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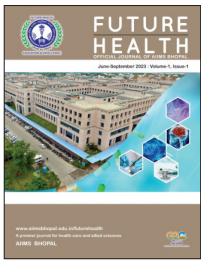

Original Article

Study of inter-relationship of thyroid and lipid profiles in obese individuals

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ABSTRACT

Objectives: Hypothyroidism may contribute to the development of atherosclerosis by increasing the quantity of LDL particles and enhancing LDL oxidability. Thyroid failure is also linked to hyperhomocysteinemia. Additionally, hypothyroidism is associated with arterial hypertension and a hypercoagulable state. Individuals with subclinical hypothyroidism have significantly higher total cholesterol, LDL cholesterol, apolipoprotein B, and Lipoprotein (a). We hypothesize that the major coronary risk factors are positively correlated with generalized obesity. In line with this, our study was designed to examine the correlation between thyroid and lipid profiles in obese individuals.

Material and Methods: This observational study was conducted at a tertiary care center in central India. The study included 101 individuals who presented to the institute during the study period and were diagnosed with obesity. Each subject was evaluated for body weight, height, BMI, and waist circumference (WC). Fasting peripheral venous blood samples were obtained for the estimation of serum lipids (S. Triglycerides, S. Cholesterol, S. HDL cholesterol, and S. LDL cholesterol) and the serum thyroid profile (S.TSH, S. T3, S. T4).

Results: In our study, 96 males and 120 females were included. A significant association was found between TSH and total cholesterol ($r=0.295$, $p=0.003$), TSH and LDL ($r=0.342$, $p<0.001$), T3 and triglyceride ($r=-0.250$, $p=0.012$), T3 and HDL ($r=0.244$, $p=0.014$) and T4, triglyceride ($r=-0.216$, $p=0.030$) and T4 and HDL ($r=0.319$, $p=0.049$).

Conclusion: In our study, we found that thyroid and lipid profiles are significantly inter-related in obese individuals. Hypothyroidism is more commonly associated with lipid abnormalities, characterized by increased serum total cholesterol, triglycerides, LDL cholesterol, and decreased HDL cholesterol. Therefore, clinicians should remain highly suspicious of obese middle-aged females with hypothyroidism for abnormalities in their lipid profile, which may enhance the risk of atherosclerosis, leading to coronary artery disease.

Keywords: Hypothyroidism, Dyslipidemia, Coronary artery disease

INTRODUCTION

Indian surgeon Sushruta (sixth century BC) related corpulence with diabetes and heart disorders.[1] Corpulence has reached epidemic proportions in India in the 21st century, with a prevalence of about 5% of the nation's population. According to the National Family Health Survey-4 (NFHS), the prevalence of overweight or obesity (BMI ≥ 25 Kg/m^2) in Madhya Pradesh is 10.9% in males and 13.6% in females.[2]

Moderate elevations of TSH are associated with changes in lipid levels that could influence cardiovascular health. Notably, modifications in thyroid function result in changes in the composition and transport of lipoproteins. Thyroid dysfunctions often go undetected and may

be linked to adverse health outcomes.[3] The alterations in the lipid profile can be explained by the regulatory effect of thyroid hormones on the activity of key lipoprotein metabolic enzymes.

Thyroid hormones exert regulatory effects by inducing the 3-hydroxy-3-methyl-glutaryl-coenzyme A (HMG-CoA) reductase, an enzyme that catalyzes the conversion of HMG-CoA to mevalonate, the first step in the biosynthesis of cholesterol. Thyroid hormones stimulate hepatic de novo cholesterol synthesis.[4-6] They also activate LDL receptors because the promoter of the LDL receptor gene contains a tri-iodo-thyronin (T3) responsive element (TRE), which regulates the gene expression of this receptor. The cholesteryl ester transfer protein (CETP), an enzyme that transports cholesteryl esters from HDL to the very low density lipoprotein (VLDL) and intermediate-density lipoproteins (IDL), and triglycerides in the opposite direction, is also affected by these hormones. Thyroid hormones inhibit LDL oxidation due to specific binding sites for thyroxine on apolipoprotein B and stimulate lipoprotein lipase (LPL), an enzyme that catabolizes triglyceride-rich lipoproteins. Hepatic lipase (HL) hydrolyzes HDL2 to HDL3 and catabolizes IDL to LDL.[5,6]

Hypothyroidism may contribute to the development of atherosclerosis by increasing the quantity of LDL particles and enhancing LDL oxidability.[7] Thyroid failure is also associated with hyperhomocysteinemia.[8] Hypothyroidism is linked to arterial hypertension and a hypercoagulable state.[9] Individuals with subclinical hypothyroidism have significantly higher total cholesterol, LDL cholesterol, apolipoprotein B, and lipoprotein (a).[10]

We hypothesize that the major coronary risk factors are positively correlated with generalized obesity. In this regard, our study was designed to study the correlation between thyroid and lipid profiles in obese individuals. Aim of this study was to determine the correlation between thyroid function and lipid profile in obese individuals. Objective of this study was to determine relationship between obesity and thyroid function test.

