



SERUM TESTOSTERONE LEVEL IN TYPE 2 DIABETES MELLITUS MALES: A REVIEW IN URBAN POPULATION OF PAKISTAN.

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ABSTRACT

Background: High prevalence of low testosterone levels is evocative due to many chronic conditions, amongst which Diabetes Mellitus is at the top most. Creating such association decisively might contain concentrated results during execution of hypogonadism and diabetes mellitus. In Pakistani atmosphere these outcomes have to be established in association to diabetic individuals, therefore an expressive study has been done to validate these results. **Objective:** This study was carried out to assess total testosterone concentration in male type 2 diabetes patients with their age and BMI corresponding controls and observe the correlation among type 2 diabetes mellitus and serum testosterone levels. **Methods:** This cross sectional study which was carried out in Baqai Institute of Diabetology and Endocrinology Karachi, and Mohtarma Shaheed Benazir Bhutto Hospital Quetta on 200 male patients of type 2 diabetes mellitus with BMI and 50 matched male controls were studied with their serum testosterone concentrations measured. **Results:** The mean age of controls was 35.9 years and that of diabetic cases was 42.7 years. The mean BMI of controls was 23.2 Kg/m² while in diabetic cases it was 28.6 Kg/m². The testosterone levels among diabetic cases was 2.47 ng/dl which was much lower than the testosterone level seen in control mean 6.23 ng/dl done in age and BMI groups. 139 (69%) diabetic cases had low testosterone level while 61 (31%) cases had normal level of testosterone. This ratio among control was 03 (6%) low testosterone level while 47 (94%) had normal testosterone levels seen. **Conclusions:** Serum testosterone levels are considerably lower in type 2 diabetes mellitus individuals irrespective of BMI and age.

KEYWORDS: Testosterone and Diabetes mellitus.

INTRODUCTION

Diabetes mellitus is rising at an alarming rate with an expected rise of 592 million patients till 2035.^[1,2] It is a complex disease characterized by hyperglycemia, dyslipidemia, metabolic disorders, and aftermaths in diverse long-standing complications. Numerous studies had concluded that type II diabetes mellitus in men lead to low serum testosterone levels or that low serum testosterone concentrations might even expect the commencement of diabetes mellitus.^[3,4]

Patients with type 2 diabetes mellitus have a low testosterone level relative to reference based on healthy young men.^[5] Low testosterone level is commonly associated with type 2 diabetes mellitus and testosterone deficiency in adult age is associated with decrease in libido, energy, hematocrit, muscle mass and bone mineralization with depression.^[6,7] These interesting findings required to be validated in diabetic men, and studies have to be made to assess if reduced serum

testosterone concentrations in diabetes mellitus are associated with obesity, age or other variables. The majority of these types of studies are western based. The present study truly concluded the association of low serum testosterone estimation amongst Pakistani diabetic population.

METHODS

This study was conducted in Baqai Institute of Diabetology and Endocrinology (BIDE) Karachi Pakistan and Mohtarma Shaheed Benazir Bhutto Hospital Quetta during the period of April 2015 to October 2015. This cross sectional study for serum estimation of free testosterone concentrations in 200 type 2 diabetic male patients with an age of 15-62 years. The control group of 50 non diabetic individuals with matched age and body mass index (BMI) were also taken. The informed consent was taken from all diabetic and non-diabetic individuals. Individuals with unwilling for any enquiry, known history of hypogonadism,

hyperthyroidism, cirrhosis, renal failure and HIV positives were excluded from study. The mean concentration of serum testosterone was determined in diverse age and BMI groups and compared with controls.

Total testosterone was calculated by Enzyme Linked Immuno Sorbant Assay (ELISA). Estimation of HbA1c (4.2-6.2%) performed by High Performance Liquid Chromatography (HPLC). Low testosterone level cut off values below 3.0 ng/dl (American urological society) whereas a normal range was taken in between 0.1-12.0 ng/dl.

