A study to assess the relation between severity of hypothyroidism and Lipid parameters

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Abstract

Background: Hypothyroidism is associated with dyslipidemia. The present study was conducted to assess the relation between hypothyroidism and lipid parameters and lipid ratios. It is also done to assess the severity of hypothyroidism on lipid parameters.
Methods: Study comprises of 120 participants were divided into four groups depending on TSH levels, each group comprising of 30 participants. Group-1 euthyroid as controls, group-2 hypothyroid patients with TSH levels between 6-20 µIU/mL, group-3 TSH levels between 21-50 µIU/mL and group-4 consists of hypothyroid patients with TSH levels of > 50 µIU/mL. Fasting venous blood was collected from all the participants and analyzed for estimation of thyroid profile and lipid profile. Lipid ratios were calculated.
Results: There was significant ($p < 0.05$) increase in total cholesterol, triglycerides, LDL-C and HDL-C in all the groups compared to group-1 i.e. controls. There was significant increase ($p<0.05$) in lipid ratios. There is positive correlation between TSH and lipid parameters.
Conclusion: Our study shows hypothyroid patients show dyslipidemia and the effect of hypothyroidism on lipid parameters is more marked in patients with higher serum TSH levels. By calculating the lipid ratios from lipid parameters are better indicators of dyslipidemia and cardiovascular risk in hypothyroid patients.

Key words: Dyslipidemia, Hypothyroidism, Lipid ratios.

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Introduction

Thyroid dysfunction is the most common endocrine disorder worldwide second only to diabetes mellitus[1]. Thyroid hormones play an important role in basal metabolism and functioning of every tissue and system in the body[2]. 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. Hypothyroidism affects the cardiovascular, pulmonary, renal, neuromuscular, nervous and reproductive system. Hypothyroid patients show elevated total cholesterol (TC), low density lipoprotein (LDL), triglyceride (TG) levels[3]. The serum thyroid stimulating hormone (TSH) assay is an accurate test for detecting either hypothyroidism or hyperthyroidism[4].

Triiodothyronine (T3) and tetraiadothyronine (T4) play an important role in lipid metabolism. It is well known that alterations in thyroid function result in changes in the composition and transport of lipoproteins[5]. Thyroid hormones stimulate the hepatic denovo cholesterol synthesis by inducing the 3-hydroxy 3-methyl glutaryl Co-A reductase (HMG-CoA) which is a key regulatory enzyme in cholesterol synthesis. Thyroid hormones especially T3 up regulates LDL receptors by controlling the LDL receptor gene activation. This T3 mediated gene activation is done by direct binding of T3 to specific thyroid hormone responsive elements (TREs). Further, T3 controls the sterol regulatory element-binding protein-2 (SREBP-2), which in turn regulates LDL receptor's gene expression. T3 has also been associated with protecting LDL from oxidation[6,7]. Thyroid hormones also stimulate the cholesteryl ester transfer protein (CETP) an enzyme which transports cholesteryl esters from high density lipoprotein (HDL) to very low density lipoprotein (VLDL). Thyroid hormones also stimulate the lipoprotein lipase (LPL) which catabolizes the TG rich lipoproteins and hepatic lipase which hydrolyzes HDL2 to HDL3[8]. Hence dyslipidemia is the common feature in thyroid dysfunction.

Many studies have reported increased levels of total cholesterol, low density lipoprotein cholesterol and triglyceride in hypothyroid subjects than euthyroid subjects[9-12]. Thus hypothyroidism constitutes a significant cause of dyslipidemia[13]. Dyslipidemia is a well-known risk factor for cardiovascular disease. The

risk of coronary heart disease and other forms of atherosclerotic vascular disease increases with rising plasma cholesterol concentration. Early diagnosis and proper management can significantly reduce the mortality and morbidity. The increase in lipid levels can be reversed by thyroid hormone supplementation[14]. Development of atherosclerosis in cholesterol fed animals is enhanced by the presence of hypothyroidism and reduced when thyroid hormones is administered[15].

Thus the present study was conducted with the objective of assessing the severity of dyslipidemia and to evaluate the role and significance of lipid ratios like Atherogenic index, Castelli's risk index-1 and Castelli's risk index-2 in early identification of individuals at risk for coronary artery disease (CAD) in hypothyroid patients beyond the routinely done lipid profile. Calculating certain lipid ratios using these parameters help in early identification of individuals at risk for CAD.

