Research Article

Relationship between lipid profile blood and thyroid hormones in patient with type 2 diabetes mellitus

Abstract

Background: Diabetes and thyroid dysfunction are commonly associated, there are few studies have actually assessed this association in type 2 diabetes mellitus (T2DM). Objective: The current study was to examine the relationship between blood lipids profile and thyroid hormones in T2DM.

Material and methods: The study population comprised 160 obese T2DM patients, the mean age was 49.28±6.17year and mean body mass index was 33.52±4.11kg/m2 and have been with diabetes above five years were included. In the other hand, 160 age and sex matched non-diabetes study subjects who were with the diabetes patients at the time of the data collection participated in the study as a control group, the mean age was 48.12±7.35year and mean body mass index was 31.74±3.82kg/m2.

Results: The biochemical characteristics of the T2DM group and the non-diabetic group, showed that T2DM study subjects had a significant higher serum TC, LDL-C and TG than non-diabetic subjects. However, T2DM study subjects had a significant lower serum HDL-C than non-diabetics. Moreover, significant lower T3 and T4; and higher TSH were observed among T2DM than non-diabetic subjects (P<0.05). In addition, there were significant positive correlations between TSH and TC, LDL-C and TG, and negative correlations between TSH and HDL-C of T2DM study subjects and non-diabetic subjects. Furthermore, there were significant negative correlations between T4 & T3 and TC, LDL-C and TG, and positive correlations between T4 & T3 and HDL-C of T2DM study subjects and non-diabetic subjects(P<0.05).

Conclusion: Low thyroid function was positively associated with a lipid dysregulation in patient with type 2 diabetes mellitus, so that we recommend thyroid screening which is essential to detect subclinical or clinical hypothyroidism among diabetics.

Keywords: blood lipids profile, non-insulin dependent diabetes mellitus, thyroid hormones

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Introduction

Type 2 diabetes mellitus (T2DM) is most commonly current metabolic disorder as it affects more than 385 million and it is expected to reach about 590 million by 2035 worldwide.[1] Type 2 diabetes mellitus is usually associated with dyslipidemia, which increase the risk of cardiovascular disorders.[2,3]

Thyroid dysfunction is a common endocrinal disorder in the general populations.[4] The prevalence rate of thyroid dysfunction is much higher among diabetic population and estimated to be from 6.9% to 16%.[5,6] Decreased thyroid function often accompanied with the elevation of total cholesterol (TC) and 4-14% of hypercholesterolemia was reported as a hypothyroid state.[7–9] Moreover, cardiovascular disorders usually associated with thyroid dysfunction.[10–12] Dyslipidemia and atherosclerosis related cardiovascular disorders were proved to be associated with hypothyroidism.[13–16] Sinus tachycardia, atrial flutter and atrial fibrillation are commonly found in patients suffering from overt or subclinical hyperthyroidism.[17] Currently, many studies stated that even with relative low thyroid functions which were commonly remain within normal range might be more dangerous in diabetics.[18,19]

Generally, no study in Saudi Arabia showing the association between thyroid hormone and dyslipidemia in diabetic and non-diabetic population while the prevalence and complication of diabetes are increasing rapidly in the country.[20–23] Thus, knowing the association of thyroid hormone parameters with dyslipidemia among T2DM patients in the study area is profoundly important to enhance the knowledge gap of the interrelation between diabetes, thyroid hormone and dyslipidemia. Therefore, the aim of the present study was to examine the relationship between blood lipids profile and thyroid hormones in T2DM.

Material and methods

Subjects

The study population comprised 160 obese T2DM patients visiting king Abdulaziz University Hospital, Jeddah, Saudi Arabia, were randomly included in this study, the mean age was 49.28±6.17year and mean body mass index was 33.52±4.11kg/m² and have been with diabetes above five years were included. Initially, a physician at King Abdulaziz University Hospital examined all participants; their medical history was taken to collect information about general condition, physical activity and current medications if any. Study participants were excluded from the study if they had a history of thyroid diseases, kidney, chronic liver and cardiovascular disorders, psychiatric disorder, administration of drugs affecting levels of thyroid hormone, pregnancy and lactation, subjects in antidepressant and/or antipsychotic therapy, HIV/AIDS patients, malignancy and type I diabetes mellitus.