RESULTS

Both control and cases were well matched with respect to age (35.9 vs 42.7 years) and BMI (23.2 vs 28.6 Kg/m²). Mean testosterone concentration was 6.23 ng /dl in control group, while this level was found significantly low 2.47 ng /dl in diabetic group. HbA1c recorded in diabetics was 9.2%. Overall demographic comparison manifest that the individuals having diabetes mellitus are more prone to abnormal levels of all constituents as shown in table-1.

In age group 15-30 years the controls have normal mean value of testosterone 5.9 ± 0.57, while this was too low 2.9 ± 0.48 recorded in individuals having diabetes. This difference is statistically significant. In age group 31-40 years a statistically significance variance level of testosterone observed as well where mean testosterone level was 6.5 ± 0.70 ng/dl in control and 2.6 ± 0.28 ng/dl in diabetic group. In age group 41-50 years the mean testosterone level of 5.6 ± 1.2ng/dl in control, while in diabetic group it was 2.3 ± 0.18 ng/dl which was quite significant. In age group 51-60 years the control mean was 6.2 ± 1.2 ng/dl a normal one, while a level of 2.6 ± 0.45 ng/dl seen in diabetic group. This was also a significant value observed. In age group of 61-70 years the control testosterone mean was 3.2 ± 1.3 ng/dl, while in diabetic group it was 2.2 ± 0.85 ng/dl. (Table-2).

Body mass index (BMI) always matters in relation to diabetes and hypogonadism. Table-3 shows testosterone level distribution in diabetic cases and non- diabetic control group in relation to BMI. With a BMI less than 20, in controls (n= 04), a mean of testosterone level was 5.3 ± 0.8 ng/dl comparing with diabetic BMI was 3.0 ± 0.7 ng/dl. There was a decrease testosterone level seen in diabetics with a BMI <20 (T value of 0.80 and 0.00 significance). A BMI of 20-24.9 in control group revealed a mean testosterone level of 6.1 ± 0.5 ng/dl and this was 2.4 ± 0.3 ng/dl in diabetic group (Significance level was 0.00 while T value was 0.67). In BMI 25-29.9, in control group the testosterone level was 6.3 ± 0.5 ng/dl and in diabetic group it was 2.4 ± 0.1 ng/dl (Significance level 0.00 and T value was 0.85). With BMI of 30-34.9 no any control individual was seen while diabetics seen with the testosterone level of 2.5 ± 0.3 ng/dl. In BMI of >35, no any control case was seen but with this BMI diabetics was found with a mean testosterone value of 2.4 ± 0.5 ng/dl.

The low serum testosterone level correlation with age. In control individuals 3 cases (6%) found with low level of testosterone while 47 (94%) was normal (r = -0.76 & p = 0.44). Patients with normal serum testosterone level (r = -0.06 & p = 0.67). In diabetic group number of low testosterone level cases were 139 (69%) with normal testosterone level 61(31%). For low testosterone level diabetic group (r = -0.01 & p = 0.90). For normal testosterone level diabetic cases (r = 0.99 and p = 0.05 respectively).

Table-1: Comparison of demographic and biochemical profiles of diabetic and control groups.

Parameters (mean)	Diabetic	Control
Number	200	50
Mean age (Years)	42.7	35.9
BMI (Kg/m ²)	28.6	23.27
Testosterone level (ng/dl)	2.47	6.23
HbA _{1c} (%)*	9.52	5.11

*DCCT unit: Diabetic Control & Complications Trial

Table-2: Testosterone distribution level in control and diabetic groups in different age groups.

Age groups Control n= 50	Control Mean value in ng/dl	Age groups Diabetic n= 200	Diabetic Mean value in ng/dl	Significance
15-30 years n= 18	5.9 ± 0.57	15-30 years n= 24	2.9 ± 0.48	<0.00
31-40 years n= 17	6.5 ± 0.70	31-40 years n= 51	2.6 ± 0.28	<0.00
41-50 years n= 07	5.6 ± 1.2	41-50 years n= 88	2.3 ± 0.18	<0.00
51-60 years n= 06	6.2 ± 1.2	51-60 years n= 33	2.6 ± 0.45	<0.00
61-70 years n= 02	3.2 ± 1.3	61-70 years n= 04	2.2 ± 0.85	<0.00

Table-3: Distribution of testosterone level in control and diabetic group in relation to BMI.

