

Pattern of Altered Lipid Profile in Patients with Subclinical and Clinical Hypothyroidism and its Correlation with Body Mass Index

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ABSTRACT

Objective: To compare the lipid profile of the subclinical and clinical hypothyroid patients and to evaluate the correlation between body mass index (BMI) and lipid profile in hypothyroidism.

Study Design: Cross-sectional study.

Place and Duration of Study: Islamic International Medical College, Riphah International University, Islamabad, and Citi Laboratory, Rawalpindi, from January to December 2013.

Methodology: The subjects were selected through non-probability, purposive sampling. On the basis of thyroid profile, the subjects were divided into 3 groups: euthyroids (n=20), subclinical hypothyroids (n=50), and clinical hypothyroids (n=30). The blood of these subjects was then analyzed for lipid profile. Data was analyzed using SPSS version 18 statistical software.

Results: Both hypothyroid groups showed altered lipid profile which was observed to be significantly raised when compared with the euthyroid subjects. Comparison of lipid profile in euthyroid, subclinical, and clinical hypothyroid groups showed significant differences by non-parametric tests ($p < 0.05$). An assessment of correlation of lipid profile with the BMI was found to be significant ($p < 0.01$).

Conclusion: Hypothyroidism causes alteration of lipid profile. Clinical and subclinical hypothyroid patients have altered lipid profile as compared to euthyroids. Thyroid status monitoring is very important, since it can induce changes in lipid profile. Such dyslipidemic status is significant not only for the management of thyroid disorders but also for common diseases like obesity and coronary atherosclerosis in the population.

Key Words: Hypothyroidism. Dyslipidemia. Cardiovascular complications. Body mass index. Thyroid stimulating hormone.

INTRODUCTION

Hypothyroidism is a common endocrine disorder resulting from decreased secretion of total thyroxine (T_4) and triiodothyronine (T_3) leading to insufficient thyroid activity. It is more prevalent in females than males.¹ It results from a primary process in which the thyroid gland produces insufficient amount of thyroid hormones. The most common cause of hypothyroidism worldwide is iodine deficiency, with an overall prevalence of hypothyroidism reported to be 2 - 5%.² The estimated prevalence rates of hypothyroidism and subclinical hypothyroidism in Pakistan are 4.1 and 5.4%, respectively.³ Biochemically, hyposecretion of T_4 and T_3 leads to marked increase in serum thyroid stimulating hormone (TSH) levels due to hypersecretion of pituitary TSH.⁴

It can be classified on the basis of serum level of TSH, which is a reliable index of the biological activity of

thyroid hormones into clinical and subclinical hypothyroidism.⁴ Thyroid dysfunction, particularly hypothyroidism, is associated with dyslipidemia as thyroid hormones are important modulators of intermediary metabolism.⁵ Biochemically, clinical hypothyroidism shows a marked increase in total cholesterol (TC) and low density lipoprotein (LDL) due to reduced number of LDL receptors in the liver leading to decreased fractional clearance of LDL.⁶ Some studies have reported that dyslipidemia may also be accompanied by increased serum triglycerides (TG) and decreased high density lipoproteins (HDL) in subclinical hypothyroidism.⁷

Hyperlipidemia, especially hypercholesterolemia, is a major risk factor for atherosclerosis.⁸ Atherosclerosis is a complex multi-factorial disease which develops in the arterial wall in response to various stimuli like hyperlipidemia and hypertension. Increased risk of atherosclerosis is associated with very low density lipoprotein (VLDL) which is a major component of the total serum cholesterol. By curing hypothyroidism, a leading cause of dyslipidemia, one can save on the possible long-term cost of cholesterol lowering drug therapy as well as reducing the incidence of cardiovascular events.⁶

The International Obesity Task Force has stated that the approach to obesity should be considered on the basis of regional variations.⁹ Among Asians, to define obesity, the cut-off value for BMI is 23 kg/m² and the classification

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of obesity is based on BMI values ranging from 22 to 26 kg/m². However, the clear cut demarcation of obesity is based on BMI values more than 26 kg/m².¹⁰

The relationship between obesity, lipid profile and thyroid dysfunction is a concern for researchers, and studies are being carried out to explore the correlation of these 3 conditions.¹¹ Lipid abnormalities have also been reported in obese individuals.⁷ Recently, an increasing prevalence of obesity has been observed in urban population of Rawalpindi and Islamabad.¹²

The objective of this study was to compare the lipid profile of the subclinical and clinical hypothyroid groups, and to assess, if there is an association between obesity and lipid profile in urban hypothyroid population of Rawalpindi and Islamabad.

