Original Article

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The Association Between Erectile Dysfunction and Subclinical Hypothyroidism in Males with Type 2 Diabetes Mellitus

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Abstract

Aim: Overt hypothyroidism is known to affect sexual functions, but data on subclinical hypothyroidism (SCH) are insufficient. We aimed to investigate the relationship between erectile dysfunction (ED) and SCH in men with type 2 Diabetes Mellitus.

Methods: This cross-sectional study included 117 diabetic patients aged between 45-70 years who applied to our outpatient clinic between March and June 2018. Biochemical blood tests and levels of hormones were analyzed. International erectile function index-5 (IIEF-5) questionnaire was applied for the assessment of ED. According to the IIEF-5 questionnaire scores, patients were grouped as severe ED (n=47), moderate ED (n=46), and no ED (n=24). Patients were also grouped according to the level of thyroid-stimulating hormone (TSH) into 3 groups; 0.27-2.49 mU/l (n=58), 2.5-4.2 mU/l (n=33), and >4.2 mU/l (n=26). Statistically significance level was set at 0.05.

Results: 40% of the patients had severe ED and 39% moderate ED, while 21% had no ED. The TSH levels were significantly different between the ED groups ($p<0.001$). A significant negative correlation was found between the IIEF-5 score and the TSH levels ($p<0.001$, $r=-0.453$). The IIEF-5 score, and duration of ED were significantly different between the TSH groups (both; $p<0.001$).

Conclusions: SCH is closely associated with ED in diabetic men. So, we recommend conducting thyroid function tests in diabetic men with ED and screening for ED in men with SCH.

Keywords: Male, thyrotropin, diabetes mellitus, type 2, erectile dysfunction, hypothyroidism

Introduction

Type 2 Diabetes Mellitus (T2DM), characterized by hyperglycemia, is a metabolic disorder resulting from insulin resistance, insufficient insulin secretion, or excessive glucagon secretion (1). There are two main polygenetically formatted basic defects in T2D, which is a progressive disease. These are insulin resistance and insulin secretion defect in beta cells (2).

Erectile dysfunction (ED), which is defined as the persistence of insufficient erection and/or failure to maintain an adequate erection for successful sexual intercourse is more common in men with T2DM (3). Diabetic ED resulting from endothelial dysfunction is known to be associated with cardiovascular diseases, obesity, hypertension, metabolic syndrome, and aging (4-6).

Hyper and hypothyroidism are the main thyroid diseases that have negative effects on the male reproductive system (7). Short-term hypothyroidism has no significant effect in men, but long-term hypothyroidism has been shown to impair male reproductive functions (8). Subclinical hypothyroidism (SCH) is a biochemical definition in which high levels of thyroid stimulating hormone (TSH) are detected when serum-free thyroid hormone levels are normal (9). It has been shown that SCH, which affects many metabolic systems, is also associated with insulin

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resistance (10). The pathophysiology of SCH and ED in these patients is multifactorial (3,9). Both SCH and ED are conditions that are increasingly prevalent, especially in the middle-aged and elderly diabetic male population, and cause metabolic and sexual dysfunction and reduce the quality of life.

In our study, we aimed to evaluate the possible relationship, which has not been evaluated before, between ED that occurs because of endothelial dysfunction and SCH that causes microscopic endothelial oedema and atherosclerosis in patients with T2DM.

Methods

Study Design

This study was designed as a cross-sectional study and was approved by the Local Ethics Committee (University of Health Sciences Turkey, Umraniye Traning and Research University Hospital Ethics Committee date: 23.02.2018; number: B, 10,1, TKH.4.34.H.GP.0.01/20). It was carried out in accordance with the Helsinki Declaration. Written informed consent was obtained from all participants. One hundred twenty-two male patients who applied to the diabetes outpatient clinic of our hospital were included in the study in order of admission according to the power analysis results. The study was conducted with 117 patients, as five patients left voluntarily after being included in the study. Patients between the ages of 45 and 70 years with a diagnosis of T2D, who have not received thyroid replacement therapy, have normal kidney and liver functions, and have a normal lifestyle with regular physical activity were included. T2DM was diagnosed according to the criteria of the American Diabetes Association (11). The exclusion criteria of the study include; type 1 diabetes mellitus, history of treated or untreated thyroid disease, taking medications that may affect thyroid functions (amiodarone, furosemide, glucocorticoids, iodine etc.), malignancy, hyperprolactinemia, major pelvic surgery, prostate cancer, abnormal rectal examination findings, prostatectomy, severe cardiovascular and neurovascular disease, acute cerebrovascular accident, acute or chronic infection, uncontrolled diabetes, major psychiatric diseases, and diabetic neuropathy.

