Iranian type 2 diabetics may not have serum testosterone level lower than healthy subjects; A case-control study

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ABSTRACT

Diabetes mellitus is a common metabolic disease. Its association with low level of testosterone is controversial. This study aimed to investigate the association between serum total testosterone, free testosterone index (FTI), and sex hormone-binding globulin (SHBG) in Iranian men with type 2 diabetic.
A case-control study was conducted on 38 non-diabetic and 36 diabetic men aged 40-60 years old with Body Mass Index (BMI) 18-40 (kg/m2). Fasting serum total testosterone, SHBG, FBS (Fasting Blood Sugar), HbA1C, and other hormone tests were measured. Logistic regression adjusted models was used to asses the association of total testosterone, free testosterone and SHBG level with type 2 diabetes.
The mean age of participants was 47.7±5.7 years. Serum total testosterone, FTI, and SHBG had no difference between case and control groups. There was no significant difference in total testosterone, FTI and SHBG between the patient with and without glycemic control.
Logistic regression analysis showed an inverse relationship for total testosterone in the lower tertile concentration and type 2 diabetes, but adjustment of HbA1c eliminated the correlation between total testosterone and diabetes. According to logistic regression analysis, SHBG and FTI were not significantly associated with type 2 diabetes.
Our findings suggest that serum testosterone level of the type 2 diabetics may not be lower than healthy subjects in Iranian men.

Keywords: Glysemic control, type 2 diabetes, serum total testosterone, free testosterone index, sex hormone-binding globulin

INTRODUCTION

Diabetes Mellitus (DM) is a major cause of renal failure, lower limb amputation for non-traumatic cause, and blindness in adults and with its rate appears to be increasing through the world becoming the most frequent cause of death[1].
Since 1960s the research has shown that the testosterone level in type 2 diabetic patients is lower than non-diabetic men. The same is true for the free testosterone level [2-4]. However, some other studies did not report such a correlation [5-6].
Lack of testosterone can cause a decrease in libido, impotency, decrease in muscle mass, fatigue, decrease in bone density and osteoporosis. Because the diabetes is a common disease and considering the importance and the role of testosterone it would be worthful to investigate the factors that can cause a decrease in testosterone level in diabetic patients. Considering the conflicting results on the correlation between serum testosterone level and diabetes and based on the fact that only a few case-control studies, especially in Iran, had been undertaken, we decided to investigate the relationship between level of testosterone hormone and type 2 diabetes in Iranian men.

MATERIALS AND METHODS

Current study was a case-control study. In this study 74 men aged 47.7±5.7 years, including 38 diabetic patients admitted into department of endocrinology at Firouzgar hospital (case) and 36 male non diabetic participants working in the department of endocrinology at Firouzgar Hospital (control) were randomly assessed. All the participants were privately interviewed during a face to face interview by one trained personnel. After receiving necessary information on the aimers of participating in the study, all patients signed a written informed consent form and then answered some questions regarding the history of a certain underlying diseases, medication use, and smoking habits. Inclusion criteria were aged 40-60 years and BMI between 18-40 kg/m^2. All the participants with a hypophyseal disease, renal failure, or thyroid disorders were excluded from the study.

The participants were then weighed with indoor clothing without shoes. Weight was measured to the nearest 100 grams using a digital personal scale. Height was measured using a tape meter, to the nearest centimeter, in standing position without shoes. Body mass index (BMI) was calculated by taking a person's weight (Kg) dividing by their height (meter) squared. All the male participants with a BMI between 18 and 40 having other inclusion criteria were included in the study.

After 8-10 hours fasting, blood samples were taken between 7 to 9 a.m. and serum total testosterone, SHBG, LH, FSH, FBS, HbA1C were measured. To increase the accuracy of the test, all the tests were performed by the same personnel at the department of endocrinology at Firouzgar Hospital. Fasting blood sugar (FBS) of sampling day was determined by the enzymatic colorimetric method with glucose oxidase.

HbA1C was determined by ion exchange chromatography (DS5, Drue Company). IRMA method was used to measure FSH, LH hormones. Serum total testosterone was measured using RIA immunoassay and SHBG was measured using ELIZA method. FTI was calculated by (total testosterone, in nmol/L) × 100 divided by (SHBG, in nmol/l)[7].

Occasional or daily smoking was defined against non-smoking. The number of cigarettes per day multiply by the number of smoking years was expressed as pack/year. BMI≤ 25 (kg per square meter) was defined against BMI above 25. Based on American Diabetes Association glycemic control was defined when HbA1C<7 percent was achieved.

