

The Evaluation of Serum Level of Testosterone and Sex Hormone- Binding Globulin in Men with Type 2 Diabetes

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ABSTRACT

OBJECTIVE: To evaluate the relationship between serum level of testosterone and sex hormone-binding globulin in men with type 2 diabetes.

MATERIALS AND METHODS: In this case-control study, forty men aged 40-70 with type 2 diabetes mellitus were randomly selected and compared with 40 non-diabetic men. The two groups were matched for their age and BMI. After complete observation and examination, fasting blood sugar, postprandial blood sugar, total and free testosterone, sex hormone-binding globulin and HbA1c were measured.

RESULTS: The mean serum level of total testosterone was 9.65 ± 2.16 mg/dl in diabetic patients and 12.77 ± 3 mg/dl in non-diabetic subjects which was significantly different ($P = 0.0001$). The mean value of free serum level of testosterone was significantly higher in non-diabetic group (14.96 ± 4.97 mg/dl) in comparison with diabetic group (9.55 ± 8.14 mg/dl, $P = 0.0001$).

CONCLUSION: In this study we found a lower level of total testosterone, free testosterone, and in lesser extent sex hormone-binding globulin in men with type 2 diabetes comparing to non-diabetic men.

KEYWORDS: Serum testosterone, Hormone-binding globulin, Type 2 diabetes.

INTRODUCTION

Over the last few years, there have been several reports demonstrating that men with type 2 diabetes mellitus (T2DM) have a higher prevalence of low circulating testosterone levels comparing with normal population (1). There is further evidence suggesting that a low testosterone level is a risk factor for development of metabolic syndrome and diabetes (2). Low concentration of sex hormone binding globulin (SHBG) is an independent risk factor for development of

type 2 diabetes mellitus in women and is strongly associated with insulin resistance (3). Hyperandrogenicity in women is also associated with an increased risk of type 2 diabetes and cardiovascular disease (4). In men, however, the low level of plasma testosterone has been observed to be associated with obesity, upper body fat distribution, and increased level of glucose and insulin (5). The signs and symptoms of low serum testosterone are: diminished interest in sex, erectile dysfunction, increased fat mass,

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reduced muscle mass, decreased strength, decreased bone density, depressed mood and fatigue. Since these symptoms are subtle and often overlap with other common medical conditions, low serum testosterone is frequently undiagnosed (6). Men with chronic conditions, such as diabetes, obesity, hypertension, hyperlipidemia and asthma/COPD are more likely to have low testosterone level compared to normal population (7). The purpose of this study, therefore, was to evaluate serum level of testosterone and SHBG in male with type 2 diabetes.

MATERIALS AND METHODS

This research was designed as a case-control study. Population-based samples of forty men with T2DM aged 40-70 years were randomly selected and referred to Yazd Diabetes Research Center.

Subjects without history of diabetes mellitus whose FBS was less than 126 mg/dl on two occasions and were matched for age and BMI were assigned to control group. Subjects with Hypogonadism, Hypopituitarism, renal or hepatic failure and those who used exogenous hormone, opium or medication which might affect sex hormone level were excluded from the study.

The institution's Research Ethics Committee approval was obtained prior to study enrollment. Informed consent was obtained from all subjects.

Anthropometric and Biochemical Measurements: BMI was computed by dividing weight (in kg) by the square of height (in meters). (kg/m^2). Fasting blood sugar and postprandial blood sugar were measured using

chromatography method. Glycosylated hemoglobin (HbA1c) was measured by HPLC method with DS5 analyzer. Testosterone and SHBG in the early morning (8:00–10:00 AM) were also measured using ELISA method.

The normal range for early morning total testosterone in adult males is considered between 300 ng/dL and 1000 ng/dL (0.35 to 10.5 nmol/L). Hypogonadism was defined as having an early morning total serum testosterone level less than 300 ng/dL.

