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TESTOSTERONE LEVELS AMONG CASES OF DIABETES MELLITUS AND RISK OF METABOLIC SYNDROME AMONG MEN WITH HYPOGONADISM: A CROSS SECTIONAL STUDY

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Abstract

Background: With the increasing prevalence of non-communicable disease the study was aimed to assess the prevalence of low serum testosterone among men diagnosed with Diabetes Mellitus along with establishing any association between testosterone levels and markers of Diabetes Mellitus and metabolic syndrome.

Objectives: to assess the prevalence of low serum testosterone among men diagnosed with Diabetes Mellitus along with establishing any association between testosterone levels and markers of Diabetes Mellitus and metabolic syndrome.

Methods and Material: This hospital based cross sectional study was conducted on 200 male diabetic patients of age 40 and above. Demographic data, physical and biochemical examination was performed on the enrolled participants. Descriptive analysis of the quantitative data was performed and mean with standard deviation was calculated. Independent t-test was used to compare means and Pearson's correlation was used to find association between two continuous variables.

Results: The prevalence of low testosterone levels among diabetics was 36% with mean testosterone levels being 4.66 ± 2.60. A significant correlation was observed between BMI (R=-0.230), HbA1c (R=-0.018), VLDL (R=-0.520) and triglyceride (R=-0.513) levels with testosterone levels. Group with low testosterone levels had significantly greater number of

participants who were obese, had waist hip ratio <0.95, high levels of VLDL and triglycerides.

Conclusions: The low testosterone levels among diabetic men were associated with high BMI, increased waist circumference and hip circumference, high blood pressure and high lipid profile hence they can be used as a significant predictor of low testosterone levels among diabetic men.

Key-words: Testosterone, hypogonadism, diabetes mellitus, diabetes, metabolic syndrome, risk factors

INTRODUCTION

Type 2 Diabetes Mellitus consists of wide variety of dysfunctions resulting from the combination of inappropriate glucagon secretion, inadequate insulin secretion and resistance to insulin action. Poorly controlled type 2 diabetes is associated with microvascular, macrovascular and neuropathic complications. Microvascular complications of diabetes include retinal, renal, along with neuropathic disease while macrovascular complications include coronary artery and peripheral vascular disease. Whereas, diabetic neuropathy affects autonomic and peripheral nerves.

The overall prevalence of diabetes in 15 states of India was reported to be 7.3% in 2017.[1] Based on the reports of International Diabetes Federation, the age adjusted prevalence of diabetes in was 9.6% and based on the increasing trend it is estimated that by the year 2045, 125 million population of India will be diagnosed with diabetes mellitus.

The relationship of diabetes with sex hormones is of utmost importance as increasing prevalence of diabetes may leads to many folds rise in the disabling morbidities associated to it. Hypogonadism is characterized by low testosterone concentration in serum and is associated with physical decline in strength, erectile dysfunction, low libido, loss of memory, difficulty in concentration and depression.[2] The studies from different countries have shown a clear association between low testosterone levels and type 2 Diabetes Mellitus.[3]Various studies have reported the prevalence of hypogonadism among men with diabetes mellitus ranging from 15- 20%.[4]

Now that low testosterone levels have also been recognized to be a predictor of cardiovascular disease, it is of utmost important to study the relationship of low testosterone levels with diabetes and other disease under the metabolic syndrome as

well.[5]The primary aim of this study was to assess the prevalence of low serum testosterone among men diagnosed with Diabetes Mellitus. The secondary aim was to establish any association between testosterone levels and markers of Diabetes Mellitus along with assessing the risk of metabolic syndrome among diabetics with low testosterone levels.

MATERIALS AND METHODS

This cross-sectional study was conducted on patients of internal medicine in the tertiary care health facility of Saifai, Etawah after the approval from ethics committee. The study included all the male participants above the age of 40 years who were either diagnosed or were known case of Diabetes Mellitus. Patients were excluded if they were undergoing Hormone Modulating Therapies, had any history of prostate or breast cancer, were cases of symptomatic Benign Prostatic Hyperplasia, had elevated age specific prostate or patients who did not consent for the study.

The necessary sample size was calculated using the formula: **Sample size== 1.96 (at 5% type I error)** Absolute error (d)= 0.05

The minimum sample size calculated was .the sample size was rounded of to 200. Patient's fulfilling the inclusion and exclusion criteria were approached for consent. The study was explained to them and consent forms were signed. Demographic and anthropometric data including height, weight, hip circumference and waist circumference were collected for all the enrolled patients. Then Blood Pressure was measured for each patient in sitting posture in the left arm using manual sphygmomanometer three times each after an interval of 5 minutes. An average value was calculated which was recorded as the final BP value of the patient. Venous blood sample (6ml) was collected in separate vacutainers for each patient for the analysis of lipid profile, HbA1C and serum testosterone levels.

