ORIGINAL RESEARCH PAPER

Endocrinology

# STUDY OF SERUM TESTOSTERONE LEVELS IN TYPE 2 DIABETES MELLITUS PATIENTS IN A TERTIARY CARE CENTRE IN NORTH INDIA

KEY WORDS:

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**ABSTRACT**

**INTRODUCTION:** Type 2 diabetes mellitus is the predominant form of diabetes worldwide, accounting for 90% of cases globally. Insulin resistance is an important feature of type 2 diabetes. Low concentrations of testosterone are linked with insulin resistance and implicated in hyperglycemia, hypertension, dyslipidemia, and an increased risk of vascular disease. The etiology of erectile dysfunction in Type 2 diabetes is often multifactorial and includes poor metabolic control, diabetes-induced micro-and macrovascular alterations, autonomic neuropathy, hypogonadism, or a combination of all these factors.

**AIMS and OBJECTIVES:** To estimate the level of serum testosterone in diabetes mellitus type-2 patients and to find co-relation between testosterone and serum glucose level in Diabetes mellitus type-2 patients.

**MATERIAL and METHODS:** A Prospective study was conducted on 100 patients diagnosed as Diabetes Mellitus Type-2 to estimate the serum testosterone levels. All the patients were selected from indoor and OPD basis of MMIMSR, Mullana,Ambala.

**OBSERVATION and RESULTS:** Plotting free testosterone levels in various age groups in Diabetes Mellitus type 2 showed that serum testosterone levels were significantly low in age group 41-60 which was statistically significant. Our study also correlated the relationship between increasing BMI, increasing duration of diabetes mellitus and the presence diabetic complications with the falling free serum testosterone levels which also came out to be statistically significant.

**CONCLUSION:** Our study concludes that there is a positive correlation between diabetes mellitus type 2 and falling serum testosterone levels.

## INTRODUCTION:

Type 2 diabetes is the predominant form of diabetes worldwide, accounting for 90% of cases globally.[1,2] Asian Indians have surprisingly higher prevalence of type 2 diabetes compared to Caucasians. Excessive insulin resistance in Asian Indians compared to Caucasians may be one of the contributing factors. This difference in the degree of insulin resistance may be explained by either an environmental or a genetic factor or by combination of both.[3-10]. Diabetes mellitus is a medical condition which is often associated with male sexual dysfunction. Erectile dysfunction (ED) is estimated to occur in 28-75% of diabetic males and its prevalence appears to increase with age & duration .[11-14] The etiology of ED in type 2 diabetes is often multifactorial and include poor metabolic control, diabetes-induced micro-and macrovascular alterations, autonomic neuropathy, hypogonadism, or a combination of all these factors.[15-17] Type 2 diabetes, which is not an autoimmune disorder is also associated with other endocrine diseases, in particular hypogonadism in men. Androgen deficiency has recently come to the forefront of the medical literature after being ignored for decades.

Important associations are being developed and confirmed in the literature between androgen deficiency and metabolic disorders. More specifically, there is an important health impact related to metabolic syndrome (MetS), insulin resistance (IR), type 2 diabetes and ultimately vascular disease and erectile dysfunction (ED). Low concentrations of testosterone are linked with IR and implicated in hyperglycaemia, hypertension, dyslipidaemia, and an increased risk of vascular disease.[18-23]

Insulin resistance is an important feature of type 2 diabetes. It is being increasingly recognized that low testosterone levels in men are associated with reduced insulin sensitivity and type 2 diabetes[24].Testosterone biosynthesis is regulated primarily by pulsatile secretion of luteinising hormone (LH) and serum testosterone levels reflect the integrity of the hypothalamic-pituitary-gonadal (HPG) axis. Therefore low testosterone levels noted in cases of insulin resistance may indicate a defect at one or more functional levels of the HPG axis.

Testosterone is the major male androgen and is produced by the interstitial cells of the leydig. It is responsible for male secondary sexual characteristics and sperm production[25]. The effects of low testosterone levels include fatigue, anaemia, bone loss, loss of sexual drive and erectile dysfunction. This last symptom in particular is important because diabetic men are highly prone to erectile dysfunction due to nerve damage, poor circulation of blood and low testosterone. These conditions are difficult to treat, and many men suffer in silence because they never bring their erectile dysfunction to their doctor or because there are few treatment options available. Hypogonadism is relatively easy to treat with testosterone supplements but this is not for everybody as testosterone replacement promotes the growth of prostate cancer and can in rare instances increases the number of red blood cells to the point that blood flow becomes sluggish[26].

