Available online at sjuoz.uoz.edu.krd

Science Journal of University of Zakho

Vol. 10, No. 4, pp. 197 –200, October-December 2022

p-ISSN: 2663-628X
e-ISSN: 2663-6298

STUDYING THE ASSOCIATION BETWEEN SYSTOLIC BLOOD PRESSURE AND THYROID STIMULATING HORMONE IN NEWLY DIAGNOSED SUBCLINICAL HYPERTHYROIDISM FEMALE PATIENTS

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Received: *04 Jul., 2022 /* ***Accepted:*** *24 Oct., 2022 /* ***Published:*** *07 Nov., 2022* ***https://doi.org/10.25271/sjuoz.2022.10.4.969***

ABSTRACT:

Background**:** Subclinical hyperthyroidism is a condition in which thyroid stimulating hormone (TSH) is mildly decreased with both free iodine thyroxine (free T4) and triiodothyronine (T3) within the normal range. The aim of this research is to determine the association between TSH with lipid profiles, age, blood pressure and body mass index (BMI) and also to evaluate lipid profiles in subclinical hyperthyroid patients.

Materials and Methods: Ninety patients with subclinical hyperthyroidism were chosen as the patient group and 50 healthy individuals age-matched were chosen as the control group. Thyroid function tests TSH, T4 and T3 were performed by VIDAS and on the same day lipid profiles were performed by (Biolis 24i Premium) in the laboratory of General Zakho Hospital, Kurdistan Region, Iraq.

Results: In subclinical hyperthyroidism the BMI and diastolic blood pressure values were non-significantly low (P=0.13 and p=0.27 respectively) whereas systolic blood pressure increased slightly but was still non-significant. TSH was significantly and negatively related to systolic blood pressure.

Conclusion: Lipid profiles and systolic and diastolic blood pressure are not altered in subclinical hyperthyroidism. However, systolic blood pressure is related to the severity of the decrease in TSH levels.

Keywords: Subclinical hyperthyroidism, Dyslipidemia, Thyroid, Hormone, Blood pressure.

1. INTRODUCTION

In recent years, thyroid diseases both hyperthyroidism and hypothyroidism have been considered the most common endocrine disorder. The prevalence of hyperthyroidism for example is 1.2% (0.5% and 0.7% clinical and subclinical hyperthyroidism respectively) (Peppa et al., 2011). This prevalence strongly depends on sex, age and iodine status (Tribulova et al., 2020). Subclinical hyperthyroidism can be defined as low (0.1 to 0.4 mIU per L) or undetectable (less than 0.1 mIU per L) level of TSH and the level of thyroxine (T4) and free T3 being within reference ranges (Family et al., 2011; Links et al., 2021).

Subclinical hyperthyroidism can be caused by exogenous and endogenous sources. Exogenous sources are related to the treatment of single thyroid nodule, multinodular goiter and thyroid carcinoma with L-thyroxine resulting in TSH suppression (Biondi et al., 2005). Endogenous sources in contrast, common causes are autonomously functioning thyroid nodule (Rudzki et al., 2019) Graves' disease and goiter (Family et al., 2011)

It is estimated that 1-5% of patients with subclinical hyperthyroidism progress to overt hyperthyroidism, which is a strong risk of cardiovascular diseases and many others (Das et al., 2012). In addition, long term subclinical hyperthyroidism without progressing to overt hyperthyroidism is associated with dementia, bone diseases, and cardiovascular diseases such as heart failure, coronary heart disease and atrial fibrillation (Biondi, 2021).

Thyroid hormones have strong effects on many enzymes that contribute to lipid metabolism such as 3-hydroxy-3-methyl-glutaryl coenzyme A reductase and lipoprotein lipase (Peppa et al., 2011, Jawzal *et al.*, 2022). Furthermore, thyroid hormones contribute to the homeostasis of blood pressure (Vö et al., 2006), systolic and diastolic functions and systematic vascular resistance (Jung et al., 2017). Therefore, this research aims to investigate the association between thyroid hormones and lipid profiles and blood pressure in subclinical hyperthyroidism.

