

Research article

Lipid Profile of Patients with Thyroid Dysfunction in Ayurveda Hospital

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Abstract

Background: Thyroid hormones play an indispensable role in various metabolic processes in the human body. Thyroid disorders other than iodine deficiency disorders in the form of thyroiditis, hypothyroidism or autoimmune thyroid dysfunctions are on rise.

Objective: This study was done to study the prevalence and pattern of dyslipidemia in patients with thyroid dysfunction.

Methods: It is a retrospective study based on the available biochemical data of 50 thyroid patients (33 females and 17 males) with age range of 26-68 years. Serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) triiodothyronine (T₃), thyroxine (T₄) and thyroid stimulating hormone (TSH), were measured using standard assays procedures.

Results: The results showed that 82% of the study population has hypothyroidism with the higher prevalence among females. The mean values of T₃, T₄ and TSH in patients with thyroid dysfunction were 0.8 ± 0.05 ng/ml, 4.2 ± 0.5 µg/dl and 9.45 ± 1.2 mIU/ml, respectively. The mean values of TC, TG, HDL-C, LDL-C, and VLDL-C were 222.4 ± 3.8 mg/dl, 180.3 ± 8.2 mg/dl, 35.6 ± 1.3 mg/dl, 151.6 ± 6.2 mg/dl and 36.5 ± 2.6 mg/dl respectively in patients with hypothyroidism. Hypothyroidism shows significant positive correlation with TC, TG and LDL. Results show that even a slight increase in serum TSH showed significant dyslipidemia.

Conclusion: This study suggests that regular monitoring of lipid level in patients with thyroid dysfunction would be helpful in preventing cardiovascular diseases.

Keywords: Lipid profile, thyroid, dyslipidemia, cholesterol, hypothyroidism

1. Introduction

Thyroid dysfunction is one of the common endocrinopathy encountered in practice, which affects the basal metabolic rate of the individual.¹ Thyroid disorders other than iodine deficiency disorders in the form of thyroiditis, hypothyroidism or autoimmune thyroid dysfunctions are on rise.² The WHO estimates that substantially greater than 190 millions suffer from iodine deficiency disorders in world.³ Thyroid dysfunction is primarily conditions that affect the amount of thyroid hormones being produced in the body. Excess production leads to hyperthyroidism while diminished production leads to hypothyroidism. They affect synthesis, mobilization and degradation of lipids, although degradation is influenced more than synthesis.⁴ Thyroid dysfunction particularly hypothyroidism is associated with dyslipidemia which increase the risk of hypertension, endothelial dysfunction, and cardiovascular diseases.⁵ Prominent cardiovascular features such as tachycardia, arrhythmias, congestive cardiac failure, and systolic hypertension are well recognized manifestations of thyrotoxicosis.

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. Such lipid abnormalities are partly reversible with thyroxine treatment in patients with co-existent diabetes. Several studies have reported inter-dependent associations between thyroid status and serum lipid levels.^{2,5} However, the controversy persists regarding the lipid level in hypothyroidism. It was observed that there was an increased frequency of thyroid dysfunction with advancing age and a higher prevalence of thyroid disease in women as compared to men.⁶ The higher incidence among females may be attributed to inhibition of disease activity by androgens and exacerbation by estrogens.⁷

Early recognition and treatment of dyslipidemia in patients with thyroid dysfunction will attenuate cardiovascular risk and improve general wellbeing. The studies focusing on the association between thyroid dysfunction and dyslipidemia are sparse. Therefore, this retrospective study has been undertaken to estimate the relationship between serum lipids and thyroid dysfunction.

2. Materials, subjects and methods

2.1 Chemical

The diagnostic kits i.e. Cholesterol, triglyceride, HDL-C, LDL-C VLDL-C and reagents were procured from Siemens Ltd, (Gujrat India). All the reagents were stored at 2-8°C after procurement. The ELISA kits for T₃, T₄, and TSH were procured from Monobind Inc. (California, USA). All the biochemical estimations were performed at room temperature.

