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A Study of Serum Total Testosterone Levels in Type 2 Diabetes Mellitus Male Patients.

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ABSTRACT

Background: Androgens not only play a crucial role in the differentiation of sex and reproductive maturity, may also help in the regulation of carbohydrate, protein, lipid metabolism and some inflammatory factors, all these may be known to influence insulin sensitivity. In recent years, testosterone deficiency has been not only associated with general health of men but also with certain common systemic disorders like abdominal obesity, type 2 diabetes mellitus & others. Aim: To compare the serum total testosterone levels in type 2 diabetes mellitus patients with that of non-diabetic healthy controls. **Methods:** In the present study, total 60 patients, 30 men aged 35-55 years who were diagnosed as type 2 diabetes mellitus patients and confirmed by the estimation of fasting plasma glucose (≥126mg/dl) on two occasions were selected from the OPD of Teerthanker Mahaveer College & Research Centre, Moradabad. 30 healthy age matched individuals, were selected as controls. **Results:** The serum total testosterone level of diabetic group was significantly lower than that non diabetic control group (p-value = 0.000). The mean of serum total testosterone of diabetic group was found 3.53 ± 1.38 ng/ml and serum total testosterone of non-diabetic control group was 5.81 ± 2.42ng/ml. **Conclusion:** As low serum total testosterone levels are found in type 2 diabetes mellitus patients, this may highlight requirement of urgent implementation of screening programs, in order to detect testosterone deficiency in all type 2 diabetes mellitus male patients at an early stage and to supplement testosterone accordingly.

Keywords: Insulin sensitivity, Testosterone, Type 2 Diabetes mellitus.

INTRODUCTION

Androgens not only play a crucial role in the differentiation of sex and reproductive maturity, may also help in the regulation of carbohydrate, protein, lipid metabolism and some inflammatory factors, all these may be known to influence insulin sensitivity. In recent years, androgen deficiency has captured interest of many researchers and they have associated testosterone not only with general health of men but also with certain common systemic disorders like abdominal obesity, type 2 diabetes mellitus & others. Various studies have suggested the effects of testosterone replacement therapy to hypogonadal male in improving glycemic status of individuals.[1] Testosterone, a steroidal hormone from androgen group, secreted into the circulation by Leydig cells of testicles, plays an important part in various biological functions during the course of male life.

Numerous studies have also identified inverse relationship between serum testosterone, insulin resistance and hyperglycemia. As Diabetes Mellitus and Testosterone hormone dysfunction are two common endocrinopathies, both may be associated with insulin resistance and defective metabolism, there seems to be some significant relation between these two and they may have tend to mutually influence each other.

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Various mechanisms by which low serum testosterone may be considered a threat for type 2 Diabetes Mellitus and metabolic syndrome include changes in the body composition, androgen receptor polymorphisms, glucose transport and decreased antioxidant effects. On the other hand, diabetes mellitus may also be considered a risk factor for hypogonadism through visceral obesity, reduced Sex Hormone Binding Globulin (SHBG), inhibition of gonadotrops secretion or production of testosterone by Leydig cells, cytokines mediated inhibition (e.g. TNF α, IL-1β, IL-6) of steroid production and increased aromatase activity resulting in estrogen excess.[2] Further, as suggested by studies, type 2 diabetes mellitus associated with testosterone dysfunction may exacerbate symptoms of sexual dysfunction by reducing libido, mood & infertility.[3]

Hence, circulating serum testosterone measurement may be recommended in patients of type 2 diabetes mellitus having erectile dysfunction.
Moreover, various studies have shown that a multidirectional relationship exists among metabolic syndrome, diabetes mellitus type 2, obesity and lower testosterone levels involving erectile dysfunction acting through pro-inflammatory agents. Thus, erectile dysfunction occurring as a result of low testosterone has been taken as one of common complication of type 2 diabetes mellitus and is one of most under diagnosed.
Hence, this study has been carried out to find out the association involving serum Total Testosterone and type 2 Diabetes Mellitus and to determine whether it should be considered as a diagnostic & prognostic marker of Diabetes Mellitus.

Aim

To compare the serum total testosterone levels in type 2 diabetes mellitus patients with that of non-diabetic healthy controls.

