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Association between Anti-thyroid Antibody and Dyslipidemia In patient with hypothyroidism

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ABSTRACT

Thyroid disease is common in the general population. Hypothyroidism is often associated with elevated serum levels of total cholesterol, LDL-C and triglycerides. Thyroid hormone (TH) affects the production, clearance and transformation of cholesterol, but current research shows that thyroid-stimulating hormone (TSH) also participates in lipid metabolism independently of TH. Therefore, the mechanism of hypothyroidism-related dyslipidemia is associated with the decrease of TH and the increase of TSH levels. The current review focuses on the updated understanding of the mechanism of hypothyroidism-related dyslipidemia. To demonstrate the relationship between the hypothyroidism and dyslipidemia and anti-thyroid antibody. This case control study was carried out on 162 adult subjects, 54 patients with overt hypothyroidism and 54 patients with subclinical hypothyroidism attended the Endocrine out-patient clinic in Internal Medicine Department, Faculty of Medicine, and Zagazig University Hospitals. The patients were divided into three groups Group (A): 54 subjects euthyroid (control), Group (B): 54 cases with SCH, and Group (C): 54 cases with Overt hypothyroidism. The results showed that TSH was significantly lower among control group with no significant difference between other two groups but regard FT3 and FT4 were significantly lower among Overt hypothyroidism Group with no significant difference between other two groups TG antibody significantly positive correlated with TAG in Overt group. TG antibody significantly positive correlated with TPO in Sub group. But No significant correlation in Control group. Thyroid dysfunction is one of the most common endocrine disorders and hypothyroidism might be associated with dyslipidemia by different mechanisms. Anti-thyroid antibody is an important index that reflects the prognosis of SH, and also aggravates vascular endothelial dysfunction leading to atherosclerosis. Anti-thyroid antibodies may also affect blood lipid level, thereby increasing the risk of cardiovascular disease.

1. INTRODUCTION

Thyroid hormones secreted by thyroid glands are important metabolic hormones regulating energy homeostasis and have control over carbohydrate and lipid metabolism [1]. Hypo and hyperthyroidism result in derangement of intermediary metabolism altering body weight, insulin resistance, and lipid profile [2]. One of the most important causes of diabetes mellitus, metabolic syndrome, and obesity is insulin resistance [3]. The thyroid axis is a classic example of an endocrine feedback loop. Hypothalamic Thyrotropin Releasing Hormone (TRH) is an important regulator of the hypothalamic-pituitary-thyroid gland axis, which causes the secretion of TSH, which in turn, stimulates thyroid hormone synthesis and secretion, all under negative feedback control [4]. Hypothyroidism is associated with decreased levels of T3, T4, and increased TSH, causing increased body weight with increased plasma lipids and lipoproteins. It is seen that the plasma lipid profile is increased in hypothyroidism and vice versa [2], [5].

Hypothyroidism. Reduced glucose absorption from the gastrointestinal tract accompanied by prolonged peripheral glucose accumulation; gluconeogenesis, diminished hepatic glucose output and reduced disposal of glucose are hallmarks of hypothyroidism [6]. Insulin resistance and oxidative stress are induced by dyslipidemia via a vice vicious cycle [1], [7]. Thyroid disease also promotes insulin resistance, hypertension, inflammation, oxidative stress, and coagulation deficits, independently of dyslipidemia. Therefore, thyroid disease with dyslipidemia plays an important role in the multifactorial origin of atherosclerosis [8], [9].

2. Patients and Methods

This case control study was carried out on 162 adult subjects,54 patients with overt hypothyroidism and 54 patients with subclinical hypothyroidism attended the Endocrine out-patient clinic in Internal Medicine Department, Faculty of Medicine, Zagazig University Hospitals from March 2021 to October 2021, and another group of 54 euthyroid individuals were enrolled as a control group. The patients were divided into three groups: Group (A): 54 subject's euthyroid (control), Group (B): 54 Patients with Subclinical hypothyroidism, and Group (C): 54 Patients with Overt hypothyroidism.

