

# TESTOSTERONE LEVEL IN TYPE 2 DIABETIC MALE PATIENTS

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## ABSTRACT

### *Background*

The relationship between diabetes mellitus and testosterone level is a remarkable issue, given the fact that diabetes is rapidly -growing disease, the morbidity is more disabling than the diabetes itself.

### *Objectives*

The aim is to study testosterone levels in men with type 2 diabetes mellitus in age group of 35-55 years.

### *Patients and Methods*

In this study 100 male type 2 diabetic patients in age group of 35-55 years were assessed by testosterone and HbA1c level estimation along with other clinical variables like BMI, smoking, alcohol drinking status and types of medications.

### *Results*

In the current study among those patients with controlled diabetes, 92.1 % had normal testosterone level as compared to 67.7% of those with uncontrolled diabetes, so there is statistically significant relationship between the control status of diabetes and testosterone level, the P-value was 0.003, while the relation of testosterone level with age of patients, BMI, smoking, alcohol drinking status and types of medication were found to be not significant.

### *Conclusion*

Uncontrolled diabetes is associated with lower testosterone level as compared to those with well-controlled status.

**Keywords:** *Type 2 diabetes, Male, Testosterone.*

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## INTRODUCTION

According to the data from the International Diabetes Federation projects, 592 million individuals will have diabetes by the year 2035<sup>(1)</sup>. Diabetes associated with different complications, low testosterone levels is one of these complications. For sex differentiation and development, along with regulating the metabolism of glucose, proteins, lipids, and androgens are very crucial<sup>(2,3)</sup>. Inverse relationships between the serum testosterone level and cardiovascular risk factors<sup>(4-8)</sup>. Cardiovascular disease (CVD) and premature mortality are also increased by testosterone deficiency<sup>(9-12)</sup>.

Low level of testosterone might exacerbate sexual dysfunction by reducing libido<sup>(13)</sup>. Approximately 34% to 45% of men with diabetes have low testosterone<sup>(14)</sup>. One-third of newly diagnosed men with diabetes at presentation have low testosterone<sup>(15)</sup>, this reaches 50%, 6 years after diagnosis<sup>(16,17)</sup>. Some recommend that in type 2 diabetic patients, morning serum total testosterone should be measured in men with symptoms of sexual dysfunction.<sup>(18)</sup>

Testosterone is primarily synthesized in Leydig cells, and it is regulated by luteinizing hormone (LH) and follicle-stimulating hormone (FSH).<sup>(19)</sup> Low testosterone in diabetic patients may be due to:

### 1. Role of sex hormone-binding globins (SHBG):

Some studies have shown a strong relationship between low testosterone and SHBG with diabetes<sup>(20-24)</sup>. Although some others have shown that this relationship is independent of SHBG<sup>(25-27)</sup>.

### 2. Role of visceral fat:

Large cross-sectional surveys showing that the inverse association of testosterone with individual has central adiposity as a component of metabolic syndrome<sup>(28-31)</sup>. Further reduction in testosterone concentrations occur with increased adipose tissue through increased conversion to estradiol by aromatase<sup>(32)</sup>.

### 3. Role of leptin:

Leptin, have a role in the regulation of body weight and food intake, also stimulates hypothalamic gonadotropin-releasing hormone neurons that induce the release of LH under normal conditions<sup>(33)</sup>. Secondarily leptin also reduce testosterone production by suppression of the stimulatory effect of gonadotrophins; therefore, elevated leptin levels in obesity may further diminish

androgen status<sup>(34)</sup>.

Low testosterone level may be challenging because of the following. First, the threshold of it is the level below which adverse clinical outcomes occur is not known<sup>(18)</sup>. Second, marked variations in the reference ranges among laboratories<sup>(35,36)</sup>.

## PATIENTS AND METHODS

One hundred male patients with T2DM were screened from the July 2015 to October 2015 at diabetic centre of Sulaimani. After ethical approval from the patients, the patients are evaluated by:

Taking history (age, duration of diabetes since diagnosis, medications, smoking, and alcohol taking).

Assessment of Body mass index (BMI)

Evaluation of HbA1c and total testosterone level.

### Inclusion criteria:

Male

Age from (35-55) years

Type 2 diabetes.

The subjects were categorized into two groups, controlled diabetes (HbA1c  $\leq$  7%) and uncontrolled diabetes (HbA1c  $>$ 7%). Normal reference range of HbA1c is according to the American diabetes association (ADA) guidelines and isolated in the laboratory of diabetic centre of Sulaimani by (HLC\_723 GX) instrument.

