overweight with respect to Group I subjects, served as healthy controls.(Table 1.0) The observation made reveal significant changes in thyroid profile (including T3, T4 and TSH levels) in both the patients group as compare to healthy controls. Alteration in serum thyroid profile was represented in Table 2. Serum T3 level was significantly low (P< 0.05, 16.59% and P< 0.001, 24.90% low) in both Group II and Group III respectively as compared to control. Similarly, serum T4 level was significantly low (P< 0.05, 21.20% and P< 0.001, 40.98% low) in both Group II and Group III respectively as compared to control. Serum TSH level was significantly high (P< 0.001, 446% and P< 0.001, 1660% high) in both Group II and Group III respectively as compared to control.

As compared to normal healthy controls, abnormalities in glycaemic and lipid profile were observed in hypothyroidism patients without and with diabetes, as represented in Table 3. In the Group II subjects, fasting blood glucose level was increased insignificantly ($P < 0.1$; 96.72 ± 8.55 mg%) with respect to Group I whereas significantly increased level of fasting blood glucose ($P < 0.001$; 163.64 ± 12.21 mg%) was observed in Group II subjects as compared to healthy controls. It was observed that dyslipidemia was highly prevalent and significantly associated with hypothyroidism patients without and with diabetes. In

both the patient groups, significantly increased level of total cholesterol ($P < 0.05$; 34.89 % high in Group II and $P < 0.001$; 63.06 % high in Group III), Triglycerides ($P < 0.05$; 34.41% high in Group II and $P < 0.001$; 70.88% high in Group III), LDL-cholesterol ($P < 0.001$; 63.87% high in Group II and $P < 0.001$; 113.7% high in Group III) and VLDL ($P < 0.05$; 33.7% high in Group II and $P < 0.001$; 70.9% high in Group III) were observed whereas HDL-cholesterol were significantly reduced in both Group II ($P < 0.05$; 14.35% low) and Group III ($P < 0.001$; 28.61% low) respectively as compared to controls.

Table 1: Demographic profile of the study group subjects (Mean \pm SD)

S.No.	Parameters	Group I (n=50)	Group II (n=50)	Group III (n=50)
1	Age (years)	46.2 \pm 7.7	45.8 \pm 8.4	46.4 \pm 6.7
2	M:F ratio	1:1	1:1	1:1
3	Height (meter)	1.61 \pm 0.048	1.62 \pm 0.046	1.61 \pm 0.044
4	Weight (Kg)	59.2 \pm 2.9	70.6 \pm 5.2	80.6 \pm 7.5
5	BMI (Kg/m ²)	22.9 \pm 1.2	27.2 \pm 1.7*	31.3 \pm 3.3**

Where, $p < 0.1$: Non-significant, $p < 0.05$: Significant; $p < 0.001$: Highly Significant;

Table 2: Serum Thyroid profile of the study group subjects (Mean \pm SD)

S.No.	Parameters	Group I (n=50)	Group II (n=50)	Group III (n=50)
1	Tri-iodo thyronin (T3) (ng/dl)	107.19 \pm 21.26	89.4 \pm 16.25**	80.49 \pm 15.31***
2	Thyroxin (T4) (μ g/dl)	8.49 \pm 1.21	6.69 \pm 1.15**	5.01 \pm 1.22***
3	Thyroid stimulating hormone (TSH) (uIU/ml)	2.60 \pm 0.89	14.22 \pm 3.53***	45.76 \pm 9.97***

Where, . * $P < 0.1$: Non-significant, ** $P < 0.05$: Significant, *** $P < 0.001$: Highly significant

Table 3: Fasting blood glucose and serum Lipid profile in the study group population. (Mean \pm SD)

S.No.	Parameters	Group I (n=50)	Group II (n=50)	Group III (n=50)
1	Fasting Blood Glucose (mg/dl)	88.35 \pm 10.69	96.72 \pm 8.55*	163.64 \pm 12.21***
2	Total cholesterol (mg/dl)	142.21 \pm 15.40	191.83 \pm 13.83**	231.89 \pm 14.31***
3	Triglyceride (mg/dl)	135.7 \pm 14.58	182.4 \pm 20.84**	231.98 \pm 20.49***
4	HDL-cholesterol (mg/dl)	42.49 \pm 3.01	36.39 \pm 2.66*	30.33 \pm 2.56**
5	LDL-cholesterol (mg/dl)	72.58 \pm 15.95	118.94 \pm 14.31***	155.16 \pm 15.35***
6	VLDL-cholesterol (mg/dl)	27.13 \pm 2.91	36.28 \pm 4.44**	46.39 \pm 4.09***

Where, . * $P < 0.1$: Non-significant, ** $P < 0.05$: Significant, *** $P < 0.001$: Highly significant

DISCUSSION:

