



Original Article

An investigation of correlation of hypothyroidism with abnormalities in levels of lipid profile constituents-A case-control study

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Abstract

Objective: To investigate correlation of hypothyroidism with abnormalities in levels of lipid profile constituents in a tertiary care hospital.

Methods: This was a case control study. The study group (cases) comprised of 50 subjects with hypothyroidism (22 subclinical hypothyroid and 28 overt hypothyroid). A total of 25 healthy subjects (controls) were also included in the study. Adults patients aged 18-60 years either of sex and high TSH contents ($>5 \mu\text{IU/mL}$) were included in the study. Fasting (12 to 14 hours) blood specimen (5 ml) from ante-cubital vein by venipuncture method in a vacutainer without anti-coagulant was collected and transferred to the laboratory under aseptic and cold conditions.

Results: Analysis of variance showed that T_3 , T_4 and TSH were significantly ($p < 0.005$) different among the groups. The post-hoc tests revealed that T_3 was found to be significantly ($p < 0.01$) higher among controls (106.94 ± 29.36) than overt hypothyroid (65.55 ± 37.83) patients. The post-hoc tests revealed that cholesterol, LDL and triglycerides were significantly ($p < 0.01$) different to each other groups. T_3 and T_4 were significantly ($p < 0.01$) negatively correlated with all the lipid profile evaluated. However, TSH was significantly ($p = 0.0005$) positively correlated with all the lipid profile evaluated.

Conclusion: Hypothyroid patients with decreased levels of T_3 & T_4 and increased levels of TSH are more susceptible to hypercholesterolemia, hyper triglyceridemia, compared to overt hypothyroid.

Keywords: Hypothyroidism, Lipid profile, Correlation.

Introduction

Hypothyroidism is a commonly prevalent endocrine disorder wherein gland becomes underactive and releases insufficient amount of thyroid hormone. Clinical presentation is well established; the classical changes include the slowing of physical and mental activities and that of all the body systems. Thyroid plays a vital role in digestion, heart & muscle function, brain

development, and maintenance of bones. The spectrum of clinical symptoms include fatigue, loss of energy, lethargy, weight gain, decreased appetite, cold intolerance, dry skin, hair loss, sleepiness, muscle pain, joint pain, weakness in the extremities, depression, emotional lability, mental impairment, forgetfulness, impaired memory, inability to concentrate, constipation, menstrual disturbances, impaired fertility,

decreased perspiration, paresthesia and nerve entrapment syndromes, blurred vision, decreased hearing, fullness in the throat, hoarseness, neck pain, sore throat, or low-grade fever (Hashimoto thyroiditis) (Bello and Bakari, 2012).

Hypothyroidism is mainly of two types (i) overt hypothyroidism (OHT), and (ii) subclinical hypothyroidism (SHT). OHT is characterized biochemically by an increase in serum TSH levels and a decrease in serum T₃ and T₄ concentrations to levels below normal; whereas SHT is characterized by mild elevation in TSH and T₃ and T₄ levels within normal range (American Association of Clinical Endocrinologists, 2002).

Thyroid gland secretes hormone T₃ and T₄ i.e. triiodothyronine and thyroxine respectively. These are iodine containing substances of physiological significance. Thyroid hormone regulates basic metabolic rate of target organs and is essential for normal growth of the human body (Guerrero et al, 1999). Cells of thyroid gland enrich actively the iodide ions from plasma. A normal thyroid gland produces all of circulating T₄ and about 20% of circulating T₃ (Surks et al, 2004). The T₄, a pro-hormone, is converted to T₃ (the active form of thyroid hormone). Nearly 80% of serum T₃ is derived from de-iodination of T₄ in peripheral tissues (Surks et al, 1973).

The objective of this study was to investigate correlation of hypothyroidism with abnormalities in levels of lipid profile constituents in a tertiary care hospital.

Material and Methods

This was a case control study conducted in the Department of Biochemistry, Hind Institute of Medical Sciences (HIMS), Safedabad, Barabanki, Uttar Pradesh. Patients attending Medicine OPD at HIMS were included in the study. The study group (cases) comprised of 50 subjects with hypothyroidism (22 subclinical hypothyroid and 28 overt hypothyroid). A total of 25 healthy subjects (controls) were also included in the study. Adults patients aged 18-60 years either of sex and high TSH contents

(>5 µIU/mL) were included in the study. Subjects with active infection, history of smoking in recent past, on treatment of diabetes, hypertension, malignancy, pituitary & rheumatologic diseases, on drugs affecting TSH, T₃ and T₄ levels (for example β blockers, dopamine, proton, pump inhibitors) and after radiation treatment or thyroidectomy were excluded from the study. The study was approved by the Ethical Committee of the Institute and consent was taken from each participant before including in the study.