Statistical Analysis: The Statistical Package for the Social Science (SPSS) version 23 IMB, USA was used for data analysis. Descriptive analysis of the quantitative data was performed and mean with standard deviation was calculated. Independent t-test was used to compare means and Pearson's correlation was used to find association between two continuous variables. A p-value of <0.05 was considered statistically significant.

RESULTS

The prevalence of low testosterone levels among diabetics was 36% (figure 1). The mean age of the study participants was 52.54 ± 10.77 while the mean BMI and waist/hip ratio was in the range of pre- obese (25.15 ± 3.23) and low risk category (0.91 ± 0.53) respectively (table 1). The mean testosterone levels of the 200 participants was 66 ± 2.60.

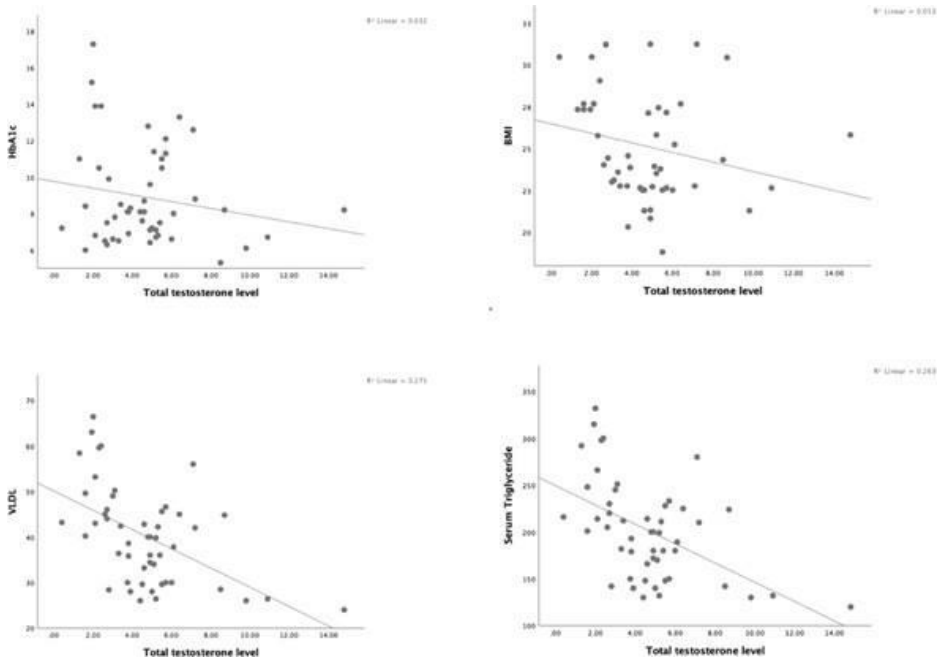

Figure 1: Significant correlation of total testosterone levels with study parameters [Hba1c (r^2=0.032), BMI (r^2=0.053), VLVL(r^2=0.271), and triglycerides (r^2=0.0.262)][SN4]

Table 1: Descriptive information of study participants

STUDY PARAMETERS	MEAN± S.D(N=200)
Age	52.54 ± 10.77
Height	168.26 ± 8.91
Weight	71.32 ± 10.82
BMI	25.15 ± 3.23
Waist	82.36 ± 8.97
Hip circumference	90.36 ± 9.25
Waist/ Hip ratio	0.91 ± 0.53

Fasting blood sugar	**175.98 ± 88.06**
Post prandial blood sugar	**280.06 ± 105.15**
Testosterone level	**4.66 ± 2.60**
HbA1C	**8.90 ± 2.67**
Systolic Blood Pressure	**137.92 ± 17.87**
Diastolic Blood Pressure	**83.68 ± 9.30**
Triglyceride	**201.28 ± 52.37**
VLDL	**40.22 ± 10.57**

Table 2: Distribution of study parameters based on the testosterone levels among the participants

The mean was found to be higher (26.9 ± 2.8) in patients with testosterone level <3.5 in comparison to patients with testosterone ≥3.5 and a significant association was observed between BMI and testosterone levels (table 2)

STUDY PARAMETERS	**Testosterone <3.5 MEAN ± S.D(n=16)**	**Testosterone ≥3.5 MEAN ± S.D (n=34)**	**t**	**P**
Age	50.8 ± 7.34	53.4 ± 12.2	2.665	0.104
Height	164.3 ± 6.5	170.4 ± 9.3	23.626	<0.01
Weight	72.8 ± 9.4	70.4 ± 11.4	2.212	0.138