METHODOLOGY

It was a cross-sectional study which was conducted in Islamic International Medical College, Riphah International University, Islamabad in collaboration with Citi Laboratory, Rawalpindi. Duration of study was one year from January to December 2013. Sample size was 100 subjects. Sampling technique was non-probability, purposive sampling. A total of 100 male or female subjects of 30 - 60 years of age were included in this study. To avoid the confounding factors, subjects with age < 30 years and > 60 years were excluded. Subjects having chronic illnesses such as coronary heart disease, diabetes mellitus, renal failure or pancreatitis, a history of smoking and treatment with thyroxine/anti-thyroid drugs or under treatment with tablet statin, pregnant women and women on oral contraceptives were excluded. Permission from Institutional Review Committee of Islamic Medical College, Riphah International University was obtained for the desired ethical considerations before start of the study.

A total of 100 subjects were enrolled for the study, who were referred from the outpatient departments of different hospitals for the evaluation of their thyroid function. Informed consent of subjects was obtained. They underwent thyroid function test and were grouped into euthyroid, subclinical, and clinical hypothyroid groups.

Height was measured in centimeters (cm) and weight in kilograms (kg), using a calibrated spring balance. The BMI was calculated by dividing weight (kg) with height (m²).

The blood was collected 12 - 14 hours after the last meal (fasting blood). From the median cubital vein 5 ml of blood was drawn. It was collected in vacutainer under aseptic condition for the estimation of serum fT₃, fT₄, TSH and lipid profile.

The blood samples were allowed to clot at room temperature and then centrifuged to separate the serum.

The serum so obtained was divided into 2 parts for thyroid profile and lipid profile.

For thyroid profile, first part of the serum was analyzed on immuno-analyzer Centaur CP by using an analyzer specific kit from Siemens for T₃, T₄ and TSH by the Chemiluminescence Microparticle Immunoassay (CMI) method.¹⁴

The second part of the serum was analyzed on chemistry analyzer, Dade Behring Dimensions Rx Max by using the Siemens kit for TC, TG and HDL cholesterol.¹⁴ The lipid concentration was considered to be altered when the total cholesterol was ≥ 200 mg/dl, the triglycerides were ≥ 160 mg/dl, HDL cholesterol was ≤ 35 mg/dl and LDL cholesterol was ≥ 130 mg/dl. The accuracy of the values was confirmed by quality control and reconfirmed by a repetitive assessment of the samples.

After the laboratory evaluations, subjects were grouped into: (1) Euthyroids: Subjects who had signs and symptoms of hypothyroidism but their thyroid profile (T₃, T₄ and TSH) were within normal reference values. (2) Subclinical hypothyroids (SCH): Subjects who had signs and symptoms of hypothyroidism. They had elevated TSH but their T₃ and T₄ were within normal reference value. (3) Clinical hypothyroids: Subjects who had signs and symptoms of hypothyroidism. They had elevated TSH and their T₃ and T₄ were below normal reference values.

Statistical Package for Social Sciences (SPSS) version 18 was employed for statistical analysis. The values for the lipid profile were calculated and documented as median (IQR). The normality distribution of each variable was checked separately through Shapiro Wilk test which showed skewness of data. Therefore, comparison of lipid parameters among the 3 groups was done by using appropriate non-parametric tests such as Mann-Whitney U test. The correlation between obesity and the lipid profile was evaluated by using Spearman's correlation analysis. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 150 subjects were initially included in the study through interviews and questionnaire. Out of whom, 100 were chosen for the study and grouped on the basis of thyroid profile and TSH. Among these, 20 subjects were euthyroid, whereas 50 and 30 subjects were in the categories of subclinical and clinical hypothyroids, respectively.

The lipid parameters were compared between euthyroids and subclinical hypothyroids (Table I) and between euthyroids and clinical hypothyroids (Table II). It can be observed from these tables, all parameters except LDL showed statistically significant differences between euthyroid and subclinical hypothyroid groups.

Table I: Comparison of lipid parameters between euthyroid and sub-clinical hypothyroid groups.

Lipid parameters	Euthyroid (n=20)		Subclinical (n=50)		p-value
	Median	IQR	Median	IQR	
TC (mmol/L)	164.00	52.75	263.0	80.5	< 0.001**
TG (mmol/L)	28.0	7.75	265.0	194.0	< 0.001**
HDL (mmol/L)	54.05	14.50	43.0	8.0	< 0.001**
LDL (mmol/L)	127.50	71.25	139.0	32.25	0.607

Mann-Whitney-U test was applied. **Highly Significant (p ≤ 0.01), *Significant (p ≤ 0.05)

Table II: Comparison of lipid parameters between euthyroid and clinical hypothyroid groups.