2.2 Subjects

It is a retrospective study based on the available biochemical data of patients visiting the Biochemistry department for the diagnosis thyroid dysfunction and lipid profile, after prescription and medication from OPD and IPD of the Ayurveda hospital at Kolkata, India. A total of 50 thyroid patients (33 females and 17 males) with age range of 26-68 years were randomly selected from the medical records. Patients reported with other ailments and metabolic disorders were excluded from the study. The individual information about clinical symptoms, weight, height and diagnosis by the hospital physicians were well documented in medical records of the hospital.

2.3 Estimation of T₃, T₄ and TSH

Venous blood samples were collected from all the subjects in the morning after fasting overnight. The assay of T₃ and T₄ was performed on the basis of competitive method of enzyme linked immune sorbent assay (ELISA) (Lisa Plus, Aspen Diagnostics, Mumbai, India), while TSH was assayed through sandwich method.

2.4 Estimation of total cholesterol

Cholesterol esters will be hydrolyzed by cholesterol esterase. Cholesterol will be oxidized into cholest-4-en-3-on and hydrogen peroxide by bacterial cholesterol oxidase. Hydrogen peroxide in the presence of phenol and amino-4-antipyrine forms a complex of red color showing absorption maximum at 500 nm by using a semi-automated enzymatic analyzer (Robonik, Mumbai, India).

2.5 Estimation of triglyceride

It is based on the principle that triglycerides in the serum sample are hydrolyzed enzymatically by the action of lipase to glycerol and fatty acids. The glycerol formed is converted to glycerol phosphate by glycerol kinase (GK). Glycerol phosphate is then oxidized to dihydroxyacetone phosphate by glycerol phosphate oxidase (GPO). The liberated hydrogen peroxide is detected by a chromogenic acceptor, chlorophenol-4-aminoantipyrine, in the presence of peroxidase (POD). The red quinone formed is proportional to the amount of triglycerides present in the sample and is measured at 546 nm.

2.6 Estimation of total HDL-cholesterol

It is measured by using phosphotungstate precipitation method based on the principle that chylomicrons, VLDL and LDL fractions in serum or plasma are separated from HDL by precipitating with phosphotungstic acid and magnesium chloride. After centrifugation the cholesterol in the HDL fraction which remains in the supernatant is assayed with enzymatic cholesterol method using cholesterol esterase, cholesterol oxidase, peroxidase and the chromogen 4-aminoantipyrine.

2.7 Estimation of total LDL-cholesterol

The LDL-Cholesterol test is a two reagent homogenous system. The assay is comprised of two distinct phases. In phase one a unique detergent solubilizes cholesterol from non-LDL- lipoprotein particles. This cholesterol is consumed by cholesterol esterase, cholesterol oxidase, peroxidase and 4-aminoantipyrine to generate a colorless end product. In phase two a second detergent in reagent 2 releases cholesterol from the LDL – lipoproteins. This cholesterol reacts with cholesterol esterase, cholesterol oxidase and a chromogen system to yield a blue color complex which can be measured bichromatically at 540/660nm. The resulting increase in absorbance is directly proportional to the LDL-C concentration in the sample.

2.8 Estimation of total VLDL-cholesterol

The value of VLDL-cholesterol was calculated as one-fifth of the concentration of triglycerides.

2.9 Statistical analysis

The data obtained was analyzed for significance between the groups by one-way analysis of variance (ANOVA). Correlation studies (Pearson's correlation coefficients and significance) were performed between the variables of thyroid assay and serum lipid profile by using statistical software programme "SPSS evaluation version 22".