In the other hand, 160 age and sex matched non-diabetes study subjects who were with the diabetes patients at the time of the data collection participated in the study as a control group, the mean age was 48.12±7.35year and mean body mass index was 31.74±3.82kg/m². Demographic (age and sex) and anthropometric (height, weight, body mass index (BMI)) data were collected from all study subjects through structured questionnaire. Any contradictions in the questionnaire completion have consulted the interviewer for clarification. All hormone measurements and biomarker analyses were blinded and conducted in batches. The original sample of the T2DM enrolled in the study was 194 participants who underwent the eligibility assessment. In the enrollment phase, 14 of them were excluded as they didn't meet inclusion criteria and 5 refused to participate, then the randomization was done. During the follow up, 7 patients discontinued intervention (5 patients had work related schedule problems and 2 patient discontinued due to unknown reason). In addition, 8 patients were excluded from the analysis due to insufficient blood sample. The Ethics Committee of the Faculty of Applied Medical Sciences, King Abdulaziz University, approved this study. All participants signed a written informed consent.

Measurements

In all subjects, independent assessors were blinded to group assignment and not involved in the routine treatment of the participants performed clinical evaluations and laboratory analysis. Body mass index (BMI) was calculated on the basis of weight (kilograms) and height (meters), and subjects were classified as normal weight (BMI 18.5-24.9kg/m²), overweight (BMI 25-29.9kg/m²), and obese (BMI ≥30kg/m²). In addition, between 07:30 and 09:00, after an overnight fast of 12hour fasting blood sample was drawn. The blood sample in EDTA.K3 containing tubes was used for fasting plasma glucose (FBG) determination. FBG were analyzed by automated chemistry analyzer (ABX Pentra 400, France) through hexokinase method. Blood sample in the plain vacutaier tube was allowed to clot and centrifuged at 3000 rpm for 10 min to separate the serum from the whole blood for lipid profile and thyroid hormone function test. Blood lipid profile

included Triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and Total blood cholesterol (TC) were measured by enzymatic determination method (ABX Pentra 400, France). Thyroid hormone function test was measured by enzyme-linked immunoassay sandwich method with a final fluorescent detection (VIDAS, biomeriux SA, France). The test included Thyroid Stimulating Hormone (TSH), Triiodothyronine (T3) and Tetraiodothyronine (T4).

Statistical analysis

SPSS (Chicago, IL, USA) version 21 was used for statistical analysis of data. Quantitative variables were described as mean±SD. An independent t-test was used to compare mean values of each parameter among the groups. To observe possible relationships between parameters, Pearson's correlation coefficient (r) was used. All assumptions were carefully appreciated in each model we followed. All variables with p- value less than 0.05 were considered as statistical significance.

Results

The anthropometric and baseline data of the whole study participants are shown in Table 1. The mean age of the no-diabetic control group was 48.12±7.35year, where the mean age of the T2DM group was 49.28±6.17year. Comparison between both groups regarding baseline variables showed that: there was no statistically significant difference between both groups as regards age, gender, BMI, urea, albumin, systolic blood pressure and diastolic blood pressure (respectively; P=0.57, P=0.62, P=0.48, P=0.61, P=0.78, P=0.53 and P=0.82). Regards the HbA1c, it was found to be more in the T2DM group than in the non-diabetic group (p=0.014). In addition, the raised FBS level was found to be more in the T2DM group than in the non-diabetic group with a statistically significant difference between the two groups (p=0.018). When comparing the PPS between the two groups, PPS level showed a statistical significant difference (p=0.025), (Table 1).