Materials and methods

The study was conducted in the department of Biochemistry, tertiary care teaching hospital in North Karnataka, India. Ethical clearance was obtained from the Institutional ethics committee. Informed consent obtained from all the participants. Study was conducted over a period of one year from March 2014 to February 2015. Among the patients who underwent thyroid profile evaluation referred from different departments, 120 participants were selected of age group between 20 to 60 years. They were divided into four groups depending on TSH levels to assess the severity of hypothyroidism. Each group composed of 30 subjects. Group-I: Patients with euthyroid state i.e TSH levels between 0.4-4.5 μIU/mL taken as controls, Group-II: TSH levels of 5-20 μIU/mL, Group-III: TSH levels of 21-50 μIU/mL and Group-IV: TSH levels of >50 μIU/mL. Patients with renal disease, hepatic disease, diabetes mellitus, myocardial infarction, patients on statins and women on oral contraceptive pills were excluded from the study.

Under aseptic precautions 5 mL of fasting venous blood was drawn from all the participants. Samples were allowed to clot, then centrifuged for ten minutes and serum was separated. The serum sample was used for estimating following biochemical tests. The serum TSH, FT3 and FT4 were estimated by chemilumine-scence immunoassay by (CLIA Maglumi 1000, SNIBE). Patients with TSH level > 5 μIU/mL were considered to be hypothyroidism. Serum cholesterol was estimated by cholesterol oxidase and peroxidase method, serum triglycerides by glycerol phosphate oxidase and peroxidase method, serum HDL-C by direct detergent method, serum LDL-C calculated by Friedewald's formula and serum VLDL-C is TG/5 in fully automated analyser (Biosystem A25) kits are from Biosystem. Lipid ratios were calculated using the following formulas i.e. Atherogenic index (AI) = log (TG/HDL-C), Castellis Risk Index -1=TC/HDL-C and Castellis Risk Index -2 = LDL-C/HDL-C.

Statistical Analysis

Statistical analysis was done using SPSS version 11. All the results were expressed as mean ± standard deviation. ANOVA test was applied and correlation was done using Pearson's correlation test. 'p' value of < 0.05 was considered statistically significant.

Results

Table 1 reveals the thyroid profile of the cases as well as controls. There was significant increase ($p < o.o5$) in TSH levels in all the groups compared to controls. There was significant decrease ($p < o.o5$) in FT3 and FT4 levels in cases compared to controls. Table-2 shows the lipid parameters and lipid ratios in different groups. In our study mean total cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol were significantly increased ($p < 0.05$) in cases compared to controls. Our results show there is increased TC, TG's and LDL-cholesterol. Lipid ratios also increases gradually in all the groups compared to group-I i.e. control. Correlation between serum TSH with lipid parameters was shown in table 3. There is significant positive correlation ($p < 0.0001$) between TSH and TC, LDL-C, TG and HDL-C.

Table 1: Thyroid profile in different groups

Parameters	Group-I	Group-II	Group-III	Group-IV	ANOVA F	p-value	Normal Range
TSH μIU/mL	2.14±0.78	11.01±3.09	30.58±9.55	83.66±17.54	391.15	0.0001	0.4-4.5
FT3 pg/mL	2.75±0.45	2.2±1.33	2.03±0.76	1.95±0.71	4.99	0.003	1.21-4.18
FT4 pg/mL	11.15±1.5	7.75±4.98	6.78±3.28	4.97±2.72	17.8	0.0001	8.9-17.8

p < 0.05 is statistically significant. **TSH**- Thyroid stimulating hormone, **FT3**- Free triiadothyroinine, **FT4**- Free tetraiadothyronine

Table 2: Lipid profile and lipid indices in different groups

Parameters	Group-I	Group-II	Group-III	Group-IV	ANOVA F	p-value
T.C mg/dL	162.49±31.17	213.56±45.9	233.97±41.68	297.06±38.11	59.91	0.0001
LDL-C mg/dL	100.9±12.43	141.23±28.36	158.16±28.55	202.5±52.57	43.79	0.0001
TGS mg/dL	121.43±10.93	168.83±35.31	183.9±29.07	261.33±45.99	93.59	0.0001
HDL-C mg/dL	37.31±4.47	38.07±5.34	38.53±5.06	42.3±7.7	4.04	0.009
VLDL mg/dL	24.28±2.18	33.76±7.06	36.78±5.81	52.26±9.1	93.59	0.001
AI	0.52±0.34	0.64±0.11	0.68±0.01	0.81±0.25	9.01	0.0001
TC/HDL CRI-1	4.41±0.97	5.59±1.26	6.01±0.85	7.31±1.76	27.0	0.0001
LDL/HDL CRI-2	2.74±0.43	3.71±0.83	4.11±0.93	4.9±1.36	26.9	0.0001