2. MATERIALS AND METHODS

A Case- control study was performed from May 2020 to September 2020 among the female population in Zakho city, Kurdistan region of Iraq. A total number of 1000 female patients were recruited in this study and their age ranged from 20 -50 years old (37.92±10.93 years). Out of 1000 female patients only 90 patients with subclinical hyperthyroidism (defined as TSH < 0.4 mU/l (Walsh et al., 2006)) and 50-matched healthy control enrolled in this study. After eight hours of fasting, 10 ml of venous blood samples using a disposable syringe were collected from all participants. TSH, T4 and T3 were performed by VIDAS, in which the principle is Enzyme Linked Fluorescent Assay. Serum glucose, serum total protein, serum globulin, serum albumin and lipid profiles were performed by (Biolis 24i Premium) using enzymatic methods, on the same day in the laboratory of General Zakho Hospital, Kurdistan Region, Iraq.

Exclusion criteria; smokers, hyperlipidemia, diabetes, blood pressure, taking any drug, alcoholic, operation.

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The ethical approval for this study was obtained from the ethical committee at the University of Zakho. All the subjects in this study participated voluntarily. Written and verbal consent was taken from all the subjects before performing biochemical measurements.

2.1 Statistical analysis

In this research, the comparison of two groups was conducted and examined using a student t-test and the Pearson correlation coefficient to find the correlation among the parameters. A *p*-value of less than 0.05 was considered to be significant. The software Statistical Package for Social Sciences version 25 (IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp) was used to find statistical calculations.

3. RESULTS

3.1 BMI and Blood Pressure

The effects of subclinical thyroid disorder on the BMI, BP, Serum glucose, TSH, T4 and T3 in female patients are shown in Table 1. Results indicate that in subclinical hyperthyroidism, the BMI and diastolic blood pressure were non-significantly reduced (P=0.13) and (p=0.27) respectively, whereas the systolic blood pressure increased slightly but was still non-significant. However, the decrease in TSH and the increase in T4 and T3 were significant (P<0.001).

The effect of subclinical hyperthyroidism on serum lipid profile is shown in Table 2. In subclinical hyperthyroidism the serum levels of total cholesterol, triglyceride, VLDL, low density lipoprotein-cholesterol (LDL-cholesterol), the ratio of total cholesterol/high density lipoprotein-cholesterol (HDL-cholesterol), and LDL-cholesterol/HDL were decreased insignificantly (p>0.05) as copmpared to the contol group. Otherwise the HDL-cholesterol level slilghtly insignificantly increased from 52.72±10.94 to 55.48±15.70 with p= 0.62.

Table 1. BMI, Waist Circumference, blood pressure, Serum Glucose, TSH, T4 and T3 in the control and subclinical hyperthyroidism groups.

Variables	Control N=50 (Mean ± SD)	Subclinical hyperthyroidism group N=90 (Mean ± SD)	P value
BMI (kg/m2)	27.61±4.85	24.94±3.38	0.13
Systolic Blood Pressure (mm Hg)	125.04±12.45	129.28±11.64	0.74
Diastolic Blood Pressure (mm Hg)	81.67±9.37	80.00±9.53	0.67
TSH mU/l	1.47±0.74	0.04±0.01	<0.001*
T4	85.14±11.64	169.57±86.64	<0.001*
T3	2.02±0.79	4.35±2.52	<0.001*

*** A *p*-value of <0.05 is considered to be statistically significant.**

3.2 Serum Lipid's Parameters

Table 2. Lipid Profile Parameters levels (Mean ± SD) in the control and subclinical hyperthyroidism groups.

Variables	Control group N=50 (Mean ± SD)	Subclinical hyperthyroidism group N=90 (Mean ± SD)	P value
Total Cholesterol (mg/dl)	160.16±32.11	148.25±26.82	0.33
Triglyceride (mg/dl)	86.58±37.22	78.35±23.85	0.52
HDL-cholesterol (mg/dl)	52.72±10.94	55.48±15.70	0.62
LDL-cholesterol (mg/dl)	90.13±27.51	77.11±24.08	0.23
VLDL (mg/dl)	17.32±7.44	15.67±4.77	0.52
Total cholesterol/HDL-cholesterol	3.12±0.84	2.78±0.61	0.26
LDL-cholesterol/HDL-cholesterol	1.78±0.73	1.47±0.56	0.26

*** A *p*-value of<0.05 is considered statistically significant (one-way ANOVA).**

3.3 Correlation between TSH Hormone and Studied Parameters

The correlation between TSH and the studied parameters in subclinical thyroid disorder is shown in Table 3. In subclinical hyperthyroidism, the result indicates that there is a negative significant correlation between TSH and systolic blood pressure (r=-0.605) and *p*-value <0.05. TSH was also negatively and non-significantly correlated with diastolic blood pressure, T4, T3, serum glucose, triglyceride, LDL-cholesterol, VLDL and serum globulin. However, TSH positively non-significantly correlated to BMI, total cholesterol, HDL-cholesterol, serum total protein and serum globulin.