MATERIAL AND METHODS

This observational study was conducted at the Department of Medicine, Sri Aurobindo Institute of Medical Sciences & Post Graduate Institute, Indore, from December 2018 to May 2023. The study included 101 individuals who presented to the institute during the study period and were diagnosed with obesity.

Inclusion Criteria: Individuals aged 18-80 years, individuals with BMI >25 Kg/m^2, and those who provided written consent to participate in the study.

Exclusion criteria: Individuals taking medication affecting thyroid function such as glucocorticoid, antiepileptic, and contraceptive drugs, pregnant women, individuals with chronic kidney disease, previously diagnosed diabetes mellitus, diseases affecting thyroid function and lipid profile.

Methodology: Purposive sampling was used to select 101 individuals diagnosed with obesity who met the JAPI criteria for Asian Indians. Informed written consent was obtained from all patients or their legally acceptable representatives. Each subject was evaluated for body weight, height, BMI, and waist circumference (WC). Fasting peripheral venous blood samples were collected for the estimation of serum lipid (S. Triglycerides, S. Cholesterol, S. HDL cholesterol, and S. LDL cholesterol) and serum thyroid profile (S.TSH, S. T3, S. T4). Laboratory investigations were performed at the Department of Biochemistry, Sri Aurobindo Medical College & Post Graduate Institute, Indore. The reference range for TSH value was considered to be 0.5 to 5.5 μIU/mL. Participants with TSH levels between 5.5 and 10 μIU/mL and normal T3 and T4 levels were classified as subclinical hypothyroidism, while those with TSH levels <0.5 μIU/mL and normal T3 and T4 levels were classified as subclinical hyperthyroidism.[11]

Statistical Analysis Plan: The data collected from the customized proforma were entered into a Microsoft Excel spreadsheet and subsequently transferred to the relevant statistical software package for analysis (SPSS). Continuous variables with a normal distribution were expressed as mean ± SD. Correlation analysis was performed using Karl Pearson's correlation coefficient. A 'P' value less than 0.05 was considered statistically significant, while a p-value greater than 0.05 was regarded as indicating no significant difference.

RESULTS

In our study, a total of 96 males and 120 females were included [Figure 1]. The highest number of subjects in our study had BMI between 25 and 30 Kg/m^2 (60.4%) followed by those with 30 and 35 Kg/m^2 (32.7%) and those >35 Kg/m^2 (6.9%). The most prevalent age group was found to be between 40 and 50 years (35.6%), followed by 30 and 40 years (21.8%), and 50 and 60 years (17.8%) [Tables 1 and 2].

A significant association was found between BMI and TSH (r=0.266, p=0.007) in our study, showing a positive correlation, while T3 and T4 were negatively correlated but not significantly. No significant association were found between WC and Thyroid Profile in our study [Table 3].

DISCUSSION

Urbanization is associated with a higher prevalence of obesity in developing countries. The primary changes related to urbanization include reduced physical movement, increased

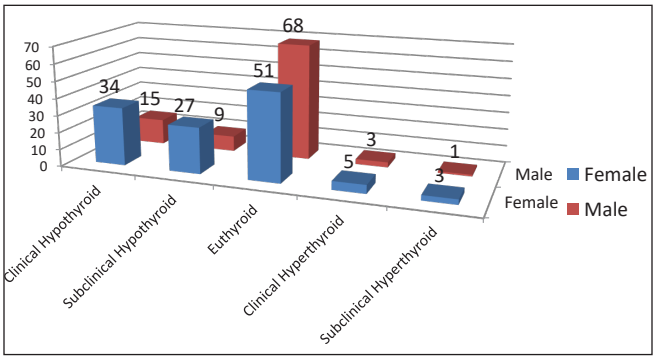

Figure 1: Distribution of study population according to thyroid status.

Table 1: Distribution of study population according to thyroid status.

Thyroid Status		Female	Male
Hypothyroid	Clinical	34	15
	Subclinical	27	9
Euthyroid		51	68
Hyperthyroid	Clinical	5	3
	Subclinical	3	1

Table 2: Correlation between thyroid profile and lipid profile.