In the insulin-resistance state, Leydig cell function, particularly steroidogenesis, may be impaired by changes in the production of hormones and cytokines locally in the target tissue and in adipose tissue. Although several studies suggest that increasing insulin resistance may be attributed to a decrease in testosterone secretion in men, it is not fully clear how the HPG axis mediates the interplay between

testosterone and insulin levels.Other potential mechanisms for low testosterone levels in type 2 diabetes mellitus include reduced or absent stimulatory effect of insulin on Leydig cells[27] , increased leptin levels in diabetes causing Leydig cell dysfunction[28] , increased TNF levels in diabetes inhibiting steroid biosynthesis in Leydig cells[29] . Clearly, additional studies are needed to fully delineate the biochemical and physiological mechanisms underlying reduced T synthesis in diabetes.

## MATERIAL AND METHODS

Study design: A Prospective study was conducted on the patients diagnosed as diabetes mellitus Type-2 to estimate the serum testosterone levels. Sample size was 100 patients selected from indoor and OPD basis of MMIMSR, Mullana Ambala.

Inclusion Criteria:All male subjects of type-2 diabetes mellitus between the age of 30-60 years irrespective of the duration of diabetes, Currently on oral hypoglycaemic drugs and or insulin.

Exclusion criteria: Subjects with age less than 30yrs and more than 60yrs,subjects with Type-1 diabetes mellitus,subjects currently on medication like corticosteroids, testosterone etc.Patients with history of hypogonadism, panhypopit uitarism.Patients with hyperthyroidism and chronic debilitating conditions like chronic renal failure, cirrhosis or HIV.

**Table 1: Age distribution of the patients enrolled**

| Age(in years) | Number of patients | Percentage (%) |
|---|---|---|
| 30 – 40 | 18 | 18.0 |
| 41 – 50 | 34 | 34.0 |
| 51 – 60 | 48 | 48.0 |

**Table 2: Smoking status of the patients**

| Smoker | Number of patients | Percentage(%) |
|---|---|---|
| Yes | 82 | 82.0 |
| No | 18 | 18.0 |

**Table 3: Distribution of patients according to their Body Mass Index (BMI)**

| BMI | Score | Number of patients | Percentage (%) |
|---|---|---|---|
| Below Normal | < 18.6 | 0 | 0.0 |
| Normal | 18.6 – 24.9 | 23 | 23.0 |
| Overweight & Obese | ≥ 25 | 77 | 77.0 |

**Table 4: Distribution of patients according to the fasting blood sugar (FBS) levels.**

| Fbs | Score(mg/dl) | Number of patients | Percentage(%) |
|---|---|---|---|
| Controlled | ≤125 | 24 | 24 |
| Uncontrolled | ≥ 126 | 76 | 76.0 |

**Table 5: Distribution of patients according to HBA1C Status.**

| HBA 1C STATUS | VALUE | Number of patients | Percentage(%) |
|---|---|---|---|
| controlled | ≤ 6.4 | 20 | 20 |
| uncontrolled | ≥ 6.5 | 80 | 80.0 |

**Table 6: Distribution of patients according to duration of disease**

| Duration(in years) | Number of patients | Percentage(%) |
|---|---|---|
| ≤ 5 | 22 | 22.0 |
| 6 – 10 | 38 | 38.0 |
| 11 – 15 | 26 | 26.0 |
| > 15 | 14 | 14.0 |

**Table 7: Distribution of patients according to Serum testosterone levels.**

| Serum testosterone | Score (ng/dl) | Number of patients | Percentage(%) |
|---|---|---|---|
| Below Normal | < 3.0 | 77 | 77.0 |
| Normal | 3.0 – 10.0 | 23 | 23.0 |

**Table 8: Distribution of serum testosterone status among patients according to age groups**

| Age(in years) | Testosterone levels <3 ng/dl (Below normal) | | Testosterone levels 3-10 ng/dl (within Normal range) | | Total | | $\chi^2$, df, p-value |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | |
| 30 – 40 | 1 | 1.3 | 17 | 73.9 | 18 | 18.0 | 66.767*** , 2, 0.000 |
| 41 – 50 | 28 | 36.4 | 6 | 26.1 | 34 | 34.0 | |
| 51 – 60 | 48 | 62.3 | 0 | 0.0 | 48 | 48.0 | |
| Total | 77 | 100.0 | 23 | 23.0 | 100 | 100.0 | |