Table 1 Descriptive study on the anthropometric and baseline data of study participants

Variable	Group (A) (T2DM)	Group (B) (Non-Diabetic)	Significance
Age	49.28±6.17	48.12±7.35	P>0.05
Sex (Male: Female)	56(35%):104(65%)	44(27%):116(73%)	P>0.05
BMI (kg/m2)	33.52±4.11	31.74±3.82	P>0.05
Urea (mg/dL)	31.87±5.19	30.62±4.76	P>0.05
Albumin (mg/dL)	4.38±0.82	4.65±0.91	P>0.05
SBP (mm Hg)	131.21±11.47	127.42±8.25	P>0.05
DBP (mm Hg)	82.13±5.22	79.85±4.61	P>0.05
HbA1c (%)	7.65±1.48*	5.23±0.97	P<0.05
FBS (mg/dl)	185.24±31.24*	125.41±16.32	P<0.05
PPS (mg/dl)	276.17±42.53*	168.78±29.46	P<0.05

(*) indicates a significant difference between groups, P<0.05.

BMI, body mass index; HBA1c, glycosylated hemoglobin; FBS, fasting blood sugar; PPS, postprandial blood sugar

Regarding the biochemical characteristics of the T2DM group and the non-diabetic group, Table 2 shows that T2DM study subjects had a significant higher serum TC, LDL-C and TG than non-diabetic subjects. However, T2DM study subjects had a significant lower serum HDL-C than non-diabetics. Moreover, significant (P<0.05) lower T3 and T4; and higher TSH were observed among T2DM than non-diabetic subjects (P<0.05).

Table 2 Biochemical characteristics of T2DM and non-diabetes study participants

Variable	Group (A) (T2DM)	Group (B) (Non-Diabetic)	Significance
T4 (pmol/l)	11.25±3.28*	13.84±4.65	P<0.05
T3 (pmol/l)	3.47±1.12*	4.61±1.23	P<0.05
TSH (mIU/ml)	5.62± 1.74*	3.85±1.31	P<0.05
TG (mg/dL)	257.17±41.38*	179.45±32.16	P<0.05
HDL-c (mg/dl)	37.15±9.24*	48.73±10.11	P<0.05
LDL-c (mg/dl)	186.21±37.53*	165.19± 28.13	P<0.05
TC (mg/dL)	271.55±46.29*	232.64±37.15	P<0.05

(*) indicates a significant difference between groups, P < 0.05.

T4, thyroxine; T3, triiodothyronine; TSH, thyroid stimulating hormone; HDL-c, high-density lipoprotein cholesterol; LDL-c, low--density lipoprotein cholesterol; TC, total cholesterol; TG, triglycerides

In Pearson correlation test, Table 3 shows that there were significant positive correlations between TSH and TC, LDL-C and TG, and negative correlations between TSH and HDL-C of T2DM study subjects and non-diabetic subjects. Furthermore, there were significant negative correlations between T4 & T3 and TC, LDL-C and TG, and positive correlations between T4 & T3 and HDL-C of T2DM study subjects and non-diabetic subjects (P<0.05).

Table 3 Pearson bivariate correlations between dependent variables (TSH, T3, T4) and studied variables (TG, HDL-c, LDL-c, TC) among T2DM and non-diabetes study participants

Tested parameters	Group (A) (T2DM)			Group (B) (Non-diabetic)		
	T4 (pmol/l)	T3 (pmol/l)	TSH (mIU/ml)	T4 (pmol/l)	T3 (pmol/l)	TSH (mIU/ml)
TG (mg/dL)	-0.532*	-0.726**	0.584*	-0.514*	-0.531*	0.728**
HDL-c (mg/dl)	0.615**	0.528*	-0.522*	0.672**	0.719**	-0.538*
LDL-c (mg/dl)	-0.519*	-0.673**	0.546*	-0.591*	-0.672**	0.655**
TC (mg/dL)	-0.622**	-0.518*	0.632**	-0.628*	-0.544*	0.512*

Spearman's correlation was used*: P<0.05**: P<0.01.