		TC	TG	LDL	HDL
TSH (μIU/mL)	r	0.295	0.167	0.342	0.030
	p	0.003	0.095	<0.001	0.763
T3 (ng/mL)	r	-0.171	-0.250	-0.123	0.244
	p	0.087	0.012	0.222	0.014
T4 (mg/dL)	r	-0.127	-0.216	-0.127	0.319
	p	0.205	0.030	0.207	0.049

A significant association was found between TSH and total cholesterol (r=0.295, p=0.003), TSH and LDL (r=0.342, p<0.001), T3 and triglycerides (r=-0.250, p=0.012), T3 and HDL (r=0.244, p=0.014) and T4 and triglycerides (r=-0.216, p=0.030) and T4 and HDL (r=0.319, p=0.049). TC: Total cholesterol, TG: Triglyceride, LDL: Low density lipoprotein, HDL: High density lipoprotein, TSH: Thyroid stimulating hormone

consumption of high-calorie foods, and increased stress.[12] The prevalence of dyslipidemia typically ranges from 10 to 73%. Serum triglyceride levels are most elevated in urban Asian Indians living in India and migrant Asian Indians.[13] The highest levels of HDL-cholesterol among Asian Indians have been observed in physically active Asian Indians residing in rural India.

Nearly 42 million people in Asia are affected by thyroid disorders.[14] Thyroid disorders are the most common endocrine disorder in India and are more frequent in women. Similar findings were observed in our study. We found a statistically significant positive correlation between BMI and TSH (r=0.266, p=0.007); similar results were reported by

Table 3: Correlation of BMI and WC with thyroid and lipid profiles.

		TSH	T3	T4	TC	TG	LDL	HDL
BMI (Kg/m^2)	r	0.266	-0.126	-0.129	0.100	0.194	0.179	-0.085
	p	0.007	0.208	0.200	0.320	0.051	0.073	0.397
WC (cm)	r	0.008	-0.062	-0.085	0.683	0.032	0.035	-0.107
	p	0.936	0.538	0.397	0.049	0.827	0.727	0.287

BMI: Body mass index, WC: Waist circumference, TSH: Thyroid stimulating hormone, LDL: Low density lipoprotein, HDL: High density lipoprotein, TC: Total cholesterol, TG: Triglyceride

Gulias-Herrero *et al.*[15] (r=0.266, p=0.007), Marzullo *et al.*[16] (r=0.05, p=0.09) explaining the relationship between obesity and hypothyroidism. Despite higher plasma TSH levels, TSH receptors are less expressed in adipocytes of obese people. This reduced expression of TSH receptor may downregulate thyroid hormone receptors and thyroid hormone activity, resulting in elevated plasma TSH and FT3 levels while creating a thyroid hormone deficit. This condition could be reversed by weight loss, which restores the capacity to develop adipocytes.[17]

In our study, a significant positive correlation was found between TSH levels and total and LDL cholesterol. Our findings were consistent with Jiffri *et al.*[18], Shashi *et al.*[19], Patel *et al.*[20], Khan *et al.*[21] However, Natah *et al.*[22] found a negative non-significant correlation between these parameters. As demonstrated by the studies mentioned, correcting hypothyroidism can help reduce lipid abnormalities, thereby lowering the risk of cardiovascular disease.

In the current study, a significant negative correlation is found between T3 and T4 levels and triglyceride levels. These findings align with Jiffri *et al.*[18] and Shashi *et al.*[19] Hypertriglyceridemia, associated with increased levels of VLDL and sometimes fasting chylomicronemia is commonly observed in this population. These elevations are attributed to the decreased action of LPL, which results in reduced clearance of triglyceride-rich lipoproteins.[23,24]

In our study, a positive correlation is found between T3, T4, and HDL cholesterol. Identical findings were reported by Jiffri *et al.*[18] and Shashi *et al.*[19] Hypothyroid patients usually have elevated levels of HDL cholesterol, primarily due to an increased concentration of HDL2 particles. The decreased activityof CETP results in decreased exchange of cholesteryl esters from HDL to VLDL, while diminished action of the hepatic lipase prompts diminished catabolism of HDL2 particles.[25-27]

This study showed that total cholesterol, LDL cholesterol, and serum triglycerides are elevated in patients with subclinical hypothyroidism, while high-density lipoprotein (HDL)

cholesterol and Lp(a) remain unaltered. Clinical studies have not shown an effect of thyroid hormone treatment on serum lipid levels in patients with subclinical hypothyroidism.[28]

CONCLUSION

In our study, we found that thyroid and lipid profiles are significantly interrelated in obese individuals. Hypothyroidism is more commonly associated with lipid abnormalities, characterized by increased serum total cholesterol, triglycerides, LDL cholesterol, and decreased HDL cholesterol. Therefore, clinicians should remain highly vigilant in suspecting lipid profile derangements in obese middle-aged females with hypothyroidism, as these abnormalities may increase the risk of atherosclerosis, potentially leading to coronary artery disease.

Author contributions

SB, AJ: Study conception and design; AJ: Data collection; SB, AS: Analysis and interpretation of results; AS, AJ: Draft manuscript preparation. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The research/study approved by the Institutional Review Board at SAIMS Indore, number SAIMS/IEC/2016/16, dated 25th November 2016.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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