BMI Kg/m ²	Control Group Mean Testosterone Level (ng/dl)	Diabetic Group Mean Testosterone Level (ng/dl)	T value	P significance
< 20	5.3 ± 0.8	3.0 ± 0.7	0.80	0.00
20-24.9	6.1 ± 0.5	2.4 ± 0.3	0.67	0.00
25-29.9	6.3 ± 0.5	2.4 ± 0.1	0.85	0.00
30-34.9	00	2.5 ± 0.3	00	0.00
>35	00	2.4 ± 0.5	00	0.00

Table 4: Correlation of normal & low testosterone level of control and diabetic groups

Parameters	Control			Diabetic		
	Numbers	Correlation r	P value	Numbers	Correlation r	P value
Patients with low Testosterone level	03	-0.76	0.44	139	-0.01	0.90
Patients with normal Testosterone level	47	-0.06	0.67	61	0.99	0.05
Total	50			200		

DISCUSSION

Testosterone is the primary anabolic steroid sex hormone in male which contributes to the sex drive. It stimulates sperm production. In men, testosterone is produced mainly in the testes, with a small amount made in the adrenal glands. The hypothalamus and pituitary gland controls testosterone production. The hypothalamus instructs the pituitary gland on how much testosterone to produce, and the pituitary gland passes the message to the testes. These communications happen through chemicals and hormones in the blood stream. Testosterone production is controlled by Luteinizing Hormone (LH) and serum testosterone level reproduces the reliability of the Hypothalamic Pituitary Gonadal (HPG) axis. A normal male testosterone level peak observed at the age 30 years, and then it slowly declines. Testosterone also maintains the bone density and muscle mass.^[8] Testosterone level above or below the normal range are considered by many to be out of balance. The lower testosterone levels marked in cases of insulin confrontation may perhaps specify a deficiency in one or more useful levels of HPG axis. During insulin resistance Leydig cell role might be weakened by transformations in the assembly of insulinemia repress the strive of LH in the testis, which may considerably lessen the production of testosterone.^[9]

The prevalence of low serum testosterone among male with type 2 diabetes is high. Age, income, BMI, and diabetic neuropathy were found to be the independent risk factors for low serum testosterone.^[10] The inverse relationships between serum testosterone level and obesity, hypertension, dyslipidemia and insulin resistance have been observed.^[11] Recent studies have shown that a low serum testosterone level is associated with an increased likelihood of the metabolic syndrome.^[12] Normal ageing is associated with a decrease in testosterone levels of the order of 0.5-2 % per year.^[13,14] In our study the occurrence of low testosterone values was much high than what was anticipated relied on the age of individuals. The major diabetic age group

which was deficient in testosterone level below (2.3 ± 0.18 ng/dl) significantly was 41-50 years, while in a study findings that low testosterone levels observed in the age of 60 years and above (Kazi M et al).^[15] In control cases, low testosterone level mean 3.2 ng/dl found in the age group 61-70 years.

Traish AM, in his study concluded that low testosterone level were found in the individuals with BMI of above 40 amongst age more than 60 years.^[16] A decrease testosterone level in a raised abdominal fat, which guides to augmented aromatase action. This boosts the exchange of testosterone to estrogens, which further condenses testosterone and enhances more abdominal fat deposition as proved in the study of Dhindsa et al.^[17,18] In our study the diabetic group had the low levels of testosterone 2.4 ± 0.3 and 2.4 ± 0.1 observed in those cases where BMI was 20-24.9 and 25-29.9 respectively. In control group BMI of <20 presents a low level of testosterone 5.3 ± 0.8 but still in normal limits. Significant difference found in BMIs of control and diabetic groups.^[19] The drop in testosterone is steady and continuous in decades and begins earlier in life.

CONCLUSION

This study concluded that low testosterone level is a common defect in type 2 diabetes mellitus in Pakistani community, while the only demarcation is the age at which the level of testosterone decline.

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