BMI	26.9 ± 2.8	24.1 ± 3.1	39.243	<0.01
Waist	83.4 ± 8.5	80.4 ± 9.4	5.231	0.023
Hip circumference	92.0 ± 7.8	87.4 ± 10.7	11.774	0.001

Waist/ Hip ratio	**0.9 ± 0.1**	**0.9 ± 0.1**	**3.350**	**0.069**
Fasting blood sugar	**188.7 ± 92.6**	**168.7 ± 84.8**	**2.393**	**0.124**
Post prandial blood sugar	**283.3 ± 81.2**	**278.1 ± 116.7**	**0.112**	**0.738**
Vbkl;HbA1C	**9.4 ± 3.4**	**8.6 ± 2.1**	**4.535**	0.034
Systolic Blood Pressure	**141.6 ± 21.9**	**135.8 ± 14.7**	**5.040**	0.026
Diastolic Blood Pressure	**84.4 ± 9.6**	**83.2 ± 9.1**	**0.758**	**0.385**
Triglycerides	**242.7 ± 49.0**	**177.9 ± 37.8**	**108.448**	<0.01
VLDL	**48.7 ± 9.6**	**35.4 ± 7.6**	**116.182**	<0.01**[SN5]**

Similarly, waist and hip circumference were found to be significantly associated with testosterone levels however no such association was observed between waist hip ratio with testosterone levels. The lipid profile including triglycerides and VLDL were found to be significantly high among patients with testosterone level <3.5. Low testosterone levels were significantly correlated with height, BMI, hip circumference, HbA1c, triglycerides and VLDL (table 3)

Table 3: Correlation of total testosterone levels with the study parameters

STUDY PARAMETERS	R	P
Age	0.191	0.17
Height	0.204	0.04
Weight	0.041	0.56
BMI	0.230	<0.01
Waist	0.166	0.19
Hip circumference	0.168	0.02
Waist/ Hip ratio	0.005	0.93
Fasting blood sugar	0.028	0.69
Post prandial blood sugar	0.029	0.68
HbA1C	0.180	0.01
Systolic Blood Pressure	0.030	0.67
Diastolic Blood Pressure	0.081	0.25
Triglycerides	0.513	<0.01

VLDL	0.520	<0.01

DISCUSSION

Male hypogonadism is characterized with abnormally low levels of serum testosterone levels which is often associated with various comorbidities.[6]In this study we found that the serum testosterone levels were low (<3.5) among 36% of the diabetics. Similar results were observed in the studies from Egypt, Pakistan and Poland which presented that 34.2%, 45.5% and 46% of the diabetic men had low testosterone levels respectively.[7]In another study on Korean population, the prevalence of low testosterone levels was 34.9% among diabetic males.

Majority of the diabetic men presented with low testosterone levels in their fifth decade with a mean age of 50.8 ± 7.34. Similar results were reported by Agarwalet al[8]. And Rabijewski et al where the mean age was reported to be 56.36 ± 10.26 and 56.4 ± 3.2 respectively.In this study we found that high BMI, waist circumference and hip circumference were a significant predictor of low testosterone levels among diabetic men. These results confirm that obesity is responsible for suppressive effects on testosterone levels as stated in other studies.[9]BMI and hip circumference were found to be negatively correlated with testosterone levels in this study. It was observed in the present study that HbA1c was significantly higher among men with low testosterone levels and it was negatively correlated with its levels. Aboelnaga et al stated similar results where mean HbA1c was higher (8.69 ± 1.89) among men with low serum testosterone levels and a negative correlation with r=-0.240 was observed between the two parameters. Prolonged hyperglycaemia impairs the synthesis and secretion of testosterone, resulting in low testosterone levels which is reflected by a high HbA1c among diabetic men with hypogonadism. The present study recorded a high blood pressure among men with hypogonadism however only systolic pressure had significant difference. Musa et al and few other stated that The association observed between hypogonadism and both systolic and diastolic blood pressure was not significant.[10]In this study it was observed that both the triglycerides and VLDL were significantly higher among the hypogonadism group of men and they were negatively correlated with serum testosterone levels. It was in

agreement with the results of other studies which correlated serum testosterone levels with VLDL and triglycerides.Through these studies we can conclude that male patients diagnosed with diabetes who have dyslipidaemia may often exhibit hypogonadism.

CONCLUSION

According to this study low testosterone levels among diabetic men was associated with high BMI, high blood pressure and high lipid profile i.e. metabolic syndrome**.**

Limitations: As the present study is a cross sectional study, it does conclude about the temporal causation. The study depicts an association between metabolic syndrome and low testosterone level but it does not establish whether low testosterone levels cause metabolic syndrome or vice versa. Therefore, an analytical or longitudinal studies need to be conducted to establish the temporal causation between risk factors and low testosterone levels. Also as this study was a hospital based study the participants, the results cannot be generalized for the whole community.

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