A detailed anamnesis was taken from all patients and physical examinations were performed [weight, height, body mass index (BMI), waist circumference and blood pressure]. BMI was calculated by dividing weight (kg) by height in meters squared (m^2). Duration of diabetes and erectile dysfunction, daily number of cigarettes smoked, and use of antihypertensive drugs and anti-hyperlipidemic drugs of all participants were recorded. The patients were divided into 3 groups according to their TSH levels as 0.27-2.49 mU/l (n=58), 2.5-4.2 mU/l (n=33), and>4.2 mU/l (n=26) (Figure 1).

Evaluation of Erectile Dysfunction

The international index of erectile function (IIEF-5) questionnaire was applied to all patients to evaluate ED (12). IIEF-5 questionnaire scores range between 5 and 25. This questionnaire has been translated into Turkish and its validity and reliability have been previously tested in Turkey (13). Patients were divided into 3 groups according to their IIEF-5 questionnaire scores. The groups were defined as the following: no ED between 21 and 25 (n=24), moderate ED 11 and 20 (n=46) and severe ED between 5 and 10 (n=47) (Figure 1).

Evaluation of Subclinical Hypothyroidism

SCH is defined as the detection of high TSH levels while free thyroid hormone levels in the serum are normal (14). The normal range was defined for serum-free thyroxine (FT4) as 7-18 pg/mL, for serum-free triiodothyronine (FT3) as 2.60-4.80 pg/mL, and for TSH as 0.3-4.0 mU/l. The inter-test variation for FT4, FT3, and TSH was 3.6%, 4.1%, and 4.3%, respectively.

Metabolic Parameters

Several types of tests were used for different parameters: Plasma glucose was measured by enzymatic test; glycosylated hemoglobin A1c (HbA1c) by HPLC method; calcium, phosphate, alanine transaminase, aspartate transaminase, gamma glutamyl transferase alkaline phosphatase, amylase, albumin, total cholesterol, high density lipoprotein (HDL) and triglyceride concentrations by enzymatic colorimetric test; creatinine by Jaffe` method; c-reactive protein by an immunoassay; blood urea nitrogen by spectrophotometer; potassium, sodium and chlorine levels by ion-selective electrode analysis with an Architect plus (Abbott Park, Illinois, USA) instrument. Serum luteinizing hormone (LH), free testosterone, FT4, TSH and prolactin (PRL) levels were measured by using the radioimmunoassay method (Brahms, Hennigsdorf, Germany). The normal range for LH was 1-9 IU/L, for free

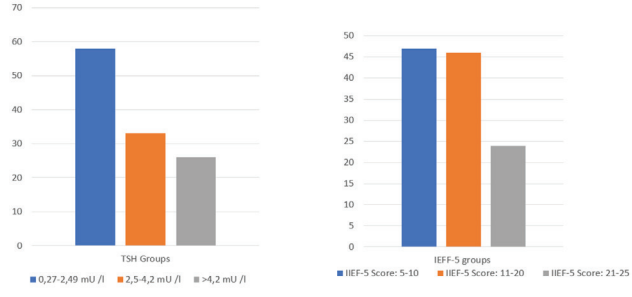

Figure 1. IEFF-5 and TSH groups
IIEF-5: International index of erectile function, TSH: Thyroid-stimulating hormone

testosterone was 8.7-54.7 pg/mL, and for PRL was 60-400 µIU/mL. The inter-test variation for LH, free testosterone, and PRL was 3.9%, 4.7% and 5.1%, respectively. Patients or controls with abnormal levels of these parameters were excluded from the study. Biochemical blood tests were carried out and levels of hormones were measured. Blood samples were taken from the patients on an empty stomach between 08:00 and 10:00 am. Samples were analyzed simultaneously and in the same laboratory.

