Original Article

Investigation of the lipid profile in patients with subclinical hypothyroidism

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Abstract

Background: Hypothyroidism is a thyroid gland-related disorder which causes lipid metabolism disturbance. Subclinical Hypothyroidism (SCH) is a compensatory stage in the course of this disease, in which TSH production increases while the levels of thyroid hormones are in normal or low-normal range. There are no studies about the lipid profile abnormalities in SCH. Therefore, the aim of this study was to evaluate the lipid profile in SCH patients and compare it with normal individuals. **Materials and Methods:** In this case-control study, subjects were randomly chosen among 800 individuals referred to Neka city hospital in Mazandaran province, Iran in order to routine biochemical and thyroid hormone checkup. Participants were divided into two groups ; cases (n=400) and controls (n=400). Thyroid hormones were measured by ELISA, and lipid profile parameters were evaluated colorimetrically by AutoAnalyzer. **Results:** There were no significant differences in age and sex distribution between the two groups. Among the measured thyroid hormones, TSH was significantly different between the two groups ($p \leq 0.05$). In case of lipid profile, high-density lipoprotein cholesterol (HDL-C) was significantly different between the two groups ($p \leq 0.05$). However, no significant differences were observed in the amount of low-density lipoprotein cholesterol (LDL-C), triglyceride (TG) and cholesterol ($p>0.05$). **Conclusion:** SCH patients, showed a decrease in HDL-C. It can be concluded that subclinical hypothyroidism similar to hypothyroidism can cause lipid metabolism disturbance.

Keywords: hypothyroidism, thyroid hormones, lipid profile, thyroid.

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Introduction

Hypothyroidism is one of the most common disorders of the endocrine system which can be considered as an autoimmune procedure that reduces the function of the thyroid gland. Hypothyroidism prevalence in various populations is between 10 to 20 percent, and after diabetes is suited at the second place among endocrine system disorders(1). In the course of hypothyroidism, there is a compensatory stage wherein the level of TSH (Thyrotropin-Stimulating Hormone) increases in order to sustain the thyroid hormones at the normal levels. At this stage, TSH level is 5 - 10 µU/ml, T4 (Thyroxine), and T3 (Triiodothyronine) are at the normal levels, and patients exhibit a slight diagnostic symptoms(2). In the subsequent stages, free T4 level drops and TSH increases to the levels higher than 10 µU/ml, moreover, signs and symptoms emerge rapidly, and the disease enters the clinical stage(3). Since hypothyroidism at its subclinical stage gradually progresses and its signs and symptoms are mild and

ambiguous, there are a little attention to disease at this stage(4). Clinical hypothyroidism is a risk factor for ischemic heart and coronary artery diseases(5). Studies have shown that hypothyroidism increases the risk of heart attacks in women(6). In subclinical hypothyroidism, atherogenic disorders might be happened which culminates in Coronary artery blockage(7). Coronary artery disease has caused 28 and 29 percent of the mortality in 1990 and 2001, respectively, however, it is predicted that it increases to 32.5 percent in 2030(8). According to statistics, 56 percent of ischemic heart disease and 18 percent of strokes caused by high blood cholesterol annually(9). There are contradictory findings in previous studies concerning the relationship between lipid profile disturbance and hypothyroidism at clinical and subclinical stages(6, 10, 11). Hence, in this study, our aim was to evaluate the lipid profile of individuals diagnosed with subclinical hypothyroidism and to compare the results with individuals with normal thyroid gland function.

Methods

Study population. In this case-control study, our study population is composed of individuals referred to Neka city hospital in Mazandaran province, Iran, between the years 2015 to 2017 for a routine checkup of thyroid hormones and lipid profile evaluations. In the subsequent steps, according to the clinical outcomes, samples were divided into cases with subclinical hypothyroidism symptoms and control group with thyroid gland normal function. In total, 400 SCH patients (200 men, and 200 women) and 400 healthy individuals (200 men, and 200 women) were selected randomly as the case and control groups, respectively. A questionnaire was arranged in order to collect demographic information such as sex, age, medication, smoking, history of cardiovascular diseases and experiments results. In this study, individuals with the serum TSH levels between 0.39-6.16 mU/L, and normal levels of thyroid hormone, total T4 (4.8-11.6 mU/L) and total T3 (0.39-6.16 mU/L) without taking any medications were considered as patients with subclinical hyperthyroidism. Prior to admission to the study, an informed consent was obtained from all participants. Questionnaires were filled by the medical staff of endocrinology section of Neka hospital. This step of the study was performed blinded both for the participant and the researchers. Fasting venous blood (10 ml) was collected from each participant by venipuncture.

