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(RESEARCH ARTICLE)

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Poor glycemic control could be the main factor impacting testosterone levels in diabetic males

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Abstract

Males with diabetes mellitus have been reported to have low serum testosterone levels relative to the general population. This study aimed to explore the impact of glycemic control, duration of diabetes (in years), comorbidities, and diabetes complications on serum testosterone levels in different age groups.

Using a cross-sectional study design, data were collected from the files and lab results of 350 diabetic male patients at King Salman Armed Forces Hospital in Saudi Arabia. We obtained data about their age, serum testosterone levels, hemoglobin A1c (HbA1c), the duration of diabetes (in years), coexisting comorbidities (if present), and diabetes mellitus complications.

Patients in this study were found to have significantly lower serum testosterone levels than the average population and by looking at each factor independently, we come to find that glycemic control was the only factor found to substantially impact testosterone levels in diabetic males.

Moreover, poor glycemic control (HbA1c ≥7%) Alone was associated with lower serum testosterone levels regardless of the presence of other factors such as the duration of diabetes (in years), age, comorbidities, and micro/macrovascular complications. In conclusion, the presence of the other factors was not found to have significant effect on serum testosterone levels unless accompanied with poor glycemic control.

Along with this finding, further studies are required to better understand the exact mechanism of glycemic control's impact on testosterone levels.

Keywords: Testosterone; Glucose; Insulin; Diabetes mellitus (DM); Glycemic control

1. Introduction

Diabetes mellitus (DM) is considered one of the most prevalent diseases affecting around 422 million people worldwide.[1] It is characterized by either decreased tissue sensitivity to insulin (type 2 diabetes mellitus) or autoimmune destruction of the cells that produce insulin in the pancreas (type 1 diabetes mellitus). Insulin is the hormone responsible for glucose uptake by the cells, thus, decreased sensitivity to insulin, or the absence of insulin leads to the accumulation of glucose in the blood, which is known as hyperglycemia. [2]

The diagnosis of DM is established with a Fasting Plasma Glucose Test (FPG) of ≥126mg/dL,[3] Oral Glucose Tolerance Test (OGTT) of ≥200mg/dL, and/or Glycosylated Hemoglobin (HbA1c) of ≥6.5% (Table 1).[4]

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Table 1 Diagnostic criteria for diabetes mellitus

	Fasting Plasma Glucose Test (mg/dL)	**Oral Glucose Tolerance Test (mg/dL)**	**HbA1c (percent)**
Diabetes	≥126	≥200	≥6.5
Prediabetes	100-125	140-199	5.7-6.4
Normal	≤99	≤139	~5.67

DM is associated with many complications and affects different organ systems in the body. Complications of DM range from microvascular to macrovascular complications. Microvascular complications affect the nerves, which is known as neuropathy, the eyes (retinopathy), and the kidneys (nephropathy), while the macrovascular complications lead to the development of cardiovascular disease, stroke, and peripheral vascular disease (e.g., non-healing ulcers).[5] Another complication that is well-documented but needs to be better understood is low testosterone level. A significant proportion of patients with DM have low serum testosterone levels relative to the general population.[6] Testosterone deficiency is associated with decreased libido, erectile dysfunction, and osteoporosis.[7] The association between low serum testosterone and diabetes mellitus has recently become an attention-grabbing subject. Therefore, we conducted a study to explore the factors that impact serum testosterone levels in diabetic males.

2. Methods

Using a cross-sectional study design, we reviewed the files of 350 patients at King Salman Armed Forces Hospital (KSAFH) in Tabuk/Saudi Arabia. We included patients from multiple departments (cardiology, endocrinology, nephrology, neurology, family medicine, general surgery, and ophthalmology). The Local Ethics Committee approved the study.

For data collection, we reviewed the files of 350 male patients aged 18 to >65 years old. Three hundred and nineteen patients were Saudis, and 31 patients were non-Saudis. We chose HbA1c as the standard to determine the patient's eligibility for this study. We only included patients with an established diabetes mellitus diagnosis with an HbA1c ≥6.5%, which is the cutoff value to diagnose diabetes mellitus. Prediabetics (HbA1c <6.5%) were not included in the study. Patients with a history of low serum testosterone due to other diseases, patients with supraphysiological levels of testosterone, and patients on hormone replacement therapy were not included in the study.