MATERIALS AND METHODS

In the present study 30 men aged 35-55 years who were diagnosed as type 2 diabetes mellitus patients and confirmed by the estimation of fasting plasma glucose (≥126mg/dl) on two occasions were selected from the OPD of Teerthanker Mahaveer College & Research Centre, Moradabad. 30 healthy age matched individuals, were selected as controls.

Exclusion Criteria: [4]

- Patients with known history of hypogonadism.
- Patients receiving exogenous testosterone.
- Patients suffering from cardiac disease, renal failure & liver cirrhosis.
- Patients suffering from AIDS.

Methodology

- Estimation of Plasma Glucose by GOD-POD, End Point method.
- Estimation of HbA1c by Particle enhanced immunoturbidimetric test.

Estimation of Serum Testosterone by ELFA (Enzyme Linked Fluorescent Assay) technique using fully automated VIDAS analyzer.

VIDAS – fully automated analyzer

Statistical Analysis

Mean ± S.D. were calculated for all the parameters analyzed and were compared by Student's t-test and the parameters were calculated using SPSS program.
P values considered significant were as follows:-
P < 0.05 – As significant
P < 0.001 – As highly significant

RESULTS

Table 1: Comparison of various measured parameters between study groups by Student's t test.

S. No.	Parameters	Diabetic Mean ± S.D.	Control Mean ± S.D.	t Value	p Value
1	Age(Years)	46.20 ± 7.17	45.83 ± 6.47	0.208	0.836
2	BMI(kg/m^2)	25.93 ± 3.36	24.10 ± 3.31	2.123	0.038
3	FPG(mg/dl)	205.33 ±81.21	85.10 ± 14.38	7.985	0.000
4	HbA1c (%)	8.01 ± 2.03	4.64 ± 0.52	8.763	0.000

The diabetic patients age group was found to be 46.20 ± 7.17years while that of control group patients was found to be 45.83± 6.47years, which was not significantly different (p=0.836).
BMI of diabetic group was 25.93± 3.36kg/m2 ,which was significantly higher than that of control group with BMI 24.10± 3.31 kg/m2 (p-value= 0.038).
FPG of diabetic group was 205.33 ± 81.21mg/dl, which was statistically higher than control group with FPG 85.10 ± 14.38 mg/dl (p-value= 0.000).
The HbA1c in diabetic group was 8.01 ± 2.03%,which was significantly higher as compared to non-diabetic individuals with HbA1c 4.64 ± 0.52 % (p- value = 0.000).