Inclusion and Exclusion Criteria. The criteria used in this study for the recruitment of patients, were age over 18, ability to give informed consent and being nonsmoker. Exclusion criteria included having a history of cardiovascular diseases, taking medications with the ability to reduce blood cholesterol and triglyceride levels, taking medications related to thyroid disorders, suffering from any other endocrinological disorder, anemia, history of thyroid surgery and other surgical operations in the last six months.

Thyroid hormones measurement and lipid profile evaluation method. After blood collection, tubes were incubated for 30 min at room temperature to let the blood samples coagulate, afterward, tubes were centrifuged and separated serums samples were collected, and stored at -70 °C until later use.

Cholesterol, HDL-C, and triglyceride levels were measured colorimetrically by using Pars Azmoon assay Kits (Tehran, Iran) in an autoanalyzer machine (Selectra-2, Netherland).

In order to measure LDL-C levels, Friedewald formula (FF) (12) was implemented. However, in cases where the triglyceride levels were higher than 400 mg/dl direct method was used to measure LDL levels. Thyroid hormone levels were measured by ELISA test using commercially available ELISA kits from Pars Azmoon Company (Tehran, Iran).

Statistical analysis. Statistical analysis was performed on SPSS software version 18. All the data are presented as mean ± SD. Testing for normality was done by Kolmogorov-Smirnov test. T-test and Mann–Whitney test was used to compare the two groups with normal and non-normal distributions, respectively. All the Statistical analysis were blind to the experimental results and groups categorization. p-Values ≤ 0.05 were considered as significant.

Results

In this study, 800 participants were investigated and according to their clinical outcomes were

Table1. Demographic information of the study groups

S.NO.	Parameters	Subclinical Hypothyroidism (N=400)cc	Healthy Control (N=400)	P Value
1	**Age (Year)**	50.73±15.30	47.12±14.95	P>0.05
2	**Sex**			
A	**men**	200	200	P>0.05
B	**women**	200	200	

categorized into two groups of cases and controls, each contained 400 individuals. Age and sex distribution of the studied groups are presented in Table 1, and as it is demonstrated, there are no significant differences between the two groups concerning age and sex ($p \geq 0.05$).

As showed in Table 2 TSH levels are significantly different between the two groups ($p \leq 0.05$), while no significant difference was observed in the level of T3 and T4 hormones ($p \geq 0.05$) In lipid profile evaluations of both groups which included HDL-C, LDL-C, TG, and cholesterol, no significant differences were observed in the measured parameters.

Table2. Association of HbA1C with lipid factors.

S.NO.	Parameters	Subclinical Hypothyroidism (N=400)	Healthy Control (N=400)	P Value
1	TSH(mIU/L)	10.61±6.70	2.3±1.32	P≤0.05*
2	T4 Total(mg/dl)	6.74±1.20	7.96±1.20	P>0.05¶
3	T3 Total(ng/ml)	1.10±0.34	1.01±0.24	P>0.05*

*Values obtained by Mann-Whitney test
¶Values obtained by T-test
P value was significant at ≤0.05
TSH: Thyrotropin-Stimulatin Hormone
T4: Thyroxine
T3: Triiodothyronin

Table3. The lipid profile of case and control groups.