Despite intense research efforts to unveil the etiology of diabetes in hypothyroidism, it remains enigmatic. However, a growing body of evidence supports the understanding that the disease begins with

reduced glucose absorption from gastrointestinal tract accompanied by prolonged peripheral glucose accumulation, gluconeogenesis, diminished hepatic glucose output and reduced disposal of glucose, which are considered as hallmarks of hypothyroidism.[13]

Some authors have indicated that hypothyroidism are associated with insulin resistance, which has been reported to be the major cause of impaired glucose metabolism in type 2 diabetes mellitus associated with thyroid disorders.[14] In the present study, fasting blood glucose was significantly increased in hypothyroidism patients with diabetes, and a slight increase in that of the nondiabetic group. The most probable mechanism underlying the etiology of diabetes in thyroid dysfunction was suggested to be the perturbed genetic expression along with impaired glucose utilization in muscles, overproduction of hepatic glucose, and enhanced absorption of splanchnic glucose [1, 15].

In addition, the present study also showed significant increases in the serum total cholesterol accompanied with a rise in the LDL-c and triglyceride levels in the hypothyroidism patients without and with diabetes as compared to healthy controls. Our findings were in congruence with the findings of previous investigators where association of hypothyroidism with altered lipid profile are well documented and the main pathophysiological basis underlying dyslipidemia along with glucose intolerance, abdominal obesity, and hypertension has been attributed to IR.[16] However, in contrast, Imaizumi *et al.* in their study observed normal cholesterol levels in patients with subclinical-hypothyroidism [17]. In the present data, the hypothyroid patients with diabetes showed a trend of increase in serum total cholesterol levels with respect to nondiabetic hypothyroidism patients but this was not statistically significant ($p < 0.1$). Combining the observations of previous studies, it is obvious that the plasma cholesterol levels are well known regulated by thyroid hormone. According to these studies, binding of T3 to a specific thyroid hormone responsive element leads to T3-mediated gene activation which in turn causes the increased expression of LDL-receptors and enhanced cellular uptake of LDL-c from circulation [18, 19].

Moreover, the role of thyroid hormone in protecting LDL particles from oxidation and in increasing the lipoprotein-lipase activity, an enzyme responsible for clearance of VLDL and chylomicron from circulation, is well documented [20, 21]. Depletion in T3 and T4 levels are responsible for decreased clearance of chylomicron remnant and intermediate density lipoprotein from circulation which, later on, taken up by macrophages in the arterial walls to produce foam cells and thereby facilitate the incidence of atherosclerosis in hypothyroidism patients [22]. These facts are well supported by outcomes of present study as serum LDL and VLDL are marked elevated ($p < 0.05$ & $P < 0.001$) in both the hypothyroidism patients group with respect to healthy controls.

HDL cholesterol is good cholesterol and it exhibits atheroprotective properties not only by

facilitating reverse cholesterol transport but also by improving endothelial function, protecting LDL from oxidation, retarding inflammation of vascular wall and limiting hemostasis [23]. Depletion in HDL levels enhances the risk of cardiovascular disease. Interestingly, serum HDL levels were found to be decreased significantly ($p < 0.05$) in hypothyroidism patients with diabetes as compared to healthy controls which reflects that hypothyroidism patients with increase in disease complexity are more susceptible to develop future cardiovascular complications. However, HDL cholesterol levels were decreased insignificantly ($p < 0.1$) in non diabetic hypothyroidism patients. Our results were in concordance with that of previous studies carried out in overt and subclinical hypothyroidism patients with diabetes [15, 23].

Apart from lipoproteins and total cholesterol levels, serum triglycerides levels were also found to be significantly high ($p < 0.05$, $p < 0.001$) in hypothyroidism patients without and with diabetes as compared to control group subjects which could be explained on the basis of increased hepatic VLDL-TG secretion rate in hypothyroidism patients. Moreover, another well accepted mechanism underlying hypertriglyceridemia in hypothyroidism patients includes abnormally low levels of post-heparin hepatic triglyceride lipase activity in hypothyroidism, as reported by Abdel Gayoum in his study on dyslipidemia and serum minerals level in thyroid disorder patients [15, 24].

CONCLUSION:

On the basis of present findings and consistent findings of previous studies, we concluded that decrease in serum T3 and T4 and altered levels of TSH in association with altered lipid profile are associated with increased risk of cardiovascular complications and play a significant role in the etiopathogenesis of diabetes in hypothyroidism patients. In addition, regular exercise, maintenance of healthy lipid profile and controlled blood glucose level are necessary to prevent hypothyroidism mediated secondary complications. However, further studies on vitamin and minerals supplementation along with iodine rich diet are needed to explore the hidden facts related to disease pathology and to overcome not only the incidence of hypothyroidism but also its associated diabetes. Furthermore, it is suggested that regular monitoring of glycemic, lipid profile along with thyroid profile may not only predict hypothyroidism development but also prevent the development of diabetes and other associated complications.

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