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Lipid parameters in a hypofunctioning thyroid gland

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Abstract

Background: Hypofunctioning of the thyroid gland is associated with lipid abnormalities. There is an inverse relation between the lipid parameters and the thyroid hormones. Management of such abnormalities becomes essential in hypothyroid patients to prevent any cardiovascular complications. In this study various lipid parameters were analysed in patients with overt hypothyroidism.
Methods: Lipid parameters such as total cholesterol, HDL cholesterol, triglycerides, LDL cholesterol were analysed in a total of 52 subjects which included 27 patients with overt hypothyroidism and 25 healthy controls. A serum level of total TSH of >20 uIU/L was included as overt hypothyroids in the study.
Results: The mean age of the overt hypothyroids was 39.56±13.01 years, among which 78.6% were females. There was a statistically significant increase in total cholesterol, LDL cholesterol and triglycerides among the cases with a significant decrease in HDL cholesterol.
Conclusion: Hypofunctioning of the thyroid gland is associated with deranged lipid parameters. This study shows that dyslipidemia could be a complication of overt hypothyroidism and periodic assessment of lipid profile may be essential in these patients.
Keywords: Overt hypothyroidism, Lipids, dyslipidemia, atherosclerosis.

1.Introduction

Thyroid stimulating hormone (TSH),secreted from anterior pituitary gland is controlled by a hypothalamic hormone, thyrotropin releasing hormone(TRH).The secretion is primarily regulated by a balance between the stimulatory action of hypothalamic thyroid releasing hormone (TRH) and the inhibitory influence of T_3. About 80% of T_4 is converted to T_3 by microsomal 5'-deiodinase. T_3 is therefore the more potent hormone, while T_4 is the storage form.[1]

T_3 and T_4 occur at a ratio of 1:40 in the plasma, where >99% of them, mainly T_4, are bound to plasma proteins-thyroxine-binding globulin (TBG), thyroxine-binding prealbumin (TBPA), and serum albumin. Less than 0.3% of the total T_3/T_4 in blood occurs in an unbound form and only the unbound molecules have an effect on the target cells.

Impaired production of thyroid hormones results in hypothyroidism which is usually due to a primary abnormality of thyroid gland or iodine deficiency; occasionally it is secondary to pituitary or hypothalamic disorders .[2]

Lipids are the sine qua non of atherosclerosis. Thyroid function is known to have a significant effect on the metabolism of lipoproteins increasing the overall risk of cardiovascular disease.

The thyroid hormone stimulates the synthesis of cholesterol in liver by inducing HMG-CoA reductase, the enzyme which catalyzes the conversion of HMG-CoA to mevalonate the first step in the biosynthesis of cholesterol. Deficiency of triiodothyronine (T_3) in hypothyroidism leads to decrease in number and activity of LDL receptors resulting in defective receptor mediated catabolism of LDL cholesterol. Thyroid hormones influence metabolism of HDL by increasing the activity of cholesteryl ester transfer protein (CETP). Decreased activity of the CETP in hypothyroidism results in

reduced transfer of cholesteryl esters from HDL_2 to VLDL which results in an increase in HDL_2 cholesterol levels.

Hypertriglyceridemia in hypothyroidism is due to increased synthesis of apolipoprotein B by the liver and a decrease in VLDL remnant receptor. There is decreased synthesis of lipoprotein lipase in hypothyroidism due to deficient thyroid hormone which plays a central role in the elimination of triglyceride particles. [3-5]

Thus it is necessary to assess the lipid parameters in patients with overt hypothyroidism as dyslipidemia is known to be a predisposing factor to the development of atherosclerotic coronary disease.

2. Materials and methods

After obtaining the approval from the institutional ethics committee 27 diagnosed patients with overt hypothyroidism (TSH value >20µIU/L) attending the outpatient department of A J Institute of Medical Sciences in the age group of15-75 years were recruited in the study. The results were compared with 25 age and sex matched healthy controls.

Patients with acute infections, hepatobiliary diseases, renal diseases, diabetes mellitus, heart diseases, myopathies, pregnant females were excluded from the study.

Blood was collected under aseptic precautions by venipuncture after obtaining informed consent. Serum separated after centrifugation was analysed for serum T3, T4 and TSH by chemiluminiscence method in immulite 1000 analyzer. [6-8] Serum cholesterol by enzymatic method (Cholesterol oxidase –Peroxidase 4-aminoantipyrine) [9], serum HDL cholesterol by enzymatic method after precipitation of polyanions [10], serum triglycerides by enzymatic method GPO-ESPAS (Glycerol 3 Phosphate Oxidase–Peroxidase N-Ethyl-N-Sulfopropyl-n-anisidine). [11] LDL cholesterol was measured by Friedwalds equation. [12]

2.1 Statistical methods

The data was analysed using SPSS v.17. Independent sample t test was applied to compare the variables between the two groups. Data is represented as mean & standard deviation. Pearson's correlation & logistic regression analysis was done to know the association and the independent risk factor after adjusting for the confounding variables respectively.