3. Results

Results of the present retrospective study showed that among 50 patients with thyroid dysfunction included in this study, female and male were 33 and 17, respectively (**Table 1**). The age range of female and male subjects was 26-65 years and 32-68 years, respectively. Results of the thyroid assay showed that, all individuals selected for the study were with thyroid dysfunction. The normal reference range considered for each parameter was already established reference value of our laboratory. The range of T₃, T₄ and TSH in patients with thyroid dysfunction were 0.2 -1.5 ng/ml, 2.4 - 8.9 µg/dl and 2.6 - 19.5 mIU/ml, respectively (**Table 2**). The mean values of T₃, T₄ and TSH in patients with thyroid dysfunction were 0.8 ± 0.05 ng/ml, 4.2 ± 0.5 µg/dl and 9.45 ± 1.2 mIU/ml, respectively. Results showed that female had higher prevalence of thyroid dysfunctions. Results of serum lipid profile showed that the mean values for TC, TG, HDL-C, LDL-C and VLDL-C were 222.4 ± 3.8 mg/dl, 180.3 ± 8.2 mg/dl, 35.6 ± 1.3 mg/dl, 151.6 ± 6.2 mg/dl and 36.5 ± 2.6 mg/dl, respectively (**Table 3**). Among all thyroid patients, hypothyroidism was found in 82%, while hypercholesterolemia was found in 92% of the individuals (**Table 4**). Similarly, hypertriglyceridemia and reduced HDL-Cholesterol was found in 76% and 42% respectively, while elevated LDL-C was found in 78 % of the individuals suffering from thyroid dysfunction. Result of the correlation studies demonstrated a negative correlation of TSH with T₃ and T₄, while a significant positive correlation of TSH was observed TC, TG and LDL.

Table 1: Gender distribution and age of patients with thyroid dysfunction

Gender	No. of patients	Age range years
Female	33	26 - 65
Male	17	32 - 68
Total	50	26 - 68

Table 2: The concentration of T₃, T₄ and TSH in patients with thyroid dysfunction

T ₃ ¹			T ₄ ²			TSH ³		
Normal Range	Calculated Range	Mean	Normal Range	Calculated Range	Mean	Normal Range	Calculated Range	Mean
0.8 -1.9	0.2 -1.5	0.8 ± 0.05*	5 - 13	2.4 - 8.9	4.2 ± 0.5*	0.4 - 5.5	2.6 - 19.5	9.45 ± 1.2*

¹Units expressed as ng/ml.; ²Units expressed as µg/dl.; ³Units expressed as mIU/ml

*Statistically significant (P<0.05) as compared to normal range for respective thyroid level.

Table 3: The concentration of cholesterol, triglyceride, HDL-Cholesterol, LDL-Cholesterol and VLDL-Cholesterol in patients with thyroid dysfunction.

Lipid parameter	Normal Range	Calculated Range	Mean
Total Cholesterol ¹	< 200	180 - 324	222.4 ± 3.8*
Triglyceride ¹	50 - 150	135 - 360	180.3 ± 8.2*
HDL-Cholesterol ¹	45 - 65	30 - 46	35.6 ± 1.3*
LDL-Cholesterol ¹	< 100	90 - 206	151.6 ± 6.2*
VLDL-Cholesterol ¹	15 - 30	27 - 75	36.5 ± 2.6

¹Units expressed as mg/dl.; *Statistically significant (P < 0.01) as compared to normal range for respective serum lipids.

Table 4: The frequency distribution of thyroid dysfunction and dyslipidemia among selected patients

Parameter	Frequency of occurrence (%)
T ₃ & T ₄ thyrotoxicosis	18
Hypothyroidism	82
Hypercholesterolemia	92
Hypertriglyceridemia	76
Reduced HDL-Cholesterol level	42
Elevated LDL-Cholesterol level	78

4. Discussion

Thyroid disorders are very common with variable prevalence among the different populations. Recent decades have seen a growing understanding of the pleiotropic effects of thyroid hormones on various vascular and metabolic processes. Furthermore, insights are being developed into the complex interactions, at the phenotypic and molecular levels, between thyroid dysfunction and cardiovascular risk. Thus, our understanding has shifted from

the simplistic concept of thyroid dysfunction as a benign disorder of hormone secretion to a more complete appreciation of its multiple deleterious effects on cardiovascular and metabolic function.^{8,9,10} Subclinical hypothyroidism is defined as an elevated TSH concentration in the presence of normal thyroid hormones.¹¹ With the advent of sensitive assays for TSH measurements subclinical hypothyroidism will increasingly be diagnosed in healthy individuals with no overt features of thyroid disease. The clinical features of thyroid disorders tend to be nonspecific and fewer in elderly compared to younger patients and the symptoms are often confused with normal ageing process and coexisting diseases which may result in greater number of elderly patients being undiagnosed.¹²