Statistical Analyses

Descriptive statistics (mean, standard deviation, minimum, median, maximum) were used to define continuous variables. The comparison of two independent and normally distributed continuous variables was made with the student's t-test, and the comparison of two independent variables that are not normally distributed was performed with the Mann-Whitney U test. The Pearson correlation coefficient was calculated to determine the relationship between two normally distributed continuous variables, and the Spearman's rho correlation coefficient to determine the relationship between two non-normally distributed continuous variables. Chi-square (or Fisher's Exact test where appropriate) was used to examine the relationship between categorical variables. The statistical significance level was set at 0.05. The analyses were performed using the MedCalc Statistical Software version 12.7.7 (MedCalc Software Bvba, Ostend, Belgium; http://www.medcalc.org; 2013) Program.

Results

While 40% of the patients participating in the study met the criteria for severe ED and 39% moderate ED, ED was not present in 21% of the patients. SCH was detected in 26 of 117 patients included in the study. The demographic data, anthropometric measurements, clinical and biochemical parameters of the patients are summarized in Table 1. The mean age of the patients was 56±8 years, the IIEF-5 score was 13±6, the TSH level was 2.70±1.76 mU/l, HbA1c level was 8.95%±2.30, and the duration of diabetes was 8±7 years. 49.2% of the patients participating in the study were smokers. In terms of using antidiabetics, while 32.4% of the patients were using only oral antidiabetic, 18.7% were using only insulin. The percentage of patients using both insulin and oral antidiabetic was 48.9%. The patients were first compared according to their IIEF-5 questionnaire scores: 21-25 points, 11-20 points, and 5-10 points (Table 2). SCH was detected in 17 of 47 patients with severe ED. There was a statistically significant difference between the 3 groups in terms of age, TSH, and duration of ED ($p<0.01$ for all). There was no difference between the IIEF-5 score and parameters such as PRL, testosterone, FSH, HbA1c, glucose, diabetes duration, waist circumference and BMI.

In the correlation analysis between the IIEF-5 score and other parameters; there was a weak negative correlation between the IIEF-5 score and hemoglobin, and a modest negative correlation between IIEF-5 age, TSH, and duration of ED (Table 3). In the regression analysis, a 1-unit change in age decreased the IIEF-5 score 0.141-fold, and a 1-unit change in TSH decreased the IIEF-5 score 0.814-fold.

When the patients were divided into 3 groups according to their TSH levels as 0.27-2.49 mU/l, 2.5-4.2 mU/l and >4.2 mU/l, a significant difference was found between

Table 1. Demographic data, anthropometric measurements, clinical and biochemical parameters of the patients

n=117	Mean ± standard deviation
Age (years)	56±8
Duration of diabetes (years)	8±7
DED (years)	5±4
IIEF-5 Score	13±6
TSH (0.3-4.0 mU/l)	2.7±1.76
FT3 (2.60-4.80 pg/mL)	2.68±0.43
FT4 (7-18 pg/mL)	1.07±0.22
Hba1c (%4.7-%5.6)	8.95±2.3
Glucose (70-100 mg/dL)	196±95
Prolactin (60-400 µIU/mL)	8.86±5.21
Free testosterone (3.7-54.7 pg/mL)	4.6±1.68
FSH (1.3-19.3 mIU/m)	5.94±4.27
Luteinizing hormone (1-9 IU/L)	4.63±2.52
Sodium (135-145 mEq/L)	139±3
Potassium (3.5-5.5 mmol/L)	4.55±0.42
Creatinine (<1 mg/dL)	0.96±0.29
Blood urea nitrogen (10-20 mg/dL)	35.7±10.86
AST (15-50 IU/L)	21±9
ALT (10-40 U/L)	30±29
C-reactive protein (<3 mg/L)	1.41±3.22
Hemoglobin (12.4-14.8 g/L)	14.01±1.76
Neutrophil (1.5-8.0 10^3/uL)	4.638±1.506
Triglyceride (<150 mg/dL)	184±137
HDL (40-60 mg/dL)	38.3±9.7
LDL (<130 mg/dL)	147±115
Total cholesterol (<200 mg/dL)	207±49

DED: Duration of erectile dysfunction, IIEF-5: international index of erectile function, TSH: Thyroid-stimulating hormone, FT3: serum-free triiodothyronine FT4: Serum-free thyroxine, HbA1c: Glycolyzed hemoglobin A1c, AST: Aspartate aminotransferase, FSH: Follicular stimulant hormone, ALT: Alanine aminotransferase, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

the groups in terms of age, the IIEF-5 score, duration of ED and hemoglobin levels (Table 4). The IIEF-5 score was statistically lower in the SCH group.