Normal reference range of total testosterone is according to an isolated in laboratory of diabetic centre of Sulaimani by (Mini ViDAS) instrument.

BMI of each patient was taken by this equation

$$\text{BMI} = \text{weight (Kg)} / (\text{height (m)})^2$$

Data were entered into an Excel sheet. After data cleaning process, data were entered into SPSS-V21 (statistical package for social science-Version 21). At the beginning, descriptive analysis (frequencies and percentages) was performed for the demographic and charters of patient rights. Chi-square test and t-test were used to find association and significant differences between studied variables. A P-value of  $<$ 0.05 was considered to be statistically significant.

## RESULTS

### 1. Relation of testosterone levels with diabetes control status

Out of 100 patients who involved in our study, 38 patients had their diabetes controlled, while the remaining were uncontrolled. Among those patients with controlled diabetes, (92.1 %) had normal testosterone level as compared to (67.7%) of those with uncontrolled diabetes, so there is a statistically significant relationship between the control status of diabetes and testosterone level, the P-value was 0.003, Figure (1).

### 2. Relation of testosterone level with age

In current study age of the involved patients was between (35-55 years), analysis of the data taking from different age groups show that there was no significant relationship between the age and testosterone level, P-value was 0.124, Table (1)

### 3. Relationship between testosterone level and duration of disease in diabetic patients

In our study duration of diabetes since diagnosis was between (1- 16 years), no significant relation was found between duration of diabetes and testosterone level, P-value was 0.309, Table (1)

### 4. Relation between BMI and testosterone levels

In current study, 29 cases have normal BMI (18.5 – 24.9 kg/m<sup>2</sup> ), 53 cases were overweight ( BMI between 25- 29.9 kg/m<sup>2</sup> ) and the remaining cases were obese ( BMI 30 kg/m<sup>2</sup> and more ). There was no significant relation between BMI and testosterone level, Figure ( 2 ).

### 5. Relation of testosterone level to drinking alcohol and smoking status

In our study, we observed that 13% and 46% of the patients were alcohol drinker and smoker respectively. No significant relationships were found between testosterone level and alcohol or smoking. Table 2.

### 6. Relation between testosterone levels and diabetes medications

In current study, those patients who were using only oral hypoglycemic agents was 76, seven patients using insulin alone and the remaining were on both insulin and oral hypoglycemic agents. As observed there was no significant relationship between type of medications and testosterone level, P-value was 0.29, Table (3).

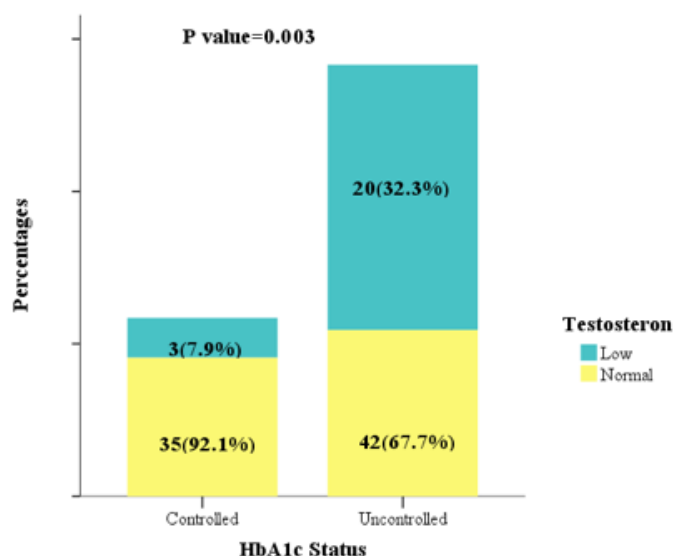


Figure 1. Relation of testosterone level to the diabetic control status.

Table 1. Relation of testosterone level with age and duration of diabetes.

Studied variables	Testosterone status		P values
	Low mean±SD	Normal mean±SD	
Age(Years)	48.0 ± 6.7	45.7±6.0	0.124
Duration of diabetes (years)	5.9±2.5	5.2±3.1	0.309