The study variables collected from the computerized hospital file system were age, nationality, serum testosterone levels, HbA1c, years of diabetes duration, comorbidities (hypertension, ischemic heart disease, stroke, dyslipidemia, and chronic kidney disease), and DM complications (diabetic neuropathy, nephropathy, and retinopathy). For serum testosterone level and HbA1c, we only considered lab tests done during the same hospital visit. Lab tests for serum testosterone and HbA1c that were done at different times were not considered.

The years of diabetes duration were determined either by looking into the patients' files and physician notes or by tracing back their blood tests until we found their prediabetic period.

Many patients have a history of admission to multiple departments. We collected data regarding their comorbidities from the departments' file system. The data about DM complications were recorded from the department of endocrinology, neurology, ophthalmology, and nephrology.

3. Results and discussion

The mean testosterone level of the study group was found to be as 391 ng/dL, lower than that of the general population at King Salman Armed Forces Hospital, which is 534 ng/dL ($p < 0.001$) (Table 2). Moreover, this significant difference in testosterone levels between diabetic male patients and the general population could be attributed to one or more factors discussed later on in this article.

Table 2 Testosterone levels in the study group

	N	Mean	Std. deviation	Minimum	Maximum
T level (ng/dL)	350	391.33	164.153	11	818

Of the 350 diabetic patients included in the study, 28.57% (100 patients) had low serum testosterone levels (≤300 ng/dL) and 71.43% (250 patients) had serum testosterone levels >300 ng/dL (Figure 1). [8]

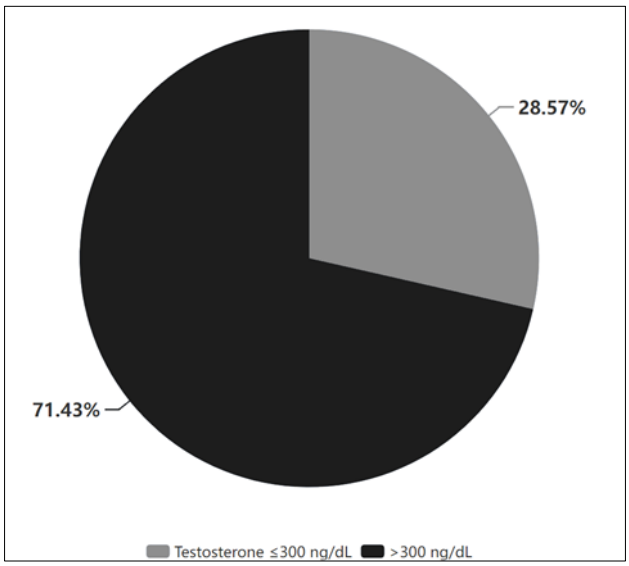

Figure 1 Percentage of diabetic patients with testosterone levels ≤300 ng/dL

3.1. Glycemic control

Looking at the degree of glycemic control, we noticed that serum testosterone levels were majorly impacted by and negatively correlated to poor glycemic control, which is defined as HbA1c ≥7%. [9] Furthermore, this negative correlation explains why it was found that, even though, diabetic patients generally have lower serum testosterone levels than the general population, those with tight glycemic control (HbA1c of 6.5-6.9%) had serum testosterone levels closer to the general population in spite of having DM (Figure 2).