In the correlation analysis between the TSH level and other parameters (Table 3); a weak statistically significant positive correlation was found between the TSH level and age, hemoglobin, and alanine aminotransferase (r= 0.210, p=0.023; r=0.217, p=0.019, r=0.202, p=0.029, respectively).

Discussion

In this study, we investigated a possible relationship between ED and SCH in men with T2DM. We found a clear relationship between ED and SCH in men with the diagnosis of T2DM. In this patient group, we found that while the TSH level increased, the IIEF-5 score decreased and as the IIEF-5 score decreased the TSH level increased.

ED, which is defined as the persistence and/or failure of sufficient penile erection for successful sexual intercourse, is more common in men with a diagnosis of T2DM (15,16). In epidemiological studies, it has been shown that approximately 30 to 90% of men with T2DM have ED (17,18). In the Massachusetts Male Aging Study, ED was shown to be 3 times higher in diabetic men compared to non-diabetics (19). The prevalence of severe ED in diabetic patients included in our study was 40% and moderate ED was 39%. Our study had a higher prevalence of diabetic ED than previously reported studies. This may be due to the differences in demographic and clinical characteristics of the patients in this study from patients in previous studies. The pathophysiology of ED is multifactorial. Mainly, hypogonadism, diabetic neuropathy and endothelial dysfunction are blamed (20). However, endocrine disorders can also cause ED. Low serum testosterone,

Table 2. Comparison of parameters according to IIEF-5 score

	IIEF-5 Score: 5-10 (n=47) Avr ± SD	IIEF-5 Score: 11-20 (n=46) Avr ± SD	IIEF-5 Score: 21-25 (n=24) Avr ± SD	p
Age (years)	59.1±7.6	56.1±7.2	51.5±5.9	<0.001*
Duration of diabetes (years)	9.2±8.4	8.4±7.1	6.1±4.7	0.852
DED (years)	6.9±4.1	4.9±3.6	0	<0.001*
TSH (0.3-4.0 mU/L)	3.3±1.4	2.5±1.9	1.7±1.4	<0.001*
FT3 (2.60-4.80 pg/mL)	2.7±0.4	2.7±0.4	2.7±0.4	0.435
FT4 (7-18 pg/mL)	1.1±0.1	1.1±0.3	1.02±0.2	0.406
Hba1c (%4.7-%5.6)	8.9±2.1	8.6±2.3	9.4±2.7	0.424
Glucose (70-100 mg/dL)	198.7±101.1	192.3±84.7	197.6±109	0.915
Prolactin (60-400 µIU/mL)	9.4±6.1	8.4±4.7	8.7±4.4	0.693
Free testosterone (3.7-54.7 pg/mL)	4.8±1.9	4.7±1.5	4.01±1.2	0.241
FSH (1.3-19.3 mlU/mL)	6.5±4.06	5.4±4.8	5.9±3.4	0.706
Luteinizing hormone (1-9 IU/L)	4.7±2.2	4.6±2.9	4.7±2.2	0.84
Sodium (135-145 mEq/L)	138.9±2.6	139.8±2.9	138.4±4.2	0.091
Potassium (3.5-5.5 mmol/L)	4.5±0.4	4.6±0.3	4.6±0.5	0.829
Creatinine (<1 mg/dL)	1.007±0.4	0.9±0.2	0.9±0.2	0.366
Blood urea nitrogen (10-20 mg/dL)	35.8±9.7	36.05±10.6	35.1±13.7	0.974
AST (15-50 IU/L)	21.04±6.5	20.3±8.7	22.8±7.6	0.159
ALT (10-40 U/L)	27.6+16.5	28.8+22.4	35.9+51.5	0.168
C-reactive protein (<3mg/L)	1.36±1.7	1.1±1.1	0.8±0.8	0.222
Hemoglobin (12.4-14.8 g/l)	14.4±1.2	14.2±1.6	13.3±1.7	0.117
Neutrophil (1.5-8.0 10^3/uL)	4.8±1.7	4.5±1.2	4.7±1.6	0.897
Triglyceride (<150 mg/dL)	188.4±178.3	163.3±92.1	206.9±113.1	0.404
HDL cholesterol (40-60 mg/dL)	40.1±10.2	37.9±8.5	36.4±9.6	0.53
LDL cholesterol (<130 mg/dL)	156.3±166.3	129.1±37.6	166.2±93.2	0.22
Total cholesterol (<200 mg/dL)	208.9±59.9	200.8±44.8	215.2±35.03	0.613