An informed consent was obtained from each patient, control or their legal guardians before enrolment in the study. This study was approved from the Institutional Review Board (IRB) of Zagazig University.

Inclusion Criteria: Patients (within the age group 15-65 years) diagnosed according to ATA with Overt hypothyroidism will be included in the study group. Patients diagnosed with subclinical hypothyroidism (SCH). SCH is defined as TSH (Thyroid Stimulating Hormone) levels above the upper defined limits with FT3 and FT4 in the reference ranges(0.35-5.5mIU/ml)/FT3(2.8-7.1)/FT4(12-22)pmol/l. Age and gender-matched healthy individuals will be taken as controls.

Exclusion Criteria:

- Known cases of diabetes mellitus, hypertension, liver and renal disorders, congestive cardiac failure, any Patients with infection/illness
- Patients' intake of medicines like statins, oral contraceptive pills, or Patients with a history of steroid use.
- Pregnant were excluded from the study
- Alcoholics and smokers.
- Obese patients, BMI not more than 30.

All cases were subjected to:

1. Full medical history including; age, family history, educational level, structured questionnaire (current or previous diseases, use of medication, and smoking).
2. Complete clinical examination.

3. Anthropometric measurement (weight, height, and BMI).
4. Laboratory findings including FBG, HbA1C, Lipid profile, Thyroid hormones, Serum TSH, Free T3, FreeT4, Thyroid Peroxidase Antibody (TPO), and Thyroglobulin Antibody

2.1 Statistical Analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) (Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent multiple groups by ANOVA or Kruskal Wallis, correlation by Pearson's correlation or Spearman's. P value was set at <0.05 for significant results & <0.001 for high significant result.

3. Results

Age was distributed as 41.96±14.62, 41.74±13.89 and 35.29±8.73 respectively with no significant difference among groups also there was no significant difference regard Weight or height or BMI but regard sex distribution female was significantly associated with Subclinical hypothyroidism Group (Table 1).

Table 1: Demographic data distribution among studied groups

			Control Group (A)	Subclinical hypothyroidism Group(B)	Overt hypothyroidism Group(C)	F	P
AGE			35.29±8.73	41.74±13.89	41.96±14.62	2.521	0.087
WEIGHT			68.35±7.35	65.83±4.85	66.11±7.52	1.214	0.298
HIGHT			167.48±7.66	159.20±32.28	165.03±8.71	1.289	0.255
BMI			24.29±0.92	24.14±1.07	24.50±0.81	1.107	0.351
SEX	**Female**	**N**	32	50	36		
		%	59.3%	92.6%	66.7%		
	Male	**N**	22	4	18	11.36	0.011
		%	40.7%	7.4%	33.3%		
Total		**N**	54	54	54		
		%	100.0%	100.0%	100.0%		

Cholesterol and triglyceride were significantly higher at group(C) and significantly lower at group (A) but LDL was significantly higher in group (C) with no significant difference between other two groups and there was no significant difference regard HDL among studied groups (Table 2)

Table 2: Lipid profile distribution among studied groups

	Control Group(A)	Subclinical hypothyroidism Group(B)	Overt hypothyroidism Group (C)	F	P
Cholesterol	163.03±28.67#	183.96±58.67	206.74±51.04*	**7.121**	**0.002***
HDL	42.87±10.58	42.87±10.16	39.03±12.28	**1.245**	**0.287**
LDL	113.33±18.6	115.78±31.39	135.17±26.02*	**6.121**	**0.003***
TAG	112.37±35.69#	125.26±39.58	139.36±48.43*	**4.521**	**0.028***

Control group was significantly lower than other groups regard FBG, HbA1C (Table 3).

