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Occurrence of Testosterone Deficiency in Males Presenting with type II Diabetes Mellitus

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Abstract

Background: Testosterone is the sex hormone, which plays important role in human body. In men, it is important to regulate the sex drive, bone mass, fat distribution, muscle mass and strength, and the production of red blood cells and sperm. Type II diabetes may cause a reduction in testosterone level which can negatively affect reproductive system of patient.

Objective: To determine the frequency of testosterone deficiency in males presenting with type II diabetes mellitus

Material and methods: This cross sectional study was done at department of Endocrinology, KEMU, Lahore for 6 months (01st January 2019 to 30th June 2019). One hundred patients diagnosed with type II diabetes mellitus were enrolled and blood samples were obtained to assess the testosterone level. SPSS v. 25 was used to analyze the data.

Results: The mean age of patients was 48.12 ± 15.16 years. Out of 100 candidates, 85 (85%) were married. There were 77 (77%) smokers, and 80 (80%) were hypertensive. Testosterone deficiency was noted in 72 (72%) patients.

Conclusion: In our study, we observed that the frequency of testosterone deficiency is high in diabetic patients.

Keywords: Testosterone deficiency; Type II diabetes mellitus; Marital status

Introduction

Diabetes affects an estimated 382 million people worldwide, with an 8.3 % prevalence rate [1]. Diabetes mellitus is a metabolic in the to illness with many etiologies defined by chronic hyperglycemia and abnormalities in carbohydrate, lipid, and protein metabolism caused by insulin production, insulin action, or both [2]. Hyperglycemia can be caused by the loss of pancreatic beta-cells or a decline in their function, resulting in decreased insulin secretion, or it can be caused by insulin resistance and varying degrees of inadequate insulin production, resulting in diabetes and its complications. Several reviews have been published on the topic of diabetes-related male infertility, although the majority of them have focused on how metabolic syndrome promotes male fertility reduction [3].

Sexual dysfunction in diabetes has a complicated pathogenesis. When compared to non-diabetic men, males with diabetes have a >3-fold increased risk of sexual dysfunction [4]. The endocrinology of the maturing male is complicated, with multiple hormones interacting in feedback along the hypothalamic-pituitary-testicular axis. Several sex hormones, particularly testosterone, drop as men age, with corresponding increases in luteinizing hormone, follicle-stimulating hormone, and sex hormone-binding globulin. Because sex hormones play such a large part in male physiology, these changes have far-reaching implications [5].

However, the decline might have a negative impact on one's quality of life as well as the operation of different organ systems. Testosterone deficiency syndrome is both underdiagnosed (the overall prevalence ranges from 6% to 9.5% in community-dwelling men aged 40 to 70 years, and jumps to 15%-30% in diabetic or obese men) and undertreated (less than 10% of men with TDS receive medication) [6]. Due to the absence of insulin's stimulatory action on these cells and an insulin-dependent decrease in FSH, which reduces LH levels, leydig cell activity and testosterone production decline in insulin-dependent diabetes. A drop in FSH produced by a fall in insulin reduces sperm production and fertility [7].

Due to increased activity of the aromatase enzyme present in fat tissues, which converts testosterone and androstenedione to estrogens, an increase in body lipids caused by diabetes lowers serum testosterone levels [8]. Significantly, this disease may have a role in the global loss in male fertility, as diabetes mellitus is becoming more prevalent in young men of reproductive age. As a result, it is critical that diabetics' reproductive health is preserved while on anti-diabetic medication [9]. Therefore, we conducted this study to find the extent of problem in local population. The findings of this study would help us to screen diabetic patient for disturbed reproductive male patients, especially in reproductive age group. So that in future, we can implement regular screening on intervals and can alter or include therapies to cure the syndrome.

Objective

To determine the frequency of testosterone deficiency in males presenting with type II diabetes mellitus

Materials and Methods

Study Design: Descriptive cross sectional study

Setting: Department of medicine in collaboration of Department of Endocrinology, KEMU, Lahore

Duration: Six months *i.e.* 01st January 2019 to 30th June 2019

Sample size: Sample size of 100 cases was estimated with 95% confidence level, 8.5% margin of error and percentage of testosterone deficiency *i.e.* 25% in diabetic patients [6].

Sampling technique: Non-probability consecutive sampling.

Sample Selection

Inclusion criteria: Male patients fall into age range of 40 years-70 years diagnosed with type II diabetes mellitus were enrolled study.