Table 3. Pearson correlation between TSH hormone and the studied parameters.

Variables	subclinical hyperthyroidism	
	Pearson Correlation	Sig. (2-tailed)
BMI (Kg/m2)	0.20	0.53
Systolic blood pressure (mm Hg)	-0.605*	0.04
Diastolic blood pressure (mm Hg)	-0.01	0.97
TSH mU/l	1.00	
T4	-0.15	0.64
T3	-0.38	0.23
Serum glucose (g/dl)	-0.14	0.66
Total cholesterol (g/dl)	0.16	0.63
Triglyceride (g/dl)	-0.47	0.12
HDL-cholesterol (g/dl)	0.55	0.06
LDL-cholesterol (g/dl)	-0.09	0.77
VLDL (g/dl)	-0.47	0.12
Serum total protein (g/dl)	0.31	0.34
Serum albumin (g/dl)	-0.29	0.36
Serum globulin (g/dl)	0.45	0.15

* Mean Correlation is significant at P<0.05 (Pearson correlation coefficient).

4. DISCUSSION

Thyroid hormones have strong effects on the metabolism of lipids including synthesis, degradation and mobilization (Erem et al., 2015).

From Tables 1 and 2, there was not any significant change in lipid profile parameters and systolic and diastolic blood pressure in both subclinical hyperthyroidism and control groups. Our results are in agreement with those of Heemstra et al., Iqbal et al., Maratou et al. (Heemstra et al., 2006; Iqbal et al., 2021; Maratou et al., 2010). Thyroid hormones participate in lipid biosynthesis and degradation. But the degradation process exceeds the biosynthesis this is why serum total cholesterol and triglyceride decreased insignificantly in the subclinical hyperthyroid group (Iqbal et al., 2021). As expected, there is a state of hypermetabolism in patients with subclinical hyperthyroidism similar to those with overt hyperthyroidism (Soni and Kaushik, 2014). The level of triglyceride is insignificantly lower in subclinical hyperthyroidism group than the control group, this is because of lower BMI in the subclinical hyperthyroidism. BMI is significantly and positively associated with triglyceride (Hami et al., 2020).

In addition, the trend of LDL-cholesterol was similar to that of total cholesterol and triglyceride in which it was lower insignificantly in subclinical hyperthyroidism. The suggested mechanism for this trend is that the T3 hormone increases the synthesis of LDL-cholesterol receptor by promoting LDL-cholesterol receptor genes (Bel Lassen et al., 2017). This is done through the reaction of T3 with specific thyroid hormone responsive elements (Rizos and Liberopoulos, 2011).

Furthermore, subclinical hyperthyroidism is not associated with systolic and diastolic blood pressure. Our result is comparable to that of a German study by Volske et al. (Völzke et al., 2006). There is a study, in which a significant increase in both systolic and diastolic blood pressure in the subclinical hyperthyroidism group was found (Kamiński et al., 2012).

However, TSH was significantly and negatively associated with systolic blood pressure. This shows that the severity of decrease of TSH in subclinical hyperthyroidism is associated with cardiovascular diseases by increasing the systolic blood pressure and increase in vascular reactivity. Correlation of TSH with other parameters are also correlated but insignificantly this is because of the well-known fact that thyroid hormones have wide range of effects on the carbohydrate, lipid and proteins metabolism (Kotwal et al., 2020)..

One limitation of our study that could be solved in further studies is not sub classifying the subclinical hyperthyroidism group based on the level of TSH and investigating the association of TSH in each subgroup with lipid profiles and systolic and diastolic blood pressure.

5. CONCLUSION

Lipid profiles and systolic and diastolic blood pressure are not altered in subclinical hyperthyroidism. However, systolic blood pressure is associated with the severity of the decrease in TSH levels.

6. CONFLICT OF INTEREST

The authors declare that they do not have any conflict of interest

7. RESEARCH FUNDING

No funding for this research

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