Data distribution was analyzed using Kolmogorov-smirnov test. For variables with a normal distribution (parametric variables) including age, BMI, HbA1C, serum total testosterone, and LH, independent sample T test was used. For non-parametric variables that did not have a normal distribution Mann- Whitney test was used. To asses the association of testosterone level with type 2 diabetes, concentration of total testosterone, free testosterone and SHBG were dichotomized by the lower tertile and entered into logistic regression models adjusting for 1) age; 2) age and smoking (pack/year); 3) variables in model 2 and BMI (overweight and non overweight); 4) variables in model 3 and HbA1c (control glycemic and non control glycemic)

The statistical significance level set at 0.05. All the statistical analyses were performed using SPSS (version 15) software.

RESULTS

The samples of this study were 74 men between 40 and 60 years (47.7±5.7) including 36 diabetic and 38 non-diabetic men. As shown in table 1, mean age and BMI did not show any significant difference between diabetic and non-diabetic groups.

Table 1: Characteristics of the type 2 diabetic patients and non-diabetic participants

	Nondiabetics (n=38)	Type2 diabetics (n=36)	95%CI	P value
Age(year)	47.6±5.5*	47.5±5.9	-2.5 , 2.77	0.92
BMI(kg/m$^{2)}$	27.2±3.4	28.0±4.1	-2.6 , 2.77	0.33
Smoking(pack/year)	3.42±8.5	3.06±6.2		0.75
FBS(mg/dl)	92.0±11.1	138.9±40.8		0.0001†
HbA1c	4.92±0.61	7.14±0.69	-2.52 , -1.91	0.0001†
Total Testosterone(ng/ml)	4.14±1.3	4.66±1.4	-1.13 , -0.08	0.09
Free Testosterone Index –FTI	102±38.6	115±64.7		0.82
Sex Hormone Globulin -SHBG(nmol/l)	15.3±6	17.8±9.7		0.69
LH	4.40±2.3	4.87±2.1	-1.50 , 0.54	0.35
FSH	6.17±3.0	4.37±1.7		0.02†
TSH	2.32±1.3	2.412.3		0.04†
Prolactin	6.96±2.8	7.86±3.4		0.17

Independed t-test was used for parametric variables (age, BMI, HbA_1C, total testosterone, LH) and Man-Whitney was used for non parametric variables.
*Mean±SD
†Significant difference ($p<0.05$)

Also, based on HbA1C, diabetic samples were subdivided into two groups of good glycemic control (n=18) and poor glycemic control (n=18) (Figure 1). There was no significant difference in total testosterone and free testosterone index between the patient with and Logistic regression analysis showed an inverse relationship for total testosterone in the lower tertile concentration and type 2 diabetes, but without glycemic control. Although poor glycemic control diabetic samples had lower SHBG in comparison to another group; the difference was not statistically significant (P=0.07).

adjustment of HbA1c eliminated the correlation between total testosterone and diabetes (Table 2)

