The relationship between thyroid hormones and lipid profile in subclinical hypothyroidism female patients

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ABSTRACT

Background and objectives: Subclinical thyroid disorder is a most common subclinical disease among many medical conditions such as cardiovascular disease and subclinical Lyme disease. The aim of this study was to determine the relationship between lipid profile results, lipid ratios, and anthropometric parameters and thyroid hormones.

Methods: One hundred patients (ages 20 to 50 years) with subclinical hypothyroidism (SHT group) and 50 healthy subjects (control group), who are age-matched with patients, were included in the current study. Thyroid function tests (TSH, T₃ and T₄) were determined by immunodiagnostic assay system (VIDAS) for all participants. The serum glucose and lipid profile tests parameters were evaluated by Biolis 24i Premium chemistry analyser. In addition, systolic and diastolic blood pressure were measured for each individual in the study using mercury sphygmomanometer.

Results: The levels of high-density lipoprotein-cholesterol (HDL-c) were significantly lower in the SHT group when compared with control group. Whereas, the level of low-density lipoprotein-cholesterol (LDL-c), the ratios total cholesterol (TC)/HDL-c and LDL-c/HDL-c were significantly higher in SHT group than in controls. Moreover, TSH was negatively correlated with diastolic blood pressure.

Conclusions: Both LDL-c and HDL-c are altered in subclinical hypothyroidism patients. And, there is a negative association between TSH and diastolic blood pressure.

Keywords: dyslipidaemia, lipid profile, subclinical hypothyroidism, thyroid hormones, TSH

INTRODUCTION

The term “subclinical” refers to the presence of a disease without clear signs, i.e. the disease maybe at an early stage.¹ This term has been used for many medical conditions such as subclinical cardiovascular disease and subclinical Lyme disease, but subclinical thyroid
disorder is probably the most common one. Therefore, subclinical thyroid disease is known as a biochemically diagnosed disorder with abnormal serum thyrotropin (TSH) with both \(T_4\) and \(T_3\) are within normal range. Subclinical thyroid disease is characterized as subclinical hyperthyroidism and subclinical hypothyroidism (SHT). The former one occurs when serum TSH concentrations are low while \(T_4\) and \(T_3\) concentrations are normal, and subclinical hypothyroidism occurs when serum TSH concentrations are elevated but serum thyroid hormones concentrations are normal.

The incidence of thyroid dysfunctions in the general population could be due to many reasons, such as ethnic, age and geographical factors as well as iodine intake. The prevalence of SHT and hyperthyroidism affects 4-10% and 1-2% of people, respectively.

Thyroid hormones play an important role in regulating a variety of metabolic processes, including lipid synthesis, mobilization, and degradation. These hormones stimulate the synthesis of cholesterol which is catalysed by 3-hydroxy-3-methyl-glutaryl coenzyme A reductase in the liver. Thyroid hormones affect the activity of lipoprotein lipase which stimulates the hydrolysis of triglycerides in chylomicrons converting it to its components, fatty acids and glycerol. SHT is linked with lipid profile alterations mainly total cholesterol (TC) and low-density lipoprotein-cholesterol (LDL-c).

It has been shown that the prevalence of hypothyroidism is higher among type II diabetes mellitus. Thyroid hormones have a significant role in glucose homeostasis by exerting antagonistic and agonistic effects on insulin actions in many organs. Thus, any alteration in the level of thyroid hormones would lead to defects in glucose metabolism. For example, hypothyroidism inactivate gluconeogenesis pathway leading to decrease in glucose levels.

The main objective of this study was to determine the relationship between lipid profile tests [TC, triglyceride (TGs), high-density lipoprotein cholesterol (HDL-c), LDL-c, very low-density lipoprotein-cholesterol (VLDL-c)] and lipid ratios (TC/HDL-c and LDL-c/HDL-c), on one hand; and thyroid function tests (TFTs: T3, T4 and TSH), on the other hand. It was sought to assess the association with anthropometric parameters such as age, blood pressure (systolic and diastolic), and BMI as well.

MATERIALS AND METHODS

Study type, participants and blood sampling

This is a case-control study (the study's type seems like a cross-sectional study and not a case-control) extended from September 2020 to December 2020 among the female population in Zakho city, Kurdistan region of Iraq. A total of 100 female patients with SHT (2.91-8.61 mIU/ml was used as a cut-off value for SHT) and age range 20 to 50 years (32.17±13.69), and 50 age-matched healthy females were recruited in the study. Blood pressure and body mass index (BMI) were recorded in all participants. And, after an overnight fasting, 10 ml of venous blood samples using disposable syringe were collected from all participants.
Participants who are smoking, diabetic and alcoholics were excluded from the study. In addition, subjects who were taking supplements or people with elevated blood pressure were also excluded from this study.

