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Original Research Article

Serum testosterone levels and clinical signs of hypogonadism in men with type 2 diabetes

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ABSTRACT

Background: Diabetes mellitus is a common metabolic disease that its association with low level of testosterone has already been shown in many studies. Considering the role of testosterone hormone in impotency, fatigue, and bone mass deficiency this study aimed to evaluate the total and free testosterone levels and clinical signs of hypogonadism in male patients with type 2 diabetes.
Methods: In this descriptive-cross sectional study, sixty-five diabetic male patients aged 35-70 years were randomly selected and enrolled to the study. The necessary information such as patient demographics, BMI, past medical history, drug history, and history of smoking, education level and employment were completed by a checklist. Then, the patients were evaluated for total and free testosterone levels and symptoms related to decreased testosterone, hypogonadism symptoms by ADAM questionnaire. Finally, the data were statistical analyzed by spss version 21.
Results: The mean age of patients was 57.12±4.7 years with age range of 38-69 years. According to the ADAM questionnaire, 51 (78.4%) of the patients were positive and 14 (21.6%) were negative. 16 (24.6%) of all patients had hypogonadism. Among ADAM positive patients, 46 (90.1%) had erectile dysfunction and 33 (64.7%) had decreased libido. Most people (75%) with hypogonadism had BMI more than 30.
Conclusions: Testosterone levels are commonly found low in diabetic men, most of whom have symptoms of hypogonadism. Body mass index is known as an independent risk factor for hypogonadism in T2D men. There was also a significant correlation between free testosterone levels and hypogonadism.

Keywords: Testosterone, Hypogonadism, Men, Diabetes

INTRODUCTION

Men are biologically more prone to type 2 diabetes than women. Studies show that the men with overweight are more likely to get the disease than women. The distribution of fat in the body of an obese person plays an important role in this regard. Because in men, most of the body fat is stored in the liver and around the abdomen and this feature is the most important factor in increasing the risk of diabetes. But instead, women store a lot of fat in the thighs and pelvis. This difference suggests that women need to be fatter than men to develop diabetes.[1-3]

Androgens play a very important role in the development and maintenance of male reproductive and sexual functions, body composition, bone health and behavior.[4] Male hypogonadism is a clinical syndrome caused by androgen deficiency and may have adverse effects on the function of various organs and their quality of life. Androgen deficiency increases by age and also slightly in healthy men. In middle-aged men, the incidence of biochemical hypogonadism varies from 2.1% to 12.8%.The incidence of low testosterone and symptoms of hypogonadism in men 40-79 years varies from 2.1% to 5.7%. Hypogonadism is more common in older men,

obese men, men with other illnesses at the same time and men who are not in good health.[5-8]

Testosterone is the most important male hormone and is very effective in the growth and development of sexual organs and the occurrence of secondary sexual characteristics such as facial hair growth, voice reduction, male pattern hair loss and anabolic properties such as muscle growth and bone mass.[9-11]

Hypogonadism is diagnosed based on persistent signs and symptoms of androgen deficiency and assessment of persistently low testosterone levels in a validated manner. Low levels of circulating androgens may be associated with signs and symptoms. Clinical signs and symptoms of androgen deficiency include delayed puberty, small testicles, male factor infertility, body hair loss, gynecomastia, decreased lean body mass and muscle strength, visceral obesity, decreased bone mineral density (osteoporosis) with low trauma fractures, decreased libido and sexual activity, erectile dysfunction, reduced or reduced night erections, hot flashes, mood swings, fatigue and anger, sleep disturbance, metabolic syndrome, insulin resistance and type 2 diabetes mellitus is a decrease in cognitive function. The most common symptoms of male hypogonadism in older men include decreased libido and sexual activity, erectile dysfunction and hot flashes. Other factors associated with low testosterone include waist circumference and somatic condition. Signs and symptoms of androgen deficiency vary depending on the age of onset, duration and severity of the deficiency.[12-15] Due to the importance of the issue and the high prevalence of diabetes among patients in the community and also the lack of further studies in this regard in the province and the country, the aim of this study was to evaluate serum levels of total and free testosterone and clinical signs of hypogonadism in male patients with type 2 diabetes.

METHODS

Study design and participants

In current cross-sectional descriptive study, 65 diabetic male patients aged 35-70 years who referred to the endocrinology clinic of Imam Khomeini hospital in Ardabil from April 2017 to March 2018 were randomly selected and entered into the study with personal consent. Based on the statistical formula, the required number of samples at 95% confidence level and the amount of test error d=35.15 and the amount of standard deviation from the study of Dhimdsa et al equal to s=144.2 were estimated to be 65 people.