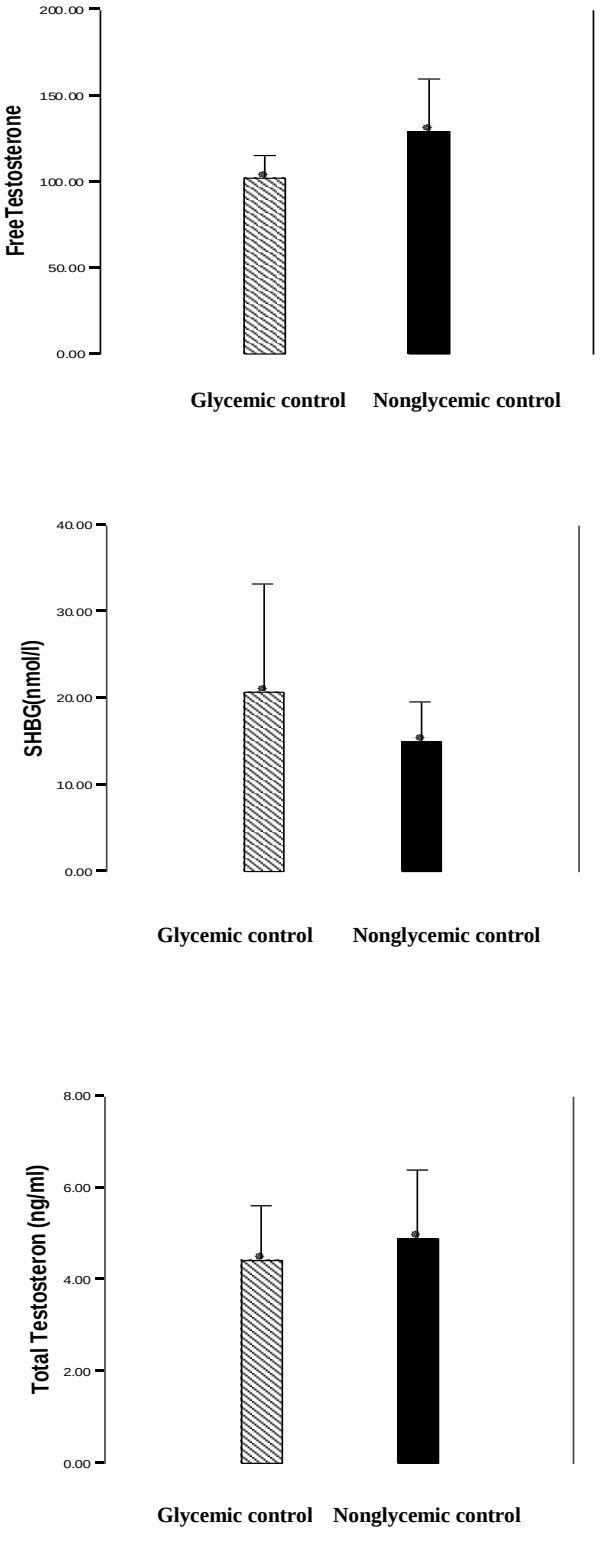

Figure 1: Plasma concentration of free testosterone index, SHBG and total testosterone in good glycemic control and poor glycemic control diabetics

Table 2: ORs for type 2 diabetes for Iranian men in the lowest third of concentrations of serum total and calculated free testosterone and SHBG

	Lowest third of total testosterone	Lowest third of calculated free testosterone	Lowest third of SHBG
Type 2 Diabetes			
Model 1	0.29(0.10-0.79)*	1.87(0.68-5.19)	1.75(0.66-4.64)
Model 2	0.20(0.06-0.67)*	2.00(0.69-5.76)	1.75(0.66-4.67)
Model 3	0.15(0.04-0.54)*	1.80(0.62-5.24)	1.45(0.49-4.27)
Model 4	0.27(0.06-1.10)	2.27(0.51-10.02)	2.26(0.61-8.27)

Data are ORs (95% CI). Model 1: age-adjusted. Model 2: adjusted for age and smoking (pack/year). Model 3: adjusted for the variables in model 2 and BMI (overweight and non overweight). Model 4: adjusted for the variables in model 3 and HbA1c (control glycemic and non control glycemic)

DISCUSSION

Mean BMI and age did not show a significant difference between diabetic and non-diabetic group. Mean FBS and HbA1C was significantly higher in diabetic patients in comparison to non-diabetic participants.

No difference was observed in LH between the two groups, However, FSH level in diabetic group was significantly lower than non-diabetic group. We could not find a clinical reason for this difference. TSH was significantly higher in the diabetic group than non-diabetic one. Since no simultaneous measurement of T4 and free T3 was performed and only one TSH test, without the possibility of repetition, was performed, it might not be possible to make a correct judgment.

Like other studies, our study showed that no significant relationship exist between the good glycemic control (based on HbA1C≤7) and serum testosterone level [2, 8-9]. In A study in 2009 on the effect of glycemic control (HbA1C≤7) on leydig cell function included 30 men with T2DM with the mean age of 57 and mean BMI of 28 without overt hypogonadism and 30 people as the control group with the same age and BMI. To study leydig cell function¸ FTI, SHBG, LH, insulin-like factor 3 (INSL3) were measured. The results of the study showed that FTI and INSL3 levels were lower in the diabetic group in comparison to the control group. The study also showed that hormonal parameters did not differ between patients with poor or good glycemic control [3]. Like our study, these studies confirm the point that there is no significant relationship between HbA1C and serum total testosterone, FTI and SHBG hyperglycemia is not the reason for the lower testosterone in diabetic patients. However, in a study on 159 diabetic patients with erectile dysfunction (ED), EI-Sakka in September of 2009 showed that after 3-6 months glycemic control (based on FBS) with insulin, hypoglycemic drugs or changes in the life style, the serum insulin decreased and serum total testosterone increased. Although they only measured FBS to study the glycemic control (and did not measure HbA1C), unlike our study and some similar studies, they reported a direct correlation between FBS and total testosterone[9].

In the present study, no significant difference was found between total testosterone level, free testosterone index and SHBG in diabetic and non-diabetic subjects. In the longitudinal study undertaken in Iran on 836 healthy adult men (20-80 years), no correlation was found between type 2 diabetes and total testosterone level, free testosterone index or SHBG [6]. This result was not in agreement with the study conducted in Boston that mentioned in white Caucasian race, the changes of sexual hormones in patients with metabolic syndrome was more than other races[10].One reason may be due to racial different and the other may be different patterns of socio-economic status [11]. It seems that Iranian diabetics have not serum testosterone level lower than healthy subjects; however our findings suggest further studies on this issue.

Limitations of this study were small sample size, the lack of repeat experiments in other laboratory and lack of direct measurement of free testosterone. However, measurement of FTI certainly did not decrease the accuracy of the study.

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