Parameters	Euthyroid (n=20)		Clinical (n=30)		p-value
	Median	IQR	Median	IQR	
TC (mmol/L)	164.00	52.75	280.0	109.75	< 0.001**
TG (mmol/L)	28.0	7.75	254.0	270.03	< 0.001**
HDL (mmol/L)	54.05	14.50	39.0	17.0	< 0.001**
LDL (mmol/L)	127.50	71.25	178.50	75.25	.023*

Mann-Whitney-U test was applied. **Highly Significant (p ≤ 0.01), *Significant (p ≤ 0.05)

Table III: Correlation between lipid parameters and obesity.

Lipid parameters	Correlation coefficient	p-value
Cholesterol	0.311	< 0.001**
Triglyceride	0.489	< 0.001**
High density lipoprotein	-0.210	<0.03*
Low density lipoprotein	0.261	<0.005**

Mann-Whitney-U test was applied. **Highly significant (p < 0.01); *Significant (p < 0.05).

All lipid parameters also showed statistically significant differences between euthyroid and clinical hypothyroid groups.

On correlating the serum levels of lipid parameters in subjects with increased BMI, serum levels of TC, TGs and LDL showed significant positive correlation with increased BMI and a negative significant correlation between serum levels of HDL and increased BMI, i.e. with obesity (Table III).

DISCUSSION

Thyroid hormones are involved in controlling metabolism of macromolecules including lipids and carbohydrates.⁵ There is a strong link between thyroid disorders and a number of common metabolic diseases including diabetes, obesity and cardiovascular diseases.¹⁵

In this study, the lipid profile and BMI of 20 euthyroid subjects were compared and evaluated with 50 subclinical and 30 clinical hypothyroid subjects. BMI values of euthyroid subjects were either normal or overweight. Out of 100 subjects, subclinical hypothyroid subjects had relatively high TSH levels (TSH > 4.94 µIU/ml). Increased levels of BMI (BMI >25) were seen in individuals within the SCH group. Clinical hypothyroid subjects had high TSH levels, i.e. > 10.0 µIU/ml. Similarly, significant increases in BMI values (BMI > 25) were seen in clinical hypothyroid group. The present study showed a high frequency of increased BMI in subclinical and clinical hypothyroid urban population of

Rawalpindi, Pakistan, strongly supporting the previously reported correlation between serum TSH levels and the degree of obesity.²⁰

In the present study, dyslipidemia was observed among obese subjects, and significantly higher levels of TC and TG's were observed in obese subjects as compared to the non-obese which concurs with the reports of the previous studies.^{10,21} Lipid abnormalities were prevalent in subclinical and clinical obese hypothyroid subjects.

The present study, observed a definite correlation between TC, TGs and LDL levels with BMI as shown in Table III. An increase in BMI was associated with a rise in TC, TGs and LDL, and a reduction in HDL levels, indicating a higher risk of cardiovascular diseases in obesity.^{22,23}

Thyroid hormones are the principal regulators of energy balance. Their role in obesity has been the focus of various scientific studies. The unfavourable effects of high levels of serum TSH on the lipid metabolism have been reported and follow-up studies have shown an increase in the risk of development of atherosclerosis and cardiovascular manifestations in clinical hypothyroid subjects with high normal serum TSH levels.^{5,7,24}

Genetic and environmental factors play an important role in the progression of such differences in BMI with deviation in thyroid functions. Such variations are probably caused by a number of environmental factors in hilly areas of Rawalpindi, of which, iodine intake level seems to be of prime importance.^{22,25}

In 2012, the clinical practice guidelines for hypothyroidism in adults, sponsored by the American Association of Clinical Endocrinologists (AACE) and the American Thyroid Association, recommended 4.12 mU/L as the upper limit of normal for TSH.²⁴

Based on the AACE guidelines, the number of subclinical subjects having high serum TSH levels is increasing, which is quite significant. TSH > 10 mU/L was found in clinical hypothyroid subjects as per the laboratory reference range. The importance of diagnosing mild thyroid disorders and subclinical hypothyroidism cannot be underestimated because if not treated, they can severely compromise the quality of life. There is an established association between clinical thyroid dysfunction and weight changes because weight gain is a consistent phenomenon in hypothyroidism.²⁴ Some studies have concluded that weight gain increases serum levels of TSH, while others showed no relationship between TSH and body weight.²⁵ A high frequency of increased serum TSH levels was observed in the urban population of Rawalpindi. This study area is an endemic area for iodine deficiency.

This study is helpful in interpreting the trends of increased BMI with increased levels of TSH in the urban community of Rawalpindi.

CONCLUSION

Thyroid dysfunction can have important effects on lipid profile in clinical as well as subclinical hypothyroidism. Thyroid hormone profile, lipid profile, and BMI correlate significantly among the hypothyroid subjects. There is a need to monitor patients with hypothyroidism for signs of obesity and various cardiovascular complications. Screening and treatment for subclinical hypothyroidism should be implemented to prevent its adverse effects on lipid metabolism.

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