Avr: Average, SD: Standard deviation, DED: Duration of erectile dysfunction, IIEF-5: International index of erectile function, TSH: Thyroid-stimulating hormone, FT3: Serum-free triiodothyronine FT4: Serum-free thyroxine, HbA1c: Glycolyzed hemoglobin A1c, AST: Aspartate Aminotransferase, FSH: Follicular stimulant hormone, ALT: Alanine aminotransferase, HDL: High density lipoprotein, LDL: Low density lipoprotein

*Kruskal-Wallis test was used. There was a statistically significant difference between the IEFF-5 groups in terms of age, TSH, and duration of ED

Table 3. Correlation of IIEF-5 score and the TSH level with all parameters

		IIEF-5 score	TSH level
Age (years)	r	-0.431*	0.21*
	p	<0.001	0.023
Duration of Diabetes (years)	r	-0.079	0.111
	p	0.398	0.232
DED (years)	r	-0.642*	0.404*
	p	<0.001	<0.001
IIEF-5 Score	r	1	-0.453*
	p		<0.001
TSH (0.3-4.0 mU/l)	r	-0.453*	1
	p	<0.001	
FT3 (2.60-4.80 pg/mL)	r	-0.028	-0.002
	p	0.768	0.986
FT4 (7-18 pg/mL)	R	-0.067	-0.014
	p	0.476	0.88
Hba1c (%4.7-%5.6)	r	-0.027	0.017
	p	0.775	0.856
Glucose (70-100 mg/dL)	r	-0.064	0.139
	p	0.493	0.136
Prolactin (60-400 µIU/mL)	r	-0.054	0.019
	p	0.564	0.839
Free testosterone (3.7-54.7 pg/mL)	r	-0.164	0.092
	p	0.077	0.324
FSH (1.3-19.3 mlU/mL)	r	-0.015	-0.05
	p	0.874	0.595
Luteinizing Hormone (1-9 IU/L)	r	0.033	-0.146
	p	0.721	0.117
Sodium (135-145 mEq/L)	r	0.022	-0.088
	p	0.811	0.347
Potassium (3.5-5.5 mmol/L)	r	0.039	-0.119
	p	0.678	0.202
Creatinin (<1 mg/dL)	r	-0.144	0.056
	p	0.121	0.545
Blood Urea Nitrogen (10-20 mg/dL)	r	-0.035	-0.092
	p	0.708	0.326
AST (15-50 IU/L)	r	0.019	-0.017
	p	0.836	0.853
ALT (10-40 U/L)	r	-0.061	0.202
	p	0.516	0.029
C-reactive protein (<3 mg/L)	r	-0.11	0.148
	p	0.237	0.11
Hemoglobin (12.4-14.8 g/l)	r	-0.231*	0.217*
	p	0.012	0.019
Neutrophil (1.5-8.0 103/uL)	r	0.052	-0.088
	p	0.576	0.348
Triglyceride (<150 mg/dL)	r	0.078	0.115
	p	0.405	0.216
HDL cholesterol (40-60 mg/dL)	r	-0.102	-0.121
	p	0.274	0.193
LDL Cholesterol (<130 mg/dL)	r	0.085	-0.055
	p	0.363	0.555
Total Cholesterol (<200 mg/dL)	r	0.095	0.019
	p	0.306	0.841

DED: Duration of erectile dysfunction, IIEF-5: International index of erectile function, TSH: Thyroid-stimulating hormone, FT3: Serum-free triiodothyronine FT4: Serum-free thyroxine, HbA1c: Glycolyzed hemoglobin A1c, AST: Aspartate aminotransferase, FSH: Follicular stimulant hormone, ALT: Alanine aminotransferase, HDL: High-density lipoprotein, LDL: Low-density lipoprotein
*Spearman's rho p<0.05 (For the correlation between two continuous variables that are not normally distributed)

hyperprolactinemia, and hypothyroidism were the most common endocrine abnormalities in patients with sexual dysfunction (21).