Measurements

Initially, all patients are screened for serum glucose and HbA1c levels. Checklist containing demographic information of patients, height, weight, BMI, patient waist (for measurement, the midline between the iliac crest and the costal margin was defined), history of the patient's past illness, history of medication, smoking and alcohol, education and job levels were completed for all patients. Patients were then assessed for signs of testosterone depletion and symptoms of hypogonadism by the ADAM questionnaire. The ADAM questionnaire has seven questions that include decreased libido, ED, fatigability, decreased muscle strength and mood changes. The sensitivity of the questionnaire was 88% and its specificity was 60%. Patients were also clinically examined for male pattern hair loss, gynecomastia ortestic size. All patient evaluations were performed between 8 and 10 am. Finally, the patients were evaluated for serum levels of total and free testosterone. In the study, overt hypogonadism was defined as the presence of clinical signs of hypogonadism and low testosterone levels (total testosterone 8 nmol/liter or testosterone available in the body 2.5 nmol/liter). Borderline hypogonadism was defined as the presence of symptoms and total testosterone 8-12 nmol/l or available testosterone available 2.5 to 4 nmol/l.

Statistical analysis

After coding, the data were entered into SPSS V22 program and analyzed using descriptive statistics method in the form of tables and graphs and analytical statistics methods using t-test and Chi square test for quantitative and qualitative data, p value level less than 0.05 was considered significant.

Inclusion and exclusion criteria

Male patients with diabetes in the age range of 35-70 years referred to the endocrinology clinic of Imam Khomeini hospital were included in the study. Patients with cardiomyopathy, valvular heart disease history of cardiovascular disease, endocrine disease that can affect serum testosterone levels, history of androgen intake and chronic disease were excluded from the study.

RESULTS

A total of 65 male diabetic patients were enrolled randomly. The average age of patients was 57.12±4.57 years with an age range of 69-38 years. According to the ADAM questionnaire, 51 patients (78.4%) were positive and 14 patients (21.6%) were negative.16 patients (24.6%) had hypogonadism. Among ADAM positive patients, 46 (90.1%) had erectile dysfunction and 33 (64.7%) decreased libido.

The average age of patients was 57.12±4.57 years with an age range of 69-38 years. Most patients with 31 cases were in the age range of 55-65 years (47.7%).The average duration of diagnosis of diabetes for patients was 9.6±41.28 years with an age range of 2-36 years. The average HbA1C of patients was 7.82±1.6% with a range of 13.7-4.9%.The average BMI of patients was 30.1±4.6 with a range of 41.5-19.2. The total average waist

circumference of patients was 107.15±3.1 cm with a range of 161-81 cm. The average of total testosterone and free testosterone (nmol/l) were 13.5±7.1 (36.8-3.1) and 0.87±0.2 (1.63-4.41)(Table 1).

Table 1: Demographic characteristics of patients.

Characteristics	Mean	Range
Diagnosis time of diabetes	6.41±6.28	2-36
HbA1C	7.82±1.6	4.9-13.7
BMI	30.1±4.6	19.2-41.5
Waist	107.3±15.1	81-166
Total testosterone	13.5±7.1	3.1-36.8
Free testosterone	0.87±0.2	0.21-1.83

Most patients with 26 patients (40%) were illiterate. There was no significant relationship between patients' education level and the incidence of hypogonadism. Most patients with 33 patients (50.7%) were self-employed. There was no significant relationship between patients' jobs and hypogonadism. A total of 16 diabetic men had hypogonadism, one in the age range of 35-45 years, 4 in the age range of 45-55, 7 in the age range of 55-65 and 4 in the age range over 65. There was no significant relationship between age of patients and hypogonadism.

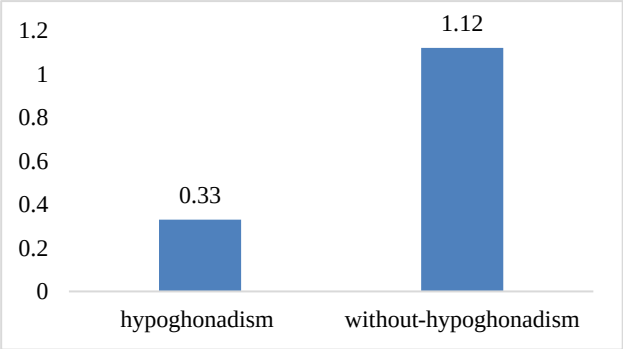

Figure 1: Frequency of free testosterone levels in patients studied based on hypogonadism.

Most people (75%) with hypogonadism had a BMI greater than 30.There was a significant relationship between patients' BMI and the incidence of hypogonadism (p=0.001).Most people (68.75%) had more than 7 HbA1C hypogonadism. There was no significant relationship between patients' HbA1C and hypogonadism. Most patients (75%) with lumbar hypogonadism had more than 94.There was no significant relationship between patients' waist circumference and hypogonadism. Most patients had a history of smoking hypogonadism. There was no significant relationship between patients' smoking and hypogonadism (Table 2). The average amount of free testosterone (nmol/l) was 0.33±0.1 in patients with hypogonadism and 1.12±0.1 in patients without hypogonadism. There was a significant relationship between patients' free testosterone levels and hypogonadism (p=0.012).