**A reference for the cut-off value should be mentioned (in addition, to which test this cut-off value is?)**

**Biolchemical analyses**

Serum TSH, T₄ and T₃ were evaluated by VIDAS (BioMérieux, France), in which the principle is Enzyme Linked Fluorescent Assay (ELFA).¹¹ Serum glucose, and lipid profile tests were performed by Biolis 24i Premium chemistry analyser (Tokyo Boeki, Japan) using enzymatic methods¹² on the same day in the laboratory of General Zakho Hospital, Kurdistan Region, Iraq.

The ethical approval of this protocol was obtained from the local health ethics committee. The subjects voluntarily participated in the study and the written informed consent was taken from all the subjects. All the ethical guidelines of the Declaration of Helsinki was followed.¹³

**Statistical analysis**

The levels of TSH, T₄, T₃, blood glucose and lipid profile parameters as well as BMI and blood pressure were expressed in mean and standard deviation. The general comparisons of these parameters among the group were examined using the student t-test and the Pearson’s correlation co-efficient was used to assess the association between the parameters. A p-value of less than or equal to 0.05 was considered statistically significant. The statistical evaluations were performed using the Statistical Package for Social Sciences version 25 (IBM SPSS Statistics for Windows, v. 25.0. Armonk, NY).

**RESULTS**

The study included 100 females diagnosed with SHT (their age of 32.17±13.69 years). Blood samples were taken from the volunteers after overnight fasting and blood pressure was taken after resting the patient for 10 minutes. The results of the study relied on the analysis of the blood samples obtained from volunteers who participated in this study.

The effects of subclinical thyroid disorder on the BMI, blood pressure, serum glucose, T₄ and T₃ are shown in Table 1. The results indicate that, the SHT lowered BMI, serum glucose, systolic and diastolic blood pressure; however, the effects were non-significant as compared to control group.

The effect of SHT on serum lipid profile is presented in Table 2. In SHT, serum levels of TC, TGs and VLDL-c, were increased when compared to control group but with not significant difference. However, HDL-c, LDL-c, the ratios TC/HDL-c and LDL-c/HDL-c
Table 1  Anthropometric and biochemical parameters in control and SHT groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n=50)</th>
<th>SHT patients (n=100)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m²)</td>
<td>27.44±4.27</td>
<td>25.78±5.12</td>
<td>0.29</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>122.81±13.65</td>
<td>114.47±15.42</td>
<td>0.09</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>80.00±10.29</td>
<td>81.36±12.44</td>
<td>0.66</td>
</tr>
<tr>
<td>TSH (mIU/ml)</td>
<td>1.48±0.86</td>
<td>3.72±29.03</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>T₄ (µg/dL)</td>
<td>8.59±1.18</td>
<td>7.72±6.03</td>
<td>0.55</td>
</tr>
<tr>
<td>T₃ (ng/ml)</td>
<td>1.94±0.68</td>
<td>1.76±0.81</td>
<td>0.54</td>
</tr>
<tr>
<td>Serum glucose (mg/dL)</td>
<td>99.27±10.22</td>
<td>98.42±11.77</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Data presented as mean±SD. * = statistically significant (unpaired t-test).

were significantly elevated in SHT in comparison with control group.

Table 2  Lipid profile parameters of control and SHT groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Control (n=50)</th>
<th>SHT (n=50)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TC (mg/dl)</td>
<td>162.38±28.43</td>
<td>182.90±47.05</td>
<td>0.12</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>92.61±39.23</td>
<td>116.59±49.94</td>
<td>0.11</td>
</tr>
<tr>
<td>HDL-c (mg/dl)</td>
<td>51.67±11.46</td>
<td>43.83±9.30</td>
<td>0.03*</td>
</tr>
<tr>
<td>LDL-c (mg/dl)</td>
<td>92.19±24.6</td>
<td>115.75±44.17</td>
<td>0.05*</td>
</tr>
<tr>
<td>VLDL-c (mg/dl)</td>
<td>18.52±7.85</td>
<td>23.32±9.99</td>
<td>0.11</td>
</tr>
<tr>
<td>TC/HDL-c</td>
<td>3.25±0.82</td>
<td>4.33±1.41</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>LDL-c/HDL-c</td>
<td>1.87±0.68</td>
<td>2.76±1.26</td>
<td>0.01*</td>
</tr>
</tbody>
</table>

Data presented as mean±SD. * = statistically significant (unpaired t-test).

Table 3 shows the correlation between TSH and the studied parameters in subclinical thyroid disorder. In SHT, the TSH levels was negatively associated to diastolic blood pressure (r= -0.482, p= 0.043). While, non-significant negative correlation was found with systolic blood pressure, T₃, serum glucose, HDL-c and VLDL-c. And, TSH levels were positively correlated to BMI, TC, TGs and T₄ but their correlations were not significant.

**DISCUSSION**

Thyroid hormones play an important role in the regulation of cell metabolism, maintaining phospholipids levels in the cell membranes as well as the fatty acid composition of lipids. The impact of thyroid hormones is well-known in all aspects of metabolism in particular lipid metabolism including synthesis, mobilization and degradation. Therefore, this study aimed to assess the role of lipid profile in SHT patients.