In general population screenings, it has been shown that the prevalence of SCH varies between 4% and 10% (9,10,22). The prevalence of SCH in the patients included in our study was 22.2%, and it was slightly higher than the general population. We think that this is since the patients included in our study were diabetic and SCH was a common endocrine disorder in diabetic patients. Although SCH is generally an asymptomatic condition, it is known to affect many organs in the body (23). SCH has been shown to be involved in the pathophysiology of atherosclerosis and cardiovascular diseases by causing endothelial dysfunction (23).

SCH and ED, both of which have multiple mechanisms in their pathogenesis, are increasingly prevalent especially in middle-aged and elderly diabetic male populations and are conditions that decrease physical function, sexual life quality, and quality of life. SCH and ED constitute an important social problem both in our country and in the world, due to their treatment process, costs, complications they cause, and their increasing prevalence in recent years. The association between SCH and T2DM is well known (24). However, the relationship of SCH to the microvascular complications of diabetes is not clear. Various mechanisms may play a role in the relationship between thyroid dysfunction and microvascular complications in diabetes. First, it has been shown that insulin resistance is associated with clinical and SCH (24). One possible mechanism may be defective fibrinolysis or impaired vasodilation associated with insulin resistance (24). There are several studies evaluating the relationship between thyroid function and microvascular complications such as diabetic retinopathy, neuropathy, and nephropathy in patients with T2DMM, but the results are controversial (25-27). To the best of our knowledge, there are no studies

investigating the relationship between SCH and diabetic ED to date. Our results showed that SCH was associated with diabetic ED in 117 type 2 diabetic patients.

Free testosterone levels drop by approximately 40% in men between the ages of 25 and 75 (3). This condition can cause ED in this age group. However, in our study, we could not find a relationship between SCH and androgenic hormones such as testosterone. This situation makes us think that SCH causes hormone-independent ED in this patient group. At this point, as shown in our study, the IIEF-5 score in the SCH group was lower than the normal group. Therefore, we believe that there are different common pathways in the pathophysiology of SCH and ED in diabetic men.

Thyroid dysfunction can affect body growth metabolism and the synthesis and secretion of sex steroids (28). Numerous clinical studies have shown that both hyperthyroidism and hypothyroidism cause sexual and reproductive problems (28,29). Additionally, it is known that thyroid hormone level affects Leydig cells, Sertoli cells and spermatogenesis. It has been shown that the risk of developing ED is higher in men with hypothyroidism (29). Our study revealed that this condition occurs when SCH is present.

It has been shown that SCH suppresses antioxidative capacity by reducing paraoxonase and arylesterase activities (30). Increased oxidative stress may play an important role in the pathogenesis of diabetes-related