Statistical Analysis: Chi square and T-student tests were used to compare variables. Results were given with their 95% confidence intervals (CIs). Data were presented as means \pm SD. For the assessment of correlation between variables, Pearson correlation was used. Statistical significance was set at $P < 0.05$.

RESULTS

In this study, 40 T2DM patients were randomly selected and compared to 40 non diabetic men. The mean of FBS was 170.3 ± 54.68 mg/dl in DM group and 90.8 ± 10.37 mg/dl in control group which reached significant level ($P = 0.0001$). The mean of 2hpp also became statistically significant between two groups (285.42 ± 104.7 mg/dl in DM group and 118.43 ± 10.7 mg/dl in control group, $P = 0.0001$). The mean of HbA1c in DM group was $9.1 \pm 1.98\%$ and in control group was $6.51 \pm 0.4\%$ ($P = 0.0001$). Total testosterone and free testosterone were significantly lower in diabetic group ($P = 0.0001$, see Table 1). The mean of SHBG was 29.04 ± 9.25 mg/dl in DM group and 36.42 ± 11.43 mg/dl in control group ($P = 0.002$).

Table 1- Comparison of variables studied in diabetic and non-diabetic control subjects.

Parameter	Diabetic group	Control group	P value
FBS (mg/dl)	170.3 ± 54.68	90.8 ± 10.37	0.0001
2hpp (mg/dl)	285.42 ± 104.7	118.43 ± 10.7	0.0001
HbA1c %	9.1 ± 1.98	6.51 ± 0.4	0.0001
Total testosterone (mg/dl)	9.65 ± 2.16	12.77 ± 3	0.0001
Free testosterone (mg/dl)	9.55 ± 8.14	14.96 ± 4.97	0.0001
SHBG	29.04 ± 9.25	36.42 ± 11.43	0.002

Comparing measurements of anthropometric variables, testosterone and SHBG, we found that type 2 diabetic patients had somewhat higher free testosterone values and lower SHBG than control subjects.

We also found that total testosterone was correlated with both free testosterone ($r = 0.71$, $P < 0.001$) and SHBG ($r = 0.30$, $P < 0.001$, the bulk of serum testosterone being bound to SHBG). By contrast, free testosterone and SHBG were virtually uncorrelated ($r = 0.04$, $P = 0.24$).

DISCUSSION

In this study, we found that the mean of total and free testosterone in men with diabetes was lower than control group. Total testosterone and SHBG were also lower in the diabetic men than in control group. The derived value of free testosterone was not different between groups.

In cross-sectional studies, low concentrations of testosterone and SHBG have been associated with visceral obesity, insulin resistance or hyperinsulinaemia and dyslipidaemia (8–12).

Regarding the relationship between insulin resistance and SHBG, it has been documented that both insulin and insulin-like growth factor 1 have inhibitory effects on SHBG secretion by Hep G2 cells in vitro (13). Insulin also suppresses hepatic SHBG synthesis (14). Thus, it has been proposed that SHBG levels could be a valuable marker of insulin resistance or hyperinsulinemia in humans (14). In a prospective nested case-control study from the Multiple Risk Factor Intervention

Trial, total and free testosterone levels were lower in 176 men who developed diabetes than those of 176 control subjects. Even after matching for fasting glucose levels and BMI, free testosterone, but not total testosterone, was still associated with incident diabetes (15). In a Massachusetts Male Aging Study (16), a cohort population-based study of men aged 40-70 years, they observed that mean testosterone level was significantly lower among men who later developed diabetes in comparison with mean levels of free testosterone and SHBG. But after controlling for all other factors in the model, lower levels of free testosterone and SHBG jointly and independently predicted incident diabetes. Haffner et al. (15) reported a retrospective association of diabetes with SHBG and free testosterone but not with total testosterone. Conversely, Tibblin et al. found an independent association for testosterone but only a marginally significant association for SHBG (17).

CONCLUSION

In our study total testosterone and free testosterone were significantly lower in diabetic group. The mean of sex hormone-binding globulin in diabetic group was also significantly lower than control group.

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