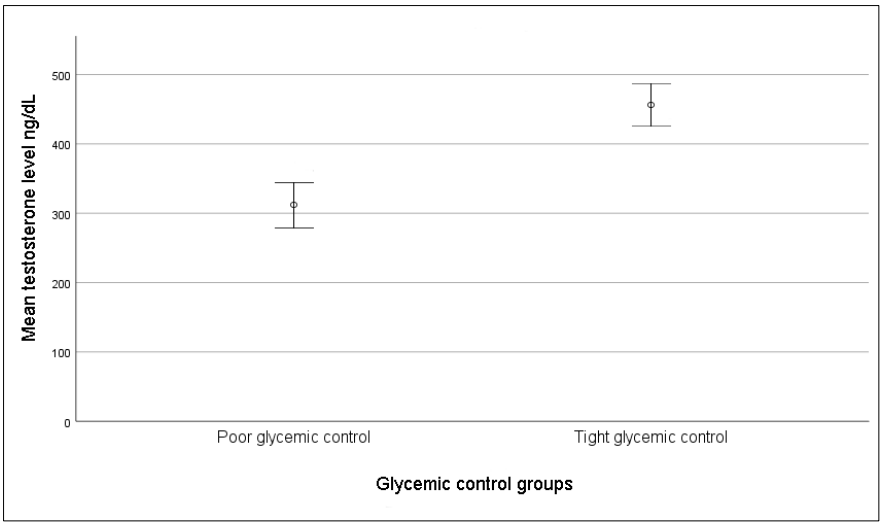

Figure 2 Poor and tight glycemic control groups (X-axis) and their mean testosterone level (Y-axis)

On the other hand, the mean testosterone level of the group with poor glycemic control was found to be 315 ng/dL compared to that of the group with tight glycemic control which is 467 ng/dL ($p < 0.001$).

3.2. Age

Serum testosterone levels are expected to decrease with age, due to normal physiological changes, by approximately 1.6% every year. [10, 11]

The patients' mean age in this study was 52 years old (±12.2 standard deviation), where the youngest patient was 20 years old and the oldest was 88 years old. Unexpectedly, young patients in this study were noted to have lower average serum testosterone than older patients. This paradoxical finding could be explained by the fact that young individuals usually do not check their serum glucose levels frequently. Therefore, due to disease unawareness, most of them have high HbA1c at the time of the diagnosis, thus, resulting in low serum testosterone levels.

Older individuals, on the other hand, typically have better glycemic control due to the chronicity and awareness of the disease. Hence, we conclude that age does not significantly impact testosterone levels in any way other than the expected normal physiological changes.

3.3. Duration of diabetes (in years)

Of the 350 diabetic patients included in the study, 6% were diagnosed with DM less than one year ago, 39.14% have had DM for 2-5 years, 21.71% have had DM for 6-9 years, and 33.14% have had DM for more than 10 years.

The results obtained indicate that there is no correlation between the duration of diabetes (in years) alone and serum testosterone levels. We found that patients with long diabetes duration and reasonable glycemic control (HbA1c <7%) tend to have higher average serum testosterone levels than those with shorter diabetes duration but poorer glycemic control.

This finding furthermore supports our point regarding the correlation between poor glycemic control and serum testosterone levels discussed earlier in the study.

3.4. Comorbidities and microvascular complications

By looking at the comorbidities while reviewing the patients' files, we found that, of the 350 diabetic patients, 31.7% (111 patients) have coexisting hypertension, 12% (42 patients) have ischemic heart disease, 20% (70 patients) have chronic kidney disease, and 36.3% (127 patients) have no comorbidities.

Patients with comorbidities were found to have an insignificant difference in their serum testosterone levels compared to those without comorbidities. Therefore, the presence of comorbidities alone was not found to impact serum testosterone levels in diabetic male patients as long as there is tight glycemic control.

On the other hand, microvascular complications of diabetes, such as neuropathy, nephropathy, and retinopathy were associated with lower serum testosterone levels but only in patients with poor glycemic control (HbA1c ≥7%). However, this finding could be due to confounding, mixing of effects, as patients with poor glycemic control are usually the ones who end up developing microvascular complications from DM.

4. Conclusion

After reviewing all of the factors that were thought to be affecting serum testosterone levels in diabetic male patients, we concluded that poor glycemic control is the main factor that is negatively impacting serum testosterone levels. On the other hand, the other factors that were discussed earlier in this study such as, age, duration of diabetes in years, comorbidities, and microvascular complications were found to have minimal to no impact on serum testosterone levels in diabetic male patients. If any impact was found, it was due to the poor glycemic control (HbA1c ≥7%) that was present along with the other factors and not due to the other factors solely. With that being stated, further studies are required in order to understand the exact mechanism of how poor glycemic control has an impact on serum testosterone levels in diabetic male patients.

Compliance with ethical standards

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Disclosure of conflict of interest

There is no conflict of interest declared.

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Statement of ethical approval

The study was approved by the local ethical committee and the permission to access the patients' files was given by the hospital.

Statement of informed consent

Informed consent was obtained from all individual participants in this study.

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