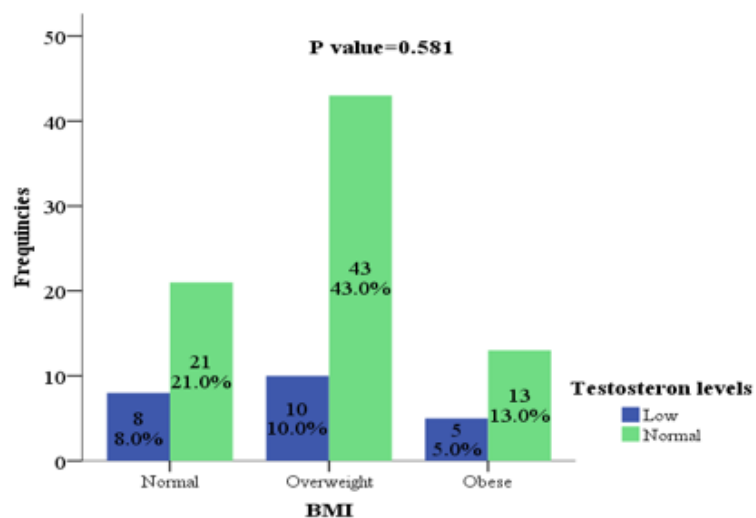


Figure 2. Relation between BMI and testosterone level.

Table 2. Alcohol and smoking status relation with testosterone level.

Studied variables	Total N(%)	Testosterone status		P values
		Low N(%)	Normal N(%)	
<b>Smoking status</b>				
Not smoker	54(54%)	15(27.8)	39(72.2)	0.160
Smoker	46(46%)	8(17.4)	38(82.6)	
<b>Alcoholic status</b>				
Non alcoholic	87(87%)	22(25.3)	65(74.7)	0.171
Alcoholic	13(13%)	1(7.7)	12(92.3)	

Table 3. Relation between diabetes medications and testosterone levels.

Diabetes medications	Testosterone level			P-value
	Normal	Low	Std. Deviation	
Insulin	2	5	1.13	0.29
Oral hypoglycemic medications	46	30	1.72	
Insulin & Oral hypoglycemic medications	7	10	1.92	

## **DISCUSSION**

### **Relation of testosterone level with diabetes control status**

In the current study, the testosterone level was significantly lower in uncontrolled diabetic patients as compared to those with well-controlled diabetes. Although a lot of studies done previously show that testosterone level is lower in diabetic patients as compared to non-diabetics<sup>(19, 37, 38, 39)</sup>, to our knowledge till now no study has been done to compare level of testosterone between controlled and uncontrolled diabetic patients. Limited number of studies was done to show that testosterone level is inversely associated with glycated hemoglobin level in non-diabetic patients and patients with metabolic syndrome<sup>(40, 41)</sup>.

### **Relation of testosterone level with age of the patients**

In our study, the relation between the age of patients and testosterone level was found to be not significant. These results are in concordance with two cross-sectional studies show that testosterone level not significantly affected by age<sup>(42, 43)</sup>. While our results are not in concordance with two other cross-sectional studies in which testosterone level declined with age, this difference possibly may be due to that these studies included older age groups than our study, also factors other than ageing might have influenced the data previously reported, and that ageing per se need not be associated with altered sex steroid levels in the human male gender<sup>(44, 45)</sup>.

### **Relationship between testosterone level and duration of disease in diabetic patients**

The results revealed no relation between testosterone level and duration of diabetes, these results were similar to a study done in 2013<sup>(46)</sup>.

### **Relation between BMI and testosterone levels**

In the present study, we found that there was no significant relationship between BMI and testosterone levels. While data from another study show that testosterone levels decreased progressively with increase in BMI<sup>(47)</sup>. There is what is called hypogonadal/obesity cycle. In this cycle, abdominal fat is increased due to low testosterone<sup>(48)</sup>.

### **Relation of testosterone level to drinking alcohol and smoking status**

Data from the current study show that 13% and 46%

of the patients were alcohol drinker and smoker respectively, but no significant relationships were found between testosterone level and alcohol or smoking. These results were not similar to studies that concluded that alcohol lead to a decline in testosterone level and Smoking may acutely increase testosterone level, but this can decrease with chronic exposure to tobacco by long-term smoking<sup>(49, 50)</sup>. These differences between our study and other studies may be due to the dose-dependent effect of alcohol on testosterone and the effects of smoking on testosterone levels depend on personal smoking pattern.

### **Relation between testosterone levels and diabetes medications**

In the present study as observed, there was no significant relationship between the type of medications and testosterone level. Recently, several studies show the role of insulin on the hypothalamic-pituitary-gonadal axis. In a randomized controlled trial of diabetic men, SHBG and total testosterone levels increased after 2 weeks of intensive insulin treatment with/without metformin, noted especially in the group treated without metformin<sup>(51)</sup>.

In conclusions, testosterone level is significantly lower in diabetic male patients with uncontrolled glycemic status as compared to those with well-controlled diabetes, so better control of diabetes will positively affect the testosterone level, prevent the progressive decline in testosterone among diabetic male patients and maintain a good sexual health.

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