$p < 0.05$ is statistically significant, TC-Total cholesterol, LDL-C – Low density lipoprotein cholesterol, TGS-Triglycerides, HDL-C – High density lipoprotein cholesterol, VLDL – Very low density lipoprotein, AI-Atherogenic index, CRI-1- Castellis Risk Index-1, CRI-2- Castellis Risk Index-2

Table 3: Pearson correlation of TSH with lipid parameters in hypothyroid cases

	r-value	Significance
TSH vs total cholesterol	0.747	0.0001
TSH vs LDL-C	0.710	0.0001
TSH vs triglyceride	0.821	0.0001
TSH vs HDL-C	0.338	0.0001
TSH vs VLDL	0.821	0.0001

p < 0.05 is statistically significant. **TSH** – Thyroid stimulating hormone, **TC**-Total cholesterol, **LDL-C** – Low density lipoprotein cholesterol, **TGS**- Triglycerides, **HDL-C** – High density lipoprotein cholesterol, **VLDL** – Very low density lipoprotein.

Discussion

Thyroid hormones have significant role to play in lipid metabolism. The current study showed significant increase in TC, TG, and LDL-C in hypothyroid patients compared to controls which is in accordance with other studies[16,17].

Our study also showed effect of hypothyroidism on lipid parameters is more marked in patients with higher serum TSH levels. As TSH levels goes on increasing dyslipidemia also increased. A study conducted in Andhra Pradesh on female patients, suggests that effect of hypothyroidism on the serum concentration of lipids is more marked in patients with higher serum TSH levels. Hence lipid abnormalities exhibit great individual variability and there might be a potential link between hypothyroidism and atherosclerosis[18].

Decreased thyroid secretion greatly increases the plasma cholesterol concentration because of decreased rate of conversion of cholesterol to bile acids and consequent diminished loss in the feces due to decreased number of LDL receptors on liver cells[19]. According to FA Khan significant increase in levels of TC in hypothyroid patients compared to controls[20]. Hypercholesterolemia is due to decreased activity of LDL receptors resulting in decreased receptor mediated catabolism of LDL and IDL in hypothyroidism[21].

Study done by Jiskra et al, in hypothyroidism the number of LDL receptors in the liver decreases and causes delayed clearance of LDL as a result there is an increase in overall cholesterol and LDL-C[22]. Our study results are in consistent with Ravi Shekhar and et al, who reports that total cholesterol and LDL levels were elevated in hypothyroidism and their levels decreases with treatment[23].

Hypothyroidism is associated with increased triglyceride levels. This is due to decreased activity of lipoprotein lipase (LPL), which results in decreased clearance of triglyceride rich lipoproteins[24]. Our study also revealed that there is significant increase in triglycerides in hypothyroid patients (all groups) compared to controls.

Hypothyroidism patients usually exhibit elevated levels of HDL cholesterol which is due to decreased activity of hepatic lipase. This leads to decreased catabolism of HDL2 particles leading to increased HDL[25]. Decreased activity of cholesteryl ester transport protein (CETP) results in reduced transfer of cholesteryl esters from HDL to VLDL, thus increasing HDL cholesterol levels[26]. Our study also showed

increase in serum HDL levels in hypothyroid patients of all the groups compared to control group. But study done by Lakshmi LJ and et al showed that there is significant decrease in HDL levels in hypothyroid patients compared to controls which is contradictory to our results[27].

The lipid ratio predicts cardiovascular disease risk better than isolated lipoprotein subfractions. Our study shows there is significant increase ($p < 0.05$) in TC/HDL and LDL/HDL ratios in cases compared to controls which is in accordance with study done by Khan FA[20]. The LDL-C/HDL-C is a better predictor for risk of heart disease than LDL-C alone. The several studies have found that the LDL-C/HDL-C ratio is an excellent monitor for effectiveness of lipid lowering therapies. If the ratio of TC/HDL is more than 3.5 risks is more. Similarly LDL/HDL ratio more than 2.5 is also detrimental[28].

Our study shows there is statistically significant (< 0.001) positive correlation between TSH with serum levels of TC, LDL-C, TGs and HDL-C. Study done by few authors also found that there was significant positive correlation between serum TSH values and lipid parameters[29,30].

Conclusion

Our study results reveal that there is dyslipidemia in hypothyroid patients and also suggests that the effect of hypothyroidism on lipid parameters is more marked in patients with higher serum TSH levels. Hence patients presenting with dyslipidemia are recommended to be investigated for hypothyroidism. Study also reveals the importance of calculating lipid ratios from individual lipid profile parameters without any economic burden to the patients. Lipid ratios are better indicators of dyslipidemia and cardiovascular risk in hypothyroid patients by these simple calculations.

Conflict of Interest: None
Source of Support: Nil

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