Methods

Fasting (12 to 14 hours) blood specimen (5 ml) from ante-cubital vein by venipuncture method in a vacutainer without anti-coagulant was collected and transferred to the laboratory under aseptic and cold conditions. Serum was separated after clotting the blood and centrifugation at 3,000 rpm for 5 min at room temperature. Serum samples were analyzed immediately or if needed stored at -20°C until analysis.

Lipid Profile estimation

- A. *Estimation of Serum Total Cholesterol:* Enzymatically by coupled reaction method
- B. *Estimation of Serum Triglyceride:* Enzymatically by coupled reactions.
- C. *Estimation of Serum HDL cholesterol:* by blocking apo B containing lipoproteins and measuring cholesterol enzymatically
- D. *Estimation of Serum LDL Cholesterol* using formula

$$\begin{aligned}
 [\text{TC}] &= [\text{VLDL-C}] + [\text{LDL-C}] + [\text{HDL-C}] \\
 &= [\text{TC}] - [\text{HDL-C} + \text{TG}/5],
 \end{aligned}$$

values in mg/dL.

Thyroid Function Tests

- **Thyroid Function Test (TSH):** Using chemiluminescent (Autodelfia method)
- **Triiodothyronine (T3):** Using chemiluminescent method
- **Thyroxine (T4):** Using chemiluminescent method

Statistical Analysis

The results are presented in frequencies, percentages and mean±SD. The Chi-square test was used to compare categorical/dichotomous variables. The one way analysis of variance (ANOVA) followed by Bonferroni post-hoc tests was used to compare continuous variables among the groups. The Pearson correlation coefficient was calculated. The p-value<0.05 was considered significant. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

The mean age of controls, subclinical hypothyroid and overt hypothyroid group was 33.08±12.61, 38.95±13.08 and 39.56±13.01 years respectively. Majority of cases and controls were males. There was no significant (p>0.05) difference in age and sex among the groups showing comparability of the groups in terms of age and sex (Table-1).

Analysis of variance showed that T₃, T₄ and TSH were significantly (p<0.005) different among the groups. The post-hoc tests revealed that T₃ was found to be significantly (p<0.01) higher among controls (106.94±29.36) than overt hypothyroid (65.55 ± 37.83) patients. T₃ was also significantly (p<0.01) among patients of subclinical hypothyroid (96.19 ± 32.78) than overt hypothyroid (65.55 ± 37.83). Almost similar pattern was observed for T₄ and reverse was for TSH (Table-2).

The analysis of variance showed that there was significant (p=0.0005) difference in cholesterol, LDL and triglycerides among the groups. The post-hoc tests revealed that cholesterol, LDL and triglycerides were significantly (p<0.01) different to each other groups (Table-3).

T₃ and T₄ were significantly (p<0.01) negatively correlated with all the lipid profile evaluated. However, TSH was significantly (p=0.0005) positively correlated with all the lipid profile evaluated (Table-4).

Table-1: Age and sex distribution among the groups

Age and sex	Controls (n=25)	Subclinical Hypothyroid (n=22)	Overt Hypothyroid (n=28)	p-value ¹
Age in years, mean±SD	33.08±12.61	38.95±13.08	39.56±13.01	0.15
Sex, no. (%)				
Male	23 (92.0)	18 (81.8)	22 (78.6)	0.39
Female	2 (8.0)	4 (18.2)	6 (21.4)	

¹ANOVA/Chi-square test

Table-2: Comparison of T₃, T₄ and TSH among the groups

Parameters	Controls (n=25)	Subclinical Hypothyroid (n=22)	Overt Hypothyroid (n=28)	p-value ¹
T ₃ (ng/dl)	106.94±29.36 ^a	96.19 ± 32.78 ^b	65.55 ± 37.83 ^{a,b}	<0.0005*
T ₄ (µg/dl)	8.36 ± 2.13 ^a	6.52 ± 2.54 ^b	3.12 ± 3.03 ^{a,b}	<0.0005*
TSH (µIU/ml)	1.91 ± 1.18 ^a	11.20 ± 4.6 ^b	66.10 ± 34.47 ^{a,b}	<0.0005*

¹ANOVA test, *Significant, ^{a,b}p<0.01 (Post-hoc tests)

Table-3: Comparison of lipid profile among the groups

Parameters	Controls (n=25)	Subclinical Hypothyroid (n=22)	Overt Hypothyroid (n=28)	p-value ¹
Total cholesterol (mg/dl)	163.4±18.84 ^a	197±48.66 ^a	262.22±43.92 ^a	0.0005*
HDL-cholesterol (mg/dl)	54.36± 8.52	52.09± 8.75	49.48± 6.830	0.09
LDL-cholesterol (mg/dl)	97.58± 23.08 ^b	121.80 ± 49.12 ^b	176.68 ± 37.89 ^b	0.0005*
Triglycerides (mg/dl)	92.80 ±36.99 ^c	135.64 ± 48.92 ^c	185.93 ± 58.60 ^c	0.0005*

¹ANOVA test, *Significant, ^{a,b,c}p<0.01 (Post-hoc tests)