Table 4. Comparison of parameters according to the TSH levels

	TSH level: 0.27-2.49 mU/l (n=58)	TSH level: 2.5-4.2 mU/L (n=33)	TSH level >4.2 mU/L (n=26)	p
	Avr ± SD	Avr ± SD	Avr ± SD	
Age (years)	54.4±6.9	59.4±8.1	57.3±7.7	0.015*
Duration of diabetes (years)	7.2±5.8	9.8±8.4	8.6±8.6	0.384
DED (years)	2.8±3.5	7.7±4.2	5.2±3.8	<0.001*
IIEF5 score	16.2±5.7	10.1±5.8	9.6±5.8	<0.001*
FT3 (2.60-4.80 pg/mL)	2.7±0.4	2.7±0.4	2.6±0.5	0.932
FT4 (7-18 pg mL)	1.1±0.2	1.02±0.1	1.1±0.2	0.222
Hba1c (%4.7-%5.6)	8.9±2.4	9±2.2	9.1±2.3	0.821
Glucose (70-100 mg/dL)	186.3±92.7	212.1±112.1	198.6±81.1	0.422
Prolactin (60-400 µIU/mL)	8.7±4.8	9.1±3.8	8.9±7.5	0.301
Free testosterone (3.7-54.7 pg/mL)	4.4±1.7	5.1±1.9	4.5±1.2	0.311
FSH (1.3-19.3 mIU/mL)	5.3±2.8	5.9±2.8	6.3±5.1	0.434
Luteinizing hormone (1-9 IU/L)	4.6±1.9	4.7±2.5	3.9±1.9	0.305
Sodium (135-145 mEq/L)	139.2±3.5	139.1±2.8	139.04±2.9	0.544
Potassium (3.5-5.5 mmol/L)	4.6±0.4	4.6±0.4	4.4±0.3	0.254
Creatinin (<1 mg/dL)	0.9±0.2	1.08±0.4	0.9±0.1	0.461
Blood urea nitrogen (10-20 mg/dL)	35.8±11.2	36.4±12.1	34±8.7	0.769
AST (15-50 IU/L)	21.2±8.7	21.4±6.9	22.1±10.8	0.924
ALT (10-40 U/L)	29.3±37.6	31.1±17.9	31.4±20.5	0.212
C-reactive protein (<3 mg/L)	1.1±1.2	1.01±1.4	2.6±6.3	0.299
Hemoglobin (12.4-14.8 g/L)	13.7±1.7	14.4±1.4	14.2±2.2	0.036*
Neutrophil (1.5-8.0 103/ul)	4.6±1.3	5.1±1.9	4.1±1.05	0.078
Triglyceride (<150 mg/dL)	170.3±97.1	210.5±214.6	177.3±75.9	0.522
HDL cholesterol (40-60 mg/dL)	39±9	39.7±11.3	35.1±8.6	0.171
LDL cholesterol (<130 mg/dL)	141.9±58.6	177.8±198.5	122.04±37.8	0.113
Total cholesterol (<200 mg/dL)	205.9±39.3	219.2±66.8	196.4±41.5	0.23

Avr: Average, SD: Standard deviation, DED: Duration of erectile dysfunction, IIEF-5: International index of erectile function, TSH: Thyroid-stimulating hormone, FT3: Serum-free triiodothyronine FT4: Serum-free thyroxine, HbA1c: Glycolyzed hemoglobin A1c, AST: Aspartate aminotransferase, FSH: Follicular stimulant hormone, ALT: Alanine aminotransferase, HDL: High density lipoprotein, LDL: Low density lipoprotein

*Kruskal-Wallis test was used. There was a significant difference between the TSH groups in terms of age, the IIEF-5 score, duration of erectile dysfunction and haemoglobin levels

complications. SCH can also cause endothelial dysfunction by causing thickening of the basement membrane (30). In our study, we believe that SCH causes ED by affecting cardiac function, peripheral vascular resistance, endothelial function, and renal hemodynamics.

In addition, it has been proven that high TSH concentration causes endothelial dysfunction by reducing the formation and availability of nitric oxide (NO) (16). It is well known that NO plays an important role in the relaxation of the corporal smooth muscle and vascular system to initiate and maintain erection (3). This pathway may be one of the possible mechanisms between SCH and ED in our study.

Study Limitations

Our study had some limitations. First, our study was single center cross-sectional analysis. We could not establish a causal relationship between SCH and diabetic ED. Second, thyroid function was evaluated at a single time point. Third, the definition of ED was based on a one-time measurement. Despite all these limitations, to the best of our knowledge, there is no study in the literature evaluating the relationship between ED and SCH in men with T2DM so that the present study is valuable for being the first study in the literature on this subject.

Conclusion

This study revealed that SCH is closely associated to ED in diabetic men. We recommend conducting thyroid function tests in diabetic men with ED and screening for ED in men with SCH. However, large randomized controlled clinical studies are needed to determine whether there is a true relationship between SCH and ED in diabetic patients.

Authorship Contributions

Concept: S.U.B., Design: R.S., S.U.B., Data Collection or Processing: R.S., S.U.B., Analysis or Interpretation: A.B., Literature Search: R.S., S.U.B., Writing: R.S., S.U.B., O.B.

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