Results showed higher prevalence of thyroid dysfunction in females which is in accordance with the earlier studies.^{2,13,14} It may be due to a sex difference in the prevalence of autoimmune diseases. Results suggested that maximum number of patients with thyroid dysfunction had one or more types of dyslipidemia. Our results reveal high prevalence of hypercholesterolemia, hypertriglyceridemia high LDL-C levels and reduced HDL level, which are well known risk factors for cardiovascular diseases among patients. These patients are on high-risk without complications but already had significant dyslipidemia, which enhances the risk of cardiovascular events, certainly required therapeutic intervention.

There was a significant association between hypothyroidism and dyslipidemia which is in accordance with the result of Regmi *et al* and Cabral *et al*.^{2,15} Increase of total cholesterol and LDL can be attributed to the effect of thyroid hormone on expression of LDL receptors and CYP7A, a rate limiting enzyme in bile acid synthesis. Decreased thyroid function not only increases the number of LDL particles but also promote LDL oxidation, thereby increasing the risk of atherosclerosis.¹⁶ HDL was increased in both overt and subclinical hypothyroidism, however, the increase was significant only in case of subclinical hypothyroidism. A study by Packard *et al.*, reported that reduced HDL-C as a powerful predictor for premature coronary heart diseases.¹⁷ Elevation in HDL cholesterol could be due to decreased activity of cholesteryl ester transfer protein and hepatic lipase. In addition, HDL-C is a ready substrate for hepatic lipase which converts it into smaller particles, which are readily cleared from the plasma. TG level is also increased in both overt and subclinical hypothyroidism which is attributable to the decreased activity of lipoprotein lipase that is responsible for the clearance of triglyceride rich lipoprotein. In subclinical hyperthyroidism, however, TC and LDL levels were slightly increased but not significant statistically. Despite the increased activity of HMG-CoA reductase, the cholesterol levels tend to be increased in hyperthyroidism due to augmented excretion of cholesterol by bile together with enhanced receptor mediated catabolism of LDL particles. Variations, generally, not very marked, observed in TG levels could be due to the action of thyroid hormone on VLDL.^{17,18}

Dyslipidemia management in people with thyroid dysfunction starts with a thorough evaluation that aims to identify secondary causes that might contribute to the abnormal lipid profile. Medication alongwith dietary modifications are the cornerstones of management. Our study clearly shows that lipid fractions are abnormal in thyroid disorders. Realizing the fact that individuals with thyroid dysfunction have a high probability of developing cardiovascular and cerebrovascular disease, it is essential that an individual who has thyroid should take care of his dyslipidemia.^{19,20} Prospective and longitudinal studies are needed at the time of diagnose to estimate true population prevalence of dyslipidemia in patients with thyroid dysfunction. Therefore, this study indicates that monitoring of lipid level in patients with thyroid dysfunction would be helpful in preventing cardiovascular diseases. As this is a retrospective study based on the available clinical records, the information related to the diabetes status and medication of the individuals was not available. Earlier studies have already established a clear association between thyroid disorders, diabetes mellitus and dyslipidemia.^{21,22,23} Unrecognized dyslipidemia in thyroid dysfunction will amplify cardiovascular risk. The increased frequency of dyslipidemia in thyroid dysfunction calls for a systematic approach to lipid profiling.

5. Conclusion

In the present study, we observed higher TSH levels or hypothyroidism in subjects with thyroid dysfunction. Therefore, selective regular screening strategy may be initiated to monitor the serum lipid profile of those patients who are at the greatest risk of thyroid dysfunction, such as those with diabetes mellitus, baseline positive antibodies or TSH concentrations in the upper half of the normal reference range. This is a preliminary study with a small sample size, hence, larger epidemiological studies is required to find out the actual prevalence and incidence of dyslipidemia in thyroid abnormality.

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