S.NO.	Parameters	Subclinical Hypothyroidism (N=400)	Healthy Control (N=400)	P Value
1	Chol(mg/dl)	196.04±40.85	191.23±48.00	P≥0.05¶
2	TG(mg/dl)	187.42±131.87	157.72±82.77	P≥0.05*
3	LDL(mg/dl)	113.67±33.12	109.66±33.59	P≥0.05¶
4	HDL(mg/dl)	42.08±12.06	46.98±10.86	P≤0.05*

V*Values obtained by Mann-Whitney test
¶Values obtained by T-test P value was significant at ≤0.05
P value was significant at ≤0.05
Chol: Cholesterol, TG: Triglycerides, HDL: High Density Lipoprotein. LDL: Low Density Lipoprotein
Mann-Whitney test
¶Values obtained by T-test

Discussion

Our findings demonstrated that there is no significant difference in lipid profile between healthy individuals and patients with subclinical hypothyroidism. The only significant difference between the two groups was observed in HDL-C levels. Moreover, TSH hormone level was significantly different between the two groups.

Studies have shown that acute administration of TSH to individuals with normal thyroids function causes disorders in the endothelium of the blood vessels and increases the level of CRP, TNFα, interleukin-6 and other oxidative stress factors. Tehrani et al. showed patients with subacute hypothyroidism exhibit a reduction in HDL-C and an increase in TG amounts when compared with normal individuals. They also showed that subclinical hypothyroidism can be a risk factor for cardiovascular disease, since it increases the TSH and TG, and reduces HDL-C levels(13). Our study also showed that HDL levels reduce in these patients compared to normal individuals, however, no significant changes were observed in triglyceride and LDL-C levels in subclinical hypothyroidism patients. Therefore, it can be concluded that one of the subclinical hypothyroidism risk factors for cardiovascular disease might be the reduction of HDL levels.

Leonidas et al. have studied the lipid profile and the cardiovascular disease risk factors in hypothyroidism patients. Their results indicated that LDL-C and TG levels increase in these patients compared to normal individuals(14). In our study, no significant changes were observed in LDL-c and TG levels between subclinical hypothyroidism patients and healthy controls.

Studies have indicated that in patients with clinical hypothyroidism, cholesterol metabolism decreases due to the reduction of cholesterol and LDL receptors on the surface of hepatocytes which in return increases the serum cholesterol and LDL-C levels and reduces HDL-C. In another study, the lipid profile of the patients with subclinical hypothyroidism was evaluated and it was shown that TG and VLDL-C levels were significantly different in these patients when compared with normal group. Their study did not find any relationship between HDL-C, LDL-C,

and cholesterol with hypothyroidism(2). Conversely, our study did not find any significant difference in TG levels between the patients and healthy controls, however, HDL-C level was significantly different between the two groups. Guntaka et al reported that cholesterol and LDL-C levels increase in patients with subclinical hypothyroidism compared two normal individuals. They also stated that increase in cholesterol and LDL-C levels can be a risk factor for atherosclerosis(15). In the current study, no significant differences were observed between the patients and healthy controls, but a significant reduction in HDL-C level was observed which can be considered as an involving factor in cardiovascular disease.

More recently, it was reported that TG level significantly increases in subclinical hypothyroidism patients compared to healthy controls, while, they did not observe any significant difference in HDL-C levels between two groups(16). In contrast to Bayar results, our findings indicated that HDL-C significantly decreases in patients with subclinical hypothyroidism and can be considered as a risk factor forcardiovascular disease in these patients.

Efstathiadou et al. reported that cholesterol, LDL and Apolipoprotein A in the lipid profile of subclinical hypothyroidism patient differ significantly from healthy controls(17). Conversely, our study could not report any significant differences in LDL-C and cholesterol levels and observed a significant decrease in HDL-C level. Inconsistency among different studies are very challenging and might be as a result of genetic variations, differences in the size, lifestyle, and the diverse diet of the study population.

Conclusion

According to our findings, it can be concluded that subclinical hypothyroidism can be considered as a possible risk factor for cardiovascular disease. Therefore, it is suggested that the lipid profile disturbance in subclinical hypothyroidism patients should be investigated in more studies and their TSH hormone should be evaluated more precisely, since the early diagnosis and treatment of such patients may prevent progression into clinical hypothyroidism and its related complications.

Conflicts of Interest

The authors have no conflict of interest to declare.

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