**Table 9: Distribution of serum testosterone status among patients according to smoking status**

| Smoker | Testosterone levels <3 ng/dl (Below normal) | | Testosterone levels 3-10 ng/dl (within Normal range) | | Total | | $\chi^2$, df, p-value |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | |
| Yes | 76 | 98.7 | 6 | 26.1 | 82 | 82.0 | 63.267*** , 1, 0.000# |
| No | 1 | 1.3 | 17 | 73.9 | 18 | 18.0 | |
| Total | 77 | 100.0 | 23 | 23.0 | 100 | 100.0 | |

**Table No. 10 Distribution of serum testosterone status among patients according to the duration of disease**

| Duration of disease (in years) | Below normal | | Normal | | Total | | $\chi^2$, df, p-value |
|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | |
| ≤ 5 | 3 | 3.9 | 19 | 82.6 | 22 | 22.0 | 65.162*** , 3, 0.000 |
| 6 – 10 | 34 | 44.2 | 4 | 17.4 | 38 | 38.0 | |
| 11 – 15 | 26 | 33.8 | 0 | 0.0 | 26 | 26.0 | |
| >15 | 14 | 18.2 | 0 | 0.0 | 14 | 14.0 | |

**Table 11: Mean Serum testosterone levels among patients according to their age groups**

| Age(in years) | No. Of patients | Mean testosterone values (in ng/dl) | Std. Deviation | F | p-value |
|---|---|---|---|---|---|
| 30 – 40 | 18 | 4.84 | 1.3 | 91.424 *** | 0.000 |
| 41 – 50 | 34 | 2.01 | 1.1 | | |
| 51 – 60 | 48 | 1.32 | 0.7 | | |

## DISCUSSION:

In the present study 77% patients have below normal serum free testosterone levels as compared to the study conducted by Sachin Verma et al[30] who included 50 diabetes mellitus 2 patients in their study, where 92% patients had free testosterone level below normal. Both the studies have this value statistically significant.However in the study done by Kapoor et al[31] only 42% patients had serum free testosterone levels below normal. Several cross-sectional studies and systemic analyses from various countries have reported that type 2 diabetes is associated with low testosterone levels. However, these studies reported differences in low testosterone levels with the varying ages of participants, cut-off points used to define hypogonadism, method of analysis, duration, and complication of diabetes are dissimilar. A study from Australia reported that 43% of type 2 diabetes patients had total testosterone levels <10 nmol/l.[32] In the United Kingdom, a cross-sectional study of 355 men with type 2 diabetic aged >30 showed that 17% had hypogonadism with total testosterone <8 nmol/1, and a further 25% had symptoms of hypogonadism associated with a total testosterone level between 8 and 12 nmol/l.[31]

In accordance with the present study; the mean free testosterone levels in patients with overweight was

1.76±1.2.This is in comparison to 0.296±0.022 in the study conducted by Dhindsa et al[33] hence there was significant decline in serum free testosterone in both the studies.(P<0.01).

In the present study 23% patients have deranged RFT, and 24% patients have macrovascular abnormalities in form of cardiovascular, cerebrovascular involvement. However 65% and 43% patients have microvascular abnormalities in the form of neuropathy and retinopathy respectively. In the study conducted by Zdravko et al[34], there was significant correlation between macrovascular and microvascular complications with free testosterone level that is p<0.05 in macrovascular, p<0.01 in microvascular. Our study had similar correlation between macrovascular and microvascular complications with free serum testosterone levels with a statistically significant p value (p<0.05).

## CONCLUSION:

From the present study it is thus concluded that free serum testosterone levels are significantly low in Type 2 diabetes mellitus and the levels further fall with increasing age of patients and increase in their body weight.

It is suggested that continuous monitoring of testosterone levels should be undertaken in every diabetic patient especially obese and of increasing age for early detection of low testosterone levels. Further work is needed to assess whether testosterone deficiency in Type 2 diabetes mellitus is responsible for the long term complication of Diabetes Mellitus and whether testosterone therapy will be beneficial in these cases

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