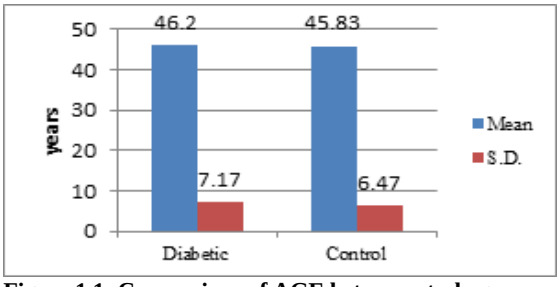

Figure 1.1: Comparison of AGE between study groups

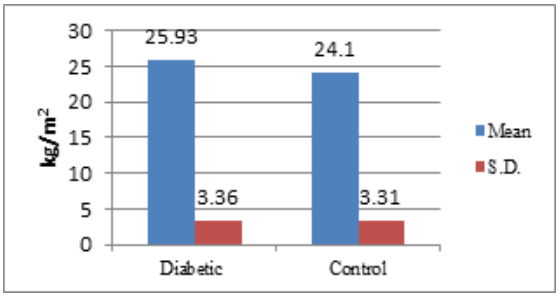

Figure 1.2: Comparison of BMI between study groups

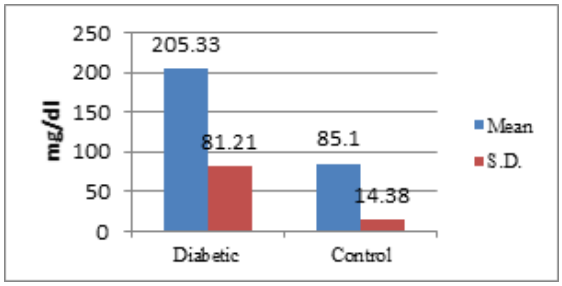

Figure 1.3 Comparison of FPG between study groups

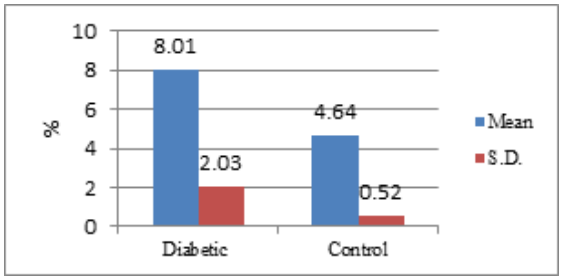

Figure 1.4: Comparison of HbA1c between study groups

Table 2: Student's t-test for Serum Total Testosterone levels between Diabetic & Non Diabetic controls

S. No.	Parameters	Diabetic Mean ± S.D.	Non diabetic Mean ± S.D.	t Value	p Value
1	Total Testosterone (ng/ml)	3.53 ± 1.38	5.81 ± 2.42	4.480	0.000

Serum Total Testosterone level of diabetic group was 3.53 ± 1.38ng/ml, which was found significantly lower than control group with serum total testosterone level 5.81 ± 2.42ng/ml, (p-value = 0.000).

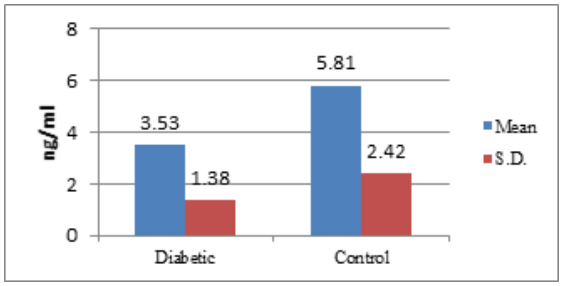

Figure 2: Comparison of Serum Total Testosterone levels between study groups

DISCUSSION

In our present study, 60 males, among them 30 male patients diagnosed as type 2 diabetes mellitus and 30 non diabetic males as controls, of age group 35-55 years, who attended the OPD of Teerthanker Mahaveer Medical College & Research Centre, Moradabad, were taken. Both control group and diabetic subjects were well matched with age.

In the present study, comparison of different parameters between diabetics and non-diabetic controls has been made. The mean age in diabetic men was 46.20 ± 7.17 years whereas that of control group were aged 45.83± 6.47years, which was not significantly different (p=0.836) i.e. the two groups taken for study were comparable with respect to age, as shown in [Table 1& Figure 1.1]. In our study, BMI of diabetic group of patients was 25.93± 3.36kg/m2 , which was significantly higher than control group BMI 24.10± 3.31 kg/m2 (p-value= 0.038), as shown in [Table 1 & Figure 1.2].

The fasting plasma glucose of diabetic group was 205.33 ± 81.21mg/dl, and for control group it was found to be 85.10 ± 14.38mg/dl. The fasting plasma glucose of diabetic group was significantly higher than control group (p-value=0.000), as shown in [Table 1 & Figure 1.3]. The level of HbA1c in diabetic patients was 8.01 ± 2.03%, which was significantly higher than control group 4.64 ± 0.52 % (p- value = 0.000), as shown in [Table 1 & Figure 1.4].

Most importantly, main objective of our study was to compare serum total testosterone levels of type 2 Diabetes mellitus patients with non-diabetic control group. Testosterone is the most important gonadal hormone that regulates the physiological functions of the body. Interestingly, in the present study, we have found that serum total testosterone level of diabetic group was significantly lower than that non diabetic control group (p-value = 0.000).

The mean of serum total testosterone of diabetic group was found 3.53 ± 1.38 ng/ml and serum total testosterone of non-diabetic control group was 5.81 ± 2.42ng/ml, as shown in [Table 2 & Figure 2]. Therefore, we concluded that the lower serum total testosterone levels were found in patients of type 2 diabetes mellitus when compared with non-diabetic control. Moreover, in our study , out of 30 diabetic patients, 13 patients i.e. about 43% had lower level of serum total testosterone when compared from the reference range (<3ng/ml).