Table 3. HbA1C and FBG distribution among studied groups

	Control Group(A)	Subclinical hypothyroidism Group(B)	Overt hypothyroidism Group(C)	F	P
FBG	**91.63±2.36***	**101.69±7.98**	**104.63±10.58**	**3.907**	**0.041***
HbA1C	**5.48±0.38**	**5.76±0.62**	**5.88±0.54**	**1.287**	**0.105**

Thyroglobulin (TG) antibody and thyroid peroxidase (TPO) antibody were significantly lower among control group than other groups (Table 4).

Table 4. TG and TPO antibody distribution among studied groups.

	Control Group(A)	Subclinical hypothyroidism GroupB	Overt hypothyroidism Group(C)	Kruskal Wallis	P
TG antibody	0.13±0.07* 0.1 (0.07-0.39)	0.43±0.39 0.22 (0.06-2.0)	0.31±0.18 0.1 (0.0-1.0)	**10.854**	**0.00****
TPO antibody	0.17±0.13* 0.11 (0.03-0.8)	0.94±0.68 0.8 (0.04-2.7)	0.87±0.59 0.4 (0.05-3.1)	**9.987**	**0.00****

Thyroglobulin (TG) antibody and thyroid peroxidase (TPO) antibody were significantly positively correlated and no significant correlate between TG antibody and TPO antibody with other variables (Table 5).

Table (5): Correlations of variable data with TG and TPO antibody

		TG antibody	TPO antibody
CHOLI	**r**	.023	.198
	P	.838	.076
HDL	**r**	.102	.033
	P	.366	.771
LDL	**r**	.168	.137
	P	.125	.149
TAG	**r**	.027	.185
	P	.823	.114
FBG	**r**	-.026-	.034
	P	.820	.760

HbA1C	**r**	.150	.034
	P	.180	.764
TPO antibody	**r**	.387**	1
	P	.000	

TG antibody was significantly positively correlated with TAG in group(C) (Table 6).

Table (6): Correlations of variable data with TG antibody and TPO antibody in group (C)

Group		TG	TPO
CHOLI	**R**	.235	.045
	P	.238	.824
HDL	**R**	-.034-	.136
	P	.867	.500
LDL	**R**	-.223-	.136
	P	.307	.537
TAG	**R**	.183	.409*
	P	.391	.047
FBG	**R**	.162	.205
	P	.419	.304
HbA1C	**R**	.253	-.050-
	P	.203	.804
TPO	**R**	.120	1
	P	.551	

TG antibody was significantly positively correlated with TPO antibody in group (B) (Table 7).

Table (7): Correlations of variable data with TG antibody and TPO antibody in group (B)

Group		TG antibody	TPO antibody
CHOLI	**R**	-.109-	.166
	P	.587	.407
HDL	**R**	.206	.007
	P	.302	.972
LDL	**R**	-.375-	.276
	P	.078	.203
TAG	**R**	-.058-	-.094-
	P	.777	.648
FBG	**R**	-.083-	-.061-
	P	.681	.764
HbA1C	**R**	.235	.129
	P	.238	.523
TPO antibody	**R**	.446*	1

	P	.020

No significant correlation was found between TG antibody and TPO antibody and variable data in group (A)(Table 8).

Table (8): Correlations of variable data with TG antibody and TPO antibody in Control group(A)

Group		TG antibody	TPO antibody
CHOLI	**R**	.272	-.212-
	P	.170	.290
HDL	**R**	-.084-	.024
	P	.678	.905
LDL	**R**	.159	-.214-
	P	.458	.316
TAG	**R**	.089	.104
	P	.680	.630
F BG	**R**	.102	-.101-
	P	.613	.617
HbA1C	**R**	-.339-	-.216-
	P	.084	.280
TPO antibody	**R**	.059	1
	P	.769	

4. Discussion

As regard demographic data among the studied groups, we found that the mean age was distributed as 41.96±14.62, 41.74±13.89 and 35.29±8.73 respectively with no significant difference among groups also there was no significant difference regard Weight or height or BMI but regard sex distribution female was significantly associated with Subclinical hypothyroidism Group.