Discussion

Diabetes is an endocrine metabolic disorder and it is a major threat to the public health and a leading cause of morbidity and mortality worldwide.[24] Thyroid dysfunction and T2DM are the most common endocrinal disorders in daily clinical practice, while the underlying mechanisms are not fully understood.[25] There is an association between diabetes and thyroid dysfunction which have important clinical implications.[26–28] Thyroid hormones are essential for lipid metabolism regulation[29,30] and thyroid dysfunction is usually associated with dyslipidemia,[31] in the other hand T2DM is associated with abnormal blood lipid profile.[32] Several studies evaluated the relationship between thyroid hormones and lipid abnormalities, few have actually assessed this association in patients with T2DM.[33,34]

In the present study, higher serum level of TC, LDL-C and TG was found among T2DM patients than non-diabetic subjects. This might be from low activity of lipoprotein lipase enzyme or the limited lipoproteins clearance, thus lead to increased TC, LDL-C and TG levels in blood.[35–37] The relationship between thyroid gland function and blood lipid profile has been proved in T2DM and non-diabetics.[38,39]

Regarding thyroid hormones, the present study revealed that the serum level of T3, T4 was significantly lower in T2DM patients while serum level of TSH was significantly higher in T2DM patients when compared to that of non-diabetic subjects. The results of present study were in accordance with the reports of.[40–44] However, Anveetha et al.,[45] reported that serum level of TSH and FBS were significantly increased among 30 patients with T2DM along with lower level of T3 and T4 than in healthy control subjects. Diabetes induced hypothalamo-pituitary-thyroid axis alterations that resulted in reduction in thyroid releasing hormone (TRH) synthesis and release that reduce iodide uptake by thyroid gland that limit T3 and T4 production.[46,47]

In the current study, a low thyroid function was positively associated with a lipid dysregulation in T2DM patients as there was a positive significant relationship between TSH and TG, LDL-C and TC in addition to negative significant correlation between TSH and HDL-C among hypothyroid T2DM study subjects. Our findings were in harmony with the report of Chubb et al.,[48] & Zhang et al.,[49] demonstrated a negative significant correlation between serum HDL-C and TSH in T2DM study participants and non-diabetic subjects. The same work result has been described by several researchers.[50–53] However, Giandalia et al.,[14] & Triolo's et al.,[54] stated that TSH was significantly associated with high triglycerides in T2DM that related to visceral obesity and high risk of atherosclerosis susceptibility in T2DM. Moreover, positive correlation between TSH and TG, TC& LDL-c may be due to activation of autoimmune that is involved in lipoprotein production.[55]

Finally, in the current study, T3 and T4 were negatively correlated to serum TC, TG and LDL-c. Thyroid hormones (T3 and T4), especially T3 have been demonstrated to regulate LDL receptors by binding directly to thyroid hormone responsive elements (TREs)[56] and controlling sterol regulatory element-binding protein.[57] Thyroid hormone also involved in hepatic expression of hydroxymethyl glutaryl coenzyme Areductase, which enhance cholesterol synthesis.[58] Thus, decreased thyroid hormones lead to reduced expression of LDL receptors and hepatic cholesterol synthesis, which may reduce cellular uptake and catabolism of LDL-C from circulation and finally result in increased levels of circulating TC. In the other hand, Spanoudi and colleagues stated that following administration of 50 μg of T4 one time daily 8 weeks resulted in significant reduction in TSH , TC, LDL-c , TG and significant increase in HDL-c in euthyroid patients with T2DM.

The current study has important strengths and limitations. The major strength is the randomized controlled nature of the study. In the other hand, the major limitation is the small sample size in both groups may limit the possibility of generalization of the findings in the present study. Finally, within the limit of this study, low thyroid function was positively associated with a lipid dysregulation in patient with T2DM, so that we recommend thyroid screening which is essential to detect subclinical or clinical hypothyroidism among diabetics.

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None.

Conflict of interest

The author declares no conflict of interest.

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