3. Results

In this study, the mean age of the healthy controls was 33.08±12.62 years and in overt hypothyroids it was 39.56±13.01 years .Among the controls 92 % were females and in cases 78.6%.

Comparison of the thyroid profile and the lipid parameters are shown in Table 1. The TSH levels were normal in controls and significantly increased in cases. The serum T3 & T4 levels were significantly decreased in the cases ($p < 0.001$). There was statistically significant ($p<0.001$) increase in the total cholesterol, LDL-C and triglycerides. There was significant decrease in HDL-C in comparison with the controls.

Table 2 shows Pearson's correlation analysis, there was a significant increase in LDL-C levels with decrease in serum T3 levels in the overt hypothyroid group.

Table 3 shows logistic regression analysis after adjusting for the confounding factors. It was found that the elevated triglyceride levels were independently associated with overt hypothyroidism with an odds ratio of 25.38 ($p<0.05$).

Table 1: Shows Pearson's correlation analysis

Parameter	Controls	Cases	p value*
Age (in years)	33.08±12.619	39.56±13.019	0.157
Females (n)	92% (23)	78.6% (22)	
Serum TSH	1.9198±1.18	55.89±20.98	<0.001
Serum T4	8.38±2.12	2.73±1.92	<0.001
Serum T3	107.55±29.04	60.67±28.93	<0.001
Serum Total Cholesterol	165.96±17.59	247.70±30.30	<0.001
Serum Triglycerides	92.80±36.99	186.26±58.41	<0.001
Serum HDL-C	54.40±8.53	49.41±6.84	<0.05#
Serum LDL-C	97.10±23.28	169.59±48.89	<0.001

*p value <0.001 is considered significant;#p value <0.05 is considered significant

Table 2: Correlation analysis of serum T3 & LDLC

	R value	P value
Controls	0.235	0.257
Cases	-0.381	0.05

*p value<0.05 is considered significant

Table 3: Logistics Regression analysis of LDL and TG with overt hypothyroidism

Parameter	B	Significance	Odds ratio	95 % CI	
				Lower	Upper
LDL	0.045	0.977	1.046	0.045	24.22
TG	3.234	0.044*	25.381	1.095	588.46
T3	-0.393	0.829	0.675	0.019	23.859

*p value <0.05 is considered significant

4. Discussion

Hypothyroidism is a graded phenomenon with biochemical abnormalities. Hypothyroidism is characterised by an elevated serum TSH and a decline in serum T4 and T3. This study shows that 78.6% of overt hypothyroids were females. Studies by Rizos *et al* [13] and Maugeri *et al* [14] showed that thyroid dysfunction has a great impact on serum concentrations of lipids. A general correlation between thyroid hormones and lipid metabolism is well established. Studies confirm that there is an inverse relationship between thyroxine serum levels and cholesterol. Though decreased thyroid function is accompanied by the reduced activity of HMG-CoA reductase, total cholesterol and LDL-C levels are increased in overt hypothyroidism. [15] This is mainly due to decrease in LDL receptors, resulting in decreased catabolism of LDL. [16] In the present study also there was statistically significant increase in total cholesterol in overt hypothyroids (247.70±30.30mg/dl) compared to controls (165.96±17.59mg/dl). There was statistically significant increase in LDL cholesterol in overt hypothyroids (169.59±48.89mg/dl) compared to controls (97.10±23.28mg/dl).

Study of Prieur *et al* shows that there is an elevation of triglycerides in hypothyroidism that is characterised by decreased clearance of VLDL-triglycerides which is due to reduced activity of lipoprotein lipase and hepatic triglyceride lipase. [17] There is a decrease in LPL activity decreasing the clearance of TG rich lipoproteins. [18] Overt hypothyroids are also known to present with raised TG levels with increased levels of VLDL .In this study we found a statistically significant increase in triglycerides in overt hypothyroids compared to controls ($p < 0.001$)(Table 1)

In logistics regression analysis there was a statistically significant odds ratio which showed that hypertriglyceridemia was independently associated with overt hypothyroidism.

These findings are in accordance with study by Efstathiadou *et al*[19], Costantini *et al*[20], Hueston *et al*[21] and Sheikh *et al* [22].

There was no statistically significant increase in HDL cholesterol in overt hypothyroids (49.48± 6.830mg/dl) compared to controls (54.36± 8.524). This finding is in accordance with study of Costantini *et al*.[20] According to a study by Abrams *et al*[23] hypertriglyceridemia is associated with a decrease in HDL cholesterol which was also seen in this study. A statistically significant correlation between T3 and LDL cholesterol was seen as deficiency of T3 down regulates LDL receptors.

5. Conclusion

This study was undertaken to study the pattern of the lipid profile in overt hypothyroidism. It was seen that there was an increase in levels of total cholesterol, LDL cholesterol and triglycerides in this group of patients. There was also a statistically significant negative correlation in T3 and LDL cholesterol levels. The findings of this study can be used for proper management of hypothyroid patients nevertheless more studies with follow up may be warranted for effective management.

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