The present study can be supported by the study by [11] aimed to identify the correlation between thyroid dysfunction and IR. The study used data from the sixth Korean National Health and Nutrition Examination Survey to evaluate a total of 5727 participants. Participants were classified into five groups according to thyroid hormone status as follows: overt hypothyroidism, subclinical hypothyroidism, euthyroid, subclinical hyperthyroidism, and overt hyperthyroidism. The mean age of the subjects was 37.99 ± 0.23 years and 47.93% of subjects were female. Though 92.32% of subjects were euthyroid, thyroid dysfunction was more common in females. Height was significantly different between groups, but weight, waist circumference, and BMI did not differ significantly.

Regarding lipid profile distribution among studied groups, our results revealed that Cholesterol and triglyceride were significantly higher at group(C) and significantly lower at group (A) but LDL was significantly higher in group (A) with no significant difference between other two groups and there was no significant difference regard HDL among studied groups. This is in consistence with the well-known association of hypothyroidism with lipid profile [12]. The study by [13] reported that CHOL, HDL-C, LDL-C and TG values in the HO group were significantly higher than those in the SHO and control groups, although there was no difference between the SHO and control groups (CHOL: 6.25 ± 1.83 vs. 5.08 ± 1.23 and 4.88 ± 0.93 mmol/l in HO, SHO and control groups, respectively; HDL-C: 1.72 ± 0.48 vs. 1.52 ± 0.33

and 1.57 ± 0.34 mmol/l, LDL-C: 3.61 ± 1.17 vs. 2.99 ± 0.92 and 2.84 ± 0.81 mmol/l; TG: 1.69 ± 1.30 vs. 1.34 ± 0.73 and 1.24 ± 0.72 mmol/l; all $p<0.05$).

Also, the study by [14] reported that the mean levels of lipid profile parameters (total cholesterol, HDL-cholesterol, LDL-cholesterol, VLDL- cholesterol and triglyceride) were significantly increased ($p < 0.01$) in hypothyroid patients when compared to controls. They also revealed that the mean levels of lipid profile parameters were almost same in clinical and subclinical groups. While the study by [11] reported that there was no statistically significant difference among the studied groups as regard Fasting glucose and HOMA_IR.

The present study also revealed that TG antibody and TPO antibody were significantly lower among control group. Autoimmune thyroid diseases are usually accompanied by the presence of anti-thyroid peroxidase (TPO), anti-thyroglobulin (Tg), and anti-thyroid-stimulating hormone receptor (TSHR) antibodies. Antibodies against thyroid antigens such as carbonic anhydrase 2, megalin, T3 and T4, sodium iodide symporter (NIS), and pendrin have also been detected, although rarely [15]. In agreement with our study [11] reported that there was high statistically significant difference among the studied groups as regard anti-TPO positivity. Our results were supported by the study by [16] who reported that both subclinical/overt hypothyroidism and hyperthyroidism showed a significantly higher percentage of subjects who had anti-TPO prior to the onset of thyroid dysfunction compared to the combined control group. However, there was no significant difference in the subjects who had anti-Tg earlier than the control group. Further assessment showed that only anti-TPO could be used as a standalone marker but not anti-Tg.

Also, [17] reported that showed that TSH levels were positively correlated with insulin and HOMA IR in patients with hypothyroidism ($r=0.927$, $P<0.01$; $r=0.835$, $P<0.01$ respectively). The serum TSH levels positively correlated with total cholesterol levels in hypothyroid subjects ($r=0.459$, $P=0.02$). Similarly, HOMA IR was also positively associated with TC with $r=0.554$ and $P=0.03$. The serum insulin levels were significantly correlated with total cholesterol ($r=0.462$, $P=0.03$).

5. Conclusion

Significantly elevated serum lipids and TSH levels, particularly TSH levels of 10 mIU/L, increased the risk for hyper triglyceridemia. Therefore, controlling TSH level during treatment for hypothyroid patient is of significant clinical importance to prevent hyperlipidemia and its associated complications.

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