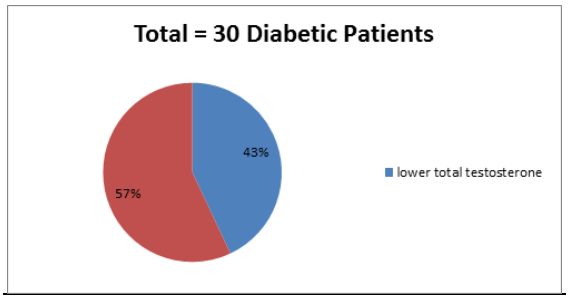

Figure 3: Graphical representation showing % of occurrence of lower serum total testosterone level in Diabetic Patients

Similar are the findings of Yeap et al., in which they have shown that diabetic men were found to have around two time's lower testosterone levels as compared to men without diabetes mellitus.[5]

Ding et al. conducted a meta-analysis which included 3825 men and confirmed that there was

higher prevalence of lower level of serum testosterone in type 2 Diabetic men.[6]

Oh et al. Also showed a reciprocal relationship between serum total testosterone and type 2 diabetes mellitus.[7]

Corona et al. conducted more recent meta-analysis including 1822 diabetic men and 10009 non diabetic controls and have found that serum total testosterone level was lower in men with diabetes mellitus than non-diabetic controls (mean difference, -2.99nmol/liter).[8]

Kupelian et al. conducted a study and suggested that low testosterone may be a marker in association of type 2 diabetes mellitus with insulin resistance.[9]

Besides this several other evidences have also been given showing the role of lower testosterone in insulin resistance.

Yialamas et al. have suggested in their study that testosterone may affect insulin resistance through changes in body composition and may also regulate insulin sensitivity.[10]

However, strong evidence may be considered which showed that low testosterone levels resulted in increased insulin resistance in males suffering from prostate cancer, receiving androgen deprivation therapy (ADT), it was seen that over 12 months of ADT resulted in decreased muscle mass by 2.7-3.6 % and gained fat mass by 9-14% resulting in increased insulin resistance.[11,12] Similarly, Yanase et al. have provided experimental evidence that included neuron specific insulin receptor knockout (NIRKO) mice with a specific knockout of the insulin receptor in neuron exhibit hypogonadotropic hypogonadism. The plasma levels of LH were found to be decreased in NIRKO mice as compared with that of controls. Further, these mice were injected with lupron, which is a GnRH receptor agonist, they found a increase in LH levels as compared with control mice.[13,14,15]

Karsenty's group recently shown in their research works that in male mice, skeleton may acts as a regulator of metabolism of glucose and testosterone. It was seen that osteocalcin, which is an osteoblast secreted molecule, stimulated testosterone secretion by testes by binding to a G- protein coupled receptor on Leydig cells, hence decreasing insulin resistance. Moreover, lower levels of osteocalcin may believe to cause increased insulin resistance, fasting glucose and metabolic syndrome.[16,17]

Marin et al. reported firstly that the testosterone replacement therapy improved insulin resistance therefore will improve the status of diabetes mellitus.[18]

However, experimental evidence, in mouse models has suggested that in vitro, testosterone encourage discrimination of pluripotent stem cells to myogenic lineage but through androgen receptor (AR) mediated pathway, control their commitment into adipocytes. These results have shown that the testosterone therapy in men results in lowering of fat mass and rise in muscle mass, these results may be likely to decline the insulin resistance.[19]

Furthermore, it was instituted that testosterone decreases insulin resistance by regulating mature adipocytes and myocytes, testosterone may lower lipoprotein lipase activity and trigylceride uptake in human adipose tissue in vivo, and increase lipolysis in vitro induced by catecholamines.[20]

Recently, micro assay studies in mice were conducted, which have shown that testosterone may have a major role in the regulating skeletal muscle genes involved in metabolism of glucose, thus it might be expected to decrease insulin resistance.[21]

CONCLUSION

This study has shown that there is a significant reduction in serum total testosterone levels in type 2 diabetes mellitus patients.. As low serum total testosterone levels are found in type 2 diabetes mellitus patients, this may highlight requirement of urgent implementation of screening programs, in order to detect testosterone deficiency in all type 2 diabetes mellitus male patients at an early stage and to supplement testosterone accordingly.

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