Table-4: Correlation of T₃, T₄ and TSH with lipid profile parameters in overt & subclinical in hypothyroid

Parameters	Lipid profile	r value	P value
T ₃ ng/dl	Total cholesterol	-0.42	0.0005*
	LDL cholesterol	-0.33	0.003*
	Triglycerides	-0.37	0.001*
T ₄ µg/dl	Total cholesterol	-0.62	0.0005*
	LDL cholesterol	-0.55	0.0005*
	Triglycerides	-0.48	0.0005*
TSH µIU/ml	Total cholesterol	0.73	0.0005*
	LDL cholesterol	0.69	0.0005*
	Triglycerides	0.65	0.0005*

Discussion

A statistically significant decrease in T₃ and the T₄ was observed in subclinical hypothyroid and in overt hypothyroid compared to control group. A statistically significant increase in TSH was seen in subclinical hypothyroid and in overt hypothyroid compared to controls. These findings were in accordance with study of Tayal et al (2009). Further, a pair wise comparison of T₃, T₄ and TSH showed that the mean difference in T₃ and T₄ between controls and subclinical hypothyroid was statistically significant. These findings were in accordance with the study of Nananda et al (2004).

The mean difference of T₃ and T₄ between controls and overt hypothyroid was also statistically significant (p<0.05). These findings are in accordance with study of Tayal et al (2009) who claimed that T₃ and T₄ were significantly lower in subclinical and overt hypothyroid than controls. Thyroid dysfunction has a great impact on serum concentrations of lipids (Rizos et al, 2011; Maugeri et al, 1999). Substitution therapy is beneficial for patients with overt hypothyroidism improving lipid profile. However, whether subclinical hypothyroidism should be treated or not is a matter of debate. A general correlation between thyroid hormones and lipid metabolism is well established. Studies confirm the presence of an inverse relationship between thyroxin serum levels and cholesterol. Other studies demonstrate the influence of iodothyronine on the catabolism of VLDL, showing increase in LDL and VLDL fractions in untreated

hypothyroidism. The data concerning a definite correlation between thyroid hormones and triglyceride is more controversial. Elevation of triglycerides in hypothyroidism characterized by decreased clearance of VLDL-triglycerides due to reduced activity of lipoprotein lipase and of hepatic triglycerid lipase is reported by Prieur et al (2005).

In the present study, there was statistically significant increase in total cholesterol of subclinical hypothyroid and overt hypothyroid as compared to controls. Statistically significant increase was observed also in LDL cholesterol of subclinical hypothyroid and overt hypothyroid compared to controls. Statistically significant increase was also found in triglycerides of subclinical hypothyroid and overt hypothyroid compared to controls (p<0.01). These findings are in accordance with other studies (Efstathiadou et al, 2001; Costantini et al, 1998; Hueston and Pearson, 2004; Sheikh et al, 2009; Adrees et al, 2009).

Our study showed an insignificant increase in the mean difference of total cholesterol and LDL cholesterol between controls and subclinical hypothyroid. This finding is similar to the observation of Hueston and Pearson (2004).

HDL cholesterol was found to remain unchanged in subclinical hypothyroid and overt hypothyroid compared to controls. This observation is similar to reports from Costantini et al (1998). However, Abrams and Grundy (1981) have reported hyper-

triglyceridemia along with decreased HDL cholesterol level.

Pair wise comparison of parameters of lipid profile showed that the mean differences in total cholesterol, LDL cholesterol and triglycerides between subclinical and overt hypothyroid were statistically significant ($p < 0.01$). Prakash and Lal (2006) have reported similar observation. Their study demonstrates that effect of hypothyroidism on lipid metabolism is more marked in patients with higher serum TSH levels. The mean difference of LDL cholesterol in subclinical hypothyroid compared to controls was insignificant. It has been observed by Hueston and Pearson (2004) also showing insignificant increase in LDL cholesterol among subclinical hypothyroid. The cause may be a less variation in thyroid hormones.

There was a statistically significant positive correlation between TSH and total cholesterol, LDL cholesterol and triglycerides among hypothyroid patients. This observation is in accordance with study done by Prakash and Lal (2006) which demonstrates that the effect of hypothyroidism in the lipid metabolism is more marked in patients with higher serum TSH levels. A statistically significant negative correlation was seen between T_3 and total cholesterol and LDL cholesterol as deficiency of tri-iodothyronine down regulates LDL receptors.

One of the limitations of this study was small sample size. The studies with larger sample size and with long study duration are recommended to have robust findings.

Conclusion

Hypothyroid patients with decreased levels of T_3 & T_4 and increased levels of TSH are more susceptible to hypercholesterolemia, hypertriglyceridemia, compared to overt hypothyroid. Dyslipidemia complications of hypothyroidism like hypercholesterolemia, atherosclerosis, can be prevented by

monitoring thyroid hormone levels along with periodic assessment of lipid profile in hypothyroid patients.

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