There are so many conflicts in the results of lipid profile in the SHT patients in the literature. This is mainly due to poor control and not adjusting for the confounding factors. In our study, TC and triglyceride did not show any significant differences between control and SHT groups despite the higher levels of these two parameters in the SHT group. These
Table 3 Correlation between TSH and other parameters in SHT.

<table>
<thead>
<tr>
<th>Variables</th>
<th>r</th>
<th>P -value (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>0.33</td>
<td>0.18</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>-0.34</td>
<td>0.17</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>-0.48</td>
<td>0.04*</td>
</tr>
<tr>
<td>T$_4$ ($\mu$g/dL)</td>
<td>0.13</td>
<td>0.61</td>
</tr>
<tr>
<td>T$_3$ (ng/mL)</td>
<td>-0.28</td>
<td>0.26</td>
</tr>
<tr>
<td>Serum glucose (g/dL)</td>
<td>-0.22</td>
<td>0.36</td>
</tr>
<tr>
<td>TC (g/dL)</td>
<td>0.28</td>
<td>0.26</td>
</tr>
<tr>
<td>Triglyceride (g/dL)</td>
<td>0.02</td>
<td>0.94</td>
</tr>
<tr>
<td>HDL-c (g/dL)</td>
<td>-0.05</td>
<td>0.84</td>
</tr>
<tr>
<td>LDL-c (g/dL)</td>
<td>0.31</td>
<td>0.21</td>
</tr>
<tr>
<td>VLDL-c (g/dL)</td>
<td>-0.02</td>
<td>0.94</td>
</tr>
</tbody>
</table>

* denotes significant correlation (Pearson’s correlation) at p<0.05.

two parameters did not correlate with TSH. Our results in this regard are in comparable to those of Staub et al. (1992). However, other studies found significant elevation in the levels of TC and triglyceride in SHT group, but the mean age in these studies were elder than our study. Age do affect the levels of TC and triglyceride, in which these two parameters are increased directly with age. This higher levels of TC and triglyceride indicates that SHT could be a risk factor for cardiovascular diseases. It seems geographical location and ethnic groups also show variation in the results. For example, a study in the United States showed significant elevations of TC and triglyceride but a European study did not show significant difference. The mechanism behind the increase in TC is the direct effect of thyroid hormone on the Niemann-Pick C1-like 1 protein in the gut which leads to increase in cholesterol absorption.

Significantly lower levels of HDL-c and significantly higher levels of LDL-c in this study indicates that thyroid hormones have widespread effects on lipid profile and also indicates that SHT can be a risk factor for atherosclerosis. These results agree with those of Wang et al. and Zha et al. However, our results do not agree with those of Vierhapper et al. who found significant difference between control and overt hypothyroidism but not control and SHT. Thyroid hormones contribute in the expression of LDL-c receptor. Thus, in SHT, the level of LDL-c receptors is decreased which in turn leads to decrease in the catabolism of LDL-c. In addition, the lower levels of HDL-c could be due to the effects of thyroid hormone on the HDL-c binding site.

Both systolic blood pressure and diastolic blood pressure is elevated in SHT but the elevation is not significant. In addition, TSH is negatively significantly associated with diastolic blood pressure. This because of T$_3$ is considered to be vasodilator, by having a direct effect on the vascular smooth muscle cells through affecting catecholamine and catecholamine receptor. Our results is parallel with those of Tseng et al.

BMI did not show any significant difference between control and SHT. Our results are in comparable with those of Caraccino et al. and Ito et al. However, a study by Knudsen et al. found a small change in TSH would significantly affect BMI.
Serum glucose levels did not affect by the change in the level of TSH despite being a little bit lower in the SHT. This difference might be more significant in the overt hypothyroidism because of the fact that thyroid hormones maintain glucose homeostasis so any alteration in the levels of thyroid hormones will obviously have an effect on glucose levels. In similarity to our study, Ganie et al. and Cheserek et al. found no significant difference in serum glucose in both control and SHT groups. Our results are not in agreement with those of Vyakaranam et al. who found significant rise in the levels of serum glucose in the SHT.

For future studies, it would be more interesting to subdivide the subclinical group into 2-3 grades based on the level of TSH.

The study’s limitations should be added.

CONCLUSIONS

In conclusion, thyroid hormones do affect the levels of some lipid profile parameters in SHT that can be seen by significant rise in the level of LDL-c and significant fall in the level of HDL-c. This association can be further studied by subdividing the subclinical group into mild and sever subclinical groups and studying the lipid profiles in them.

ACKNOWLEDGEMENTS

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DECLARATIONS

Authors’ contributions

The authors have equally contributed to this work. They reviewed and approved the final draft before publication.

Conflict of interest

The authors declare no conflict of interest.

Ethical approval and consent to participate

The ethical approval of this protocol was obtained from the local health ethics committee. The subjects voluntarily participated in the study and the written informed consent was taken from all the participants. All the ethical guidelines of the Declaration of Helsinki were followed.
Data availability

The data that support the findings of this study is available from the corresponding author, upon reasonable request.

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