DISCUSSION

A clinical and biochemical study of hypogonadism in men with type 2 diabetes was conducted in 2013 by Kapoor et al in the journal diabetes care. In this cross-sectional study, 355 men with type 2 diabetes with an average age of 30 years, accumulated and biophysical testosterone, sex hormone binding globulin, BMI and waist circumference were measured and free testosterone was calculated. Obvious hypogonadism was defined as the presence of clinical signs of hypogonadism and low testosterone levels, (total testosterone 8 nmol/l or available testosterone 2.5 nmol/l). Borderline hypogonadism was defined as the presence of symptoms and total testosterone available at 8-12 nmol/l or available testosterone at 2.5-4 nmol/l. They found that blood testosterone levels were low in diabetic men and that a significant proportion of these men had symptoms of hypogonadism. Clear hypogonadism was 17 nmol/l in 17% of men with testosterone total and 2.5 nmol/l in 14% with available testosterone. Borderline hypogonadism was found in 25% of men with total testosterone 8-12 nmol/l and available testosterone between 2.5-4 nmol/l; 42% of men had free testosterone less than 0.25 nmol/l. Both BMI and waist circumference were negatively correlated with testosterone levels in men and this correlation was stronger for waist circumference. The results of the above study were consistent with the present study.[8] The results of the present study showed that testosterone levels in men with type 2 diabetes are often low and most of these men have symptoms of hypogonadism. Obesity is associated with decreased testosterone levels in diabetic men.

Most people (75%) with hypogonadism had a BMI greater than 30. There was a significant relationship between patients' BMI and hypogonadism (p=0.001). Most people (68.75%) had more than 7 HbA1C hypogonadism. There was no significant relationship between patients' HbA1C and hypogonadism. Most patients (75%) with lumbar hypogonadism had more than 94.There was no significant relationship between patients' waist circumference and hypogonadism (p=0.48). Most patients with hypogonadism were smokers or had previously smoked. There was no significant relationship between patients' smoking and hypogonadism (p=0.16). According to the results of this study, the average level of free testosterone (nmol/l) in patients with hypogonadism was 0.33±0.1 and in patients without hypogonadism was 1.12±0.1.There was a significant relationship between patients' free testosterone levels and hypogonadism (p=0.012). A 2014 study on testosterone concentrations in obese and non diabetic obese men was conducted by Diandesa et al in the journal diabetes care. In current study, free testosterone concentrations in 1849 male hypogonadism (HIM) (1451 non-diabetic and 398 diabetic) were analyzed. They concluded that the prevalence of abnormally free testosterone concentrations in lean, overweight and obese individuals was 26%, 29% and 40% (p<0.001) and 44%, 44% and 50% in diabetic men, (p=0.46 for intra group trends and p<0.05 compared to non-diabetic men).

Table 2: Characteristics of patients by incidence or non-incidence of hypogonadism.

Characteristics		With hypogonadism		Without hypogonadism		P value
		N	%	N	%	
Age groups	35-45	1	12.5	7	87.5	0.41
	45-55	4	40	6	60	
	55-65	7	22.5	24	77.5	
	>65	4	25	12	75	
BMI	≤24.9	1	25	3	75	0.001
	25-29.9	3	21.4	11	78.6	
	≥30	12	24.5	37	75.5	
HbA1c	≥7	11	22.9	37	77.1	0.58
	<7	5	26.3	14	73.7	
Waist	≥94	12	25	36	75	0.48
	<94	4	21.1	15	78.9	
Smoking	None	4	22.3	14	77.7	0.16
	History of smoking	7	25	21	75	
	Smoker	5	23.8	16	76.2	

The average free testosterone concentration in diabetic men was significantly lower than in non-diabetic men. There was a significant relationship between free testosterone concentration and age, BMI and sex hormone binding globulin ($p<0.001$). The average decrease in free testosterone concentration was 8.7 pg/ml every 10 years in non-diabetic men and 8.4 pg/ml every 10 years in diabetic men. The study found that 40% of obese non-diabetic men and 50% of obese 45 year old diabetic men had abnormally free testosterone levels. Due to its high prevalence, obesity is probably a condition that is often associated with abnormal free testosterone levels in men. Occurrence with diabetes is associated with an additional increase in abnormal free testosterone levels, which is consistent with the results of the present study.[9] Less of samples in this study and non-repeated all tests in another visits or tests by patients is one of the limitation of this study.

CONCLUSION

According to the results of this study, testosterone levels are often low in men with diabetes, most of whom show symptoms of hypogonadism. Most people (75%) with hypogonadism had a BMI greater than 30. There was a significant relationship between patients' BMI and hypogonadism. Body mass index is recognized as an independent risk factor for hypogonadism in T2D men. According to the results of this study, the average level of free testosterone (nmol/l) in patients with hypogonadism was 0.33±0.1 and in patients without hypogonadism 1.12±0.1. There was a significant relationship between patients' free testosterone levels and hypogonadism. Considering the important role of physicians, especially endocrinologists in screening patients for low testosterone, providing patient education and increasing patient awareness about hypogonadism, it is recommended to take the necessary measures and recommendations for diabetic patients in this field. It is also suggested that more effective strategies for patient education and communication be implemented to ensure that sexual health issues are addressed in men with diabetes. In addition, due to the importance of the subject, it is suggested that studies be conducted with a larger statistical population and focusing on preventive interventions such as education.

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