Exclusion criteria: Patients with chronic infertility issues before diagnosis of diabetes and taken treatment, renal failure, alcohol or drug abuser were excluded from the study.

Data collection procedure: After approval from the hospital ethical committee, all the patients of diabetes were enrolled from wards of department of medicine. Informed written consent was taken from all patients. Demographics like name, age, BMI, duration of diabetes, history of smoking, hypertension, dyslipidemia, marital status, number of children were also noted. Then blood samples were obtained in a 5 cc disposable syringe for routine investigations along in with serum testosterone level and sent to the laboratory of the hospital. Reports were assessed and serum testosterone level was noted. All the information was recorded in proforma.

Data analysis: Data was entered and analyzed through Statistical Package for Social Sciences (SPSS) version 25. Frequency and percentage of testosterone deficiency was calculated.

Results

The mean age of patients was 48.12 ± 15.16 years. The mean BMI of patients was 31.27 ± 13.69 kg/m^2. The mean duration of diabetes was 10.19 ± 9.94 years. Out of 100 patients, 37 (37%) were taking insulin (insulin dependent), 29 (29%) were taking oral metformin alone, 19 (19%) were taking combination of metformin with other anti-glycemic drugs while 15 (15%) were taking insulin with oral treatment. There were 77 (77%) smokers, 80 (80%) were hypertensive, 52 (52%) had dyslipidemia, 39 (39%) had obesity and 29 (29%) had positive family history of diabetes. Out of 100 candidates, 85 (85%) were married while 15 (15%) were unmarried. About 66 (66%) were came from rural region, 29 (29%) were came from semi urban region while 5 (5%) came from urban region. Out of 100 patients, 18 (18%) were illiterate, 34 (34%) were matric pass, 29 (29%) had education up to graduation while 19 (19%) had post-graduation. The mean serum testosterone level was noted as 300.20 ± 146.08 ng/ml. (Table 1)

Testosterone deficiency was noted in 72 (72%) patients while 28 (28%) patients had normal testosterone level. (Figure 1)

Findings	F (%), mean ± SD
n	100
Age (years)	48.12 ± 15.16
BMI	31.27 ± 13.69
Duration of diabetes	10.19 ± 9.94
Diabetes treatment	
Insulin	37 (37%)
Oral metformin alone	29 (29%)
Combination oral	19 (19%)
Insulin plus oral	15 (15%)
Hypertension	80 (80%)
Smoking	77 (77%)
Dyslipidemia	52 (52%)
Obesity	39 (39%)
Family history of diabetes	29 (29%)
Marital status	
Married	85 (85%)
Unmarried	15 (15%)
No. of children	
0	15 (15%)
1	13 (13%)
2	9 (9%)
3	31 (31%)

4	12 (12%)
5	5 (5%)
6	8 (8%)
7	2 (2%)
8	2 (2%)
9	2 (2%)
10	1 (1%)
Residence	
Rural	66 (66%)
Semi urban	29 (29%)
Urban	5 (5%)
Education	
Illiterate	18 (18%)
Matric	34 (34%)
Graduation	29 (29%)
Postgraduate	19 (19%)
Serum testosterone level	300.20 ± 146.08

Table 1: Demographics of patients.

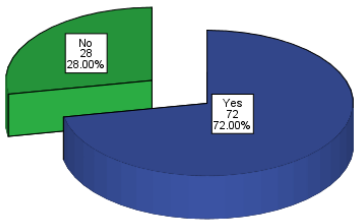

Figure 1: Testosterone deficiency.

Discussion

Diabetes mellitus is one of the most serious public health concerns in today's world. Although it was once believed that diabetes mellitus had no influence on male reproductive function, this belief has been questioned in recent years [10]. Insulin receptors have been found in Leydig cells, and insulin has been linked to the growth and proliferation of these cells. In primary Leydig cell cultures, insulin was also found to boost testosterone synthesis. As a result, insulin may have direct impacts on Leydig cells or indirectly through its action on LH, which will further regulate Leydig cell function [11,12].

Testosterone deficiency and sex steroid status are both risk factors for type 2 diabetes. Some research looked into the relationship between testosterone levels and the risk of diabetes in males, but their results were mixed [13]. Lower blood testosterone is not only frequent in men with type 2 diabetes who have already been diagnosed, but it also predicts future diabetic risks and death, according to epidemiological studies. Low testosterone may be a mediator of dysglycemia, according to preclinical investigations [14].

In our study, we observed that Testosterone deficiency was noted in 72 (72%) patients. Despite this, total testosterone levels in diabetic males were consistently lower in all individual investigations compared to nondiabetic controls, with a mean pooled difference of 2.66 nmol/liter [95% Confidence Interval (CI), 3.45 to 1.86].
After adjusting for age and crude markers of body fat, such as BMI and waist circumference, the difference in total testosterone was reduced, at 1.61 nmol/liter (95% CI, 2.56 to 0.65), although it was still significant [15].

According to a more recent meta-analysis by Corona et al., of 28 cross-sectional studies including 1,822 men with diabetes and 10,009 nondiabetic controls, total testosterone was lower in men with diabetes than controls [mean difference, 2.99 nmol/liter (95% CI, 3.59 to 2.40) and diabetes remained associated with lower total testosterone in the levels independent of age and BMI (adjusted r=0.568; P 0.0001). But Corona et al., could not determine the relationship between free testosterone levels and diabetes, because of scarce reliable information and data [16].

Nevertheless, a cross-sectional study of 1413 adult men from the Third National Health and Nutrition Examination Survey (NHANES)

cohort found that men in the lowest tertile of calculated free testosterone were more likely to have prevalent diabetes (odds ratio, 4.12; 95% CI, 1.25–13.55; P=0.04), even after controlling for the main age, ethnicity, and adiposity [17]. A research in Australia found that 43% of senior, obese men with type 2 diabetes had low total testosterone levels and 53% had low estimated free testosterone levels.

In these individuals, serum testosterone levels were inversely related to age and BMI; however, low testosterone levels were not limited to these characteristics, as low circulating testosterone was seen in 20% of youthful and 40% of underweight males [19].

Total testosterone levels were adequately lowered in diabetics, according to a meta-analysis of 20 cross-sectional studies involving 850 type 2 diabetes men [20]. Brand et al., found that diabetic men had not only lower testosterone but also lower levels of sex hormone binding globulin when compared to non-diabetic men in a cross-sectional study of 1,292 males [21]. Grossmann et al. observed testosterone deficiency to be more common in males with diabetes, regardless of type of diabetes, in a cross-sectional study of 574 men with type 2 diabetes and 69 men with type 1 diabetes [18].

Kumari et al. also found that diabetic patients had significantly lower mean total testosterone levels than non-diabetic patients (8.9 5.1 *versus* 14.1 7.2 mmol/L; p-value: 0.0001), and diabetic patients had significantly higher prevalence of androgen deficiency (45.5% *vs.* 20% ; p-value: 0.00001) [22].

This conjunction of diabetes and testosterone insufficiency in males has sparked a heated debate about whether low testosterone causes metabolic dysfunction, if it is simply a biomarker associated with diabetes, or whether low total serum testosterone is a result of long-term diabetes [15]. Thus according to current research, Asian and Caucasian men with low serum testosterone levels are more likely to develop metabolic syndrome, which includes type 2 diabetes and has negative cardiovascular clinical consequences [23].

Low blood testosterone concentrations are common in overweight or obese men, and are linked to an increased risk of type II diabetes [24]. In our study, there were 35 (35%) obese patients. Given that diabetes is becoming a fast-growing epidemic with morbidity that is more disabling than the disease itself, the association between testosterone and diabetes is a critical topic. Various studies have shown an increase in the prevalence of hypogonadism in diabetics, although whether this is a cause or a consequence is still being investigated. The number of testosterone prescriptions has risen in recent decades, despite the fact that the link between testosterone therapy and cardiovascular effects is still unclear [25].

Hypogonadism is a condition that affects both men and women. A study of 1,849 men (398 diabetic *versus* 1451 non-diabetics) found that obesity affects testosterone levels, as they discovered a negative correlation between testosterone and body mass index, regardless of whether the subjects had diabetes or not, though diabetic men had high risk of low free testosterone across all BMI categories [26].

Conclusion

In our study, we observed that the frequency of testosterone deficiency is high in diabetic patients. Thus, in future we can screen diabetic patients for testosterone deficiency, especially in patients of reproductive age group in order to prevent infertility. Further studies should be done with large sample size to determine the testosterone deficiency and its treatment protocol along with treatment protocol for diabetes.

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