

Testosterone Levels in Male Type-II Diabetic Patients and its Association with HbA_{1c} Levels and Duration of the Disease

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ABSTRACT

OBJECTIVE: To measure serum testosterone levels in type-II diabetes mellitus male subjects and to correlate its association with blood glycated haemoglobin A1 (HbA_{1c}) levels and - duration of the disease.

METHODOLOGY: This cross sectional study was carried out at Biochemistry department, LUMHS, Jamshoro, from December 2015 to May 2016. One hundred male subjects including 50 DM patients and 50 age matched with no family history of DM, were enrolled by purposive sampling technique. Study population excluded those patients diagnosed as diabetic erectile dysfunction, diabetic nephropathy, diabetic renal failure, metformin therapy, familial dyslipidemia, and hypercholesterolemia. Serum testosterone (ELISA assay) and whole blood HbA_{1c} levels (TINIA assay) were measured by standard laboratory methods using Hitachi Roche Diagnostic Chemistry Analyzer. The obtained results were analysed by SPSS version 21.0 (IBM, Incorporation, and USA) and is reported as Mean± SD. The $p \leq 0.05$ was considered to indicate statistical significance.

RESULTS: The ages of diabetes mellitus patients and control subjects were 58.24 ± 11.13 and 54.56 ± 10.44 years respectively. Serum testosterone levels were observed to be more significant ($p < 0.004$) in control subjects (3.53 ± 0.74 mg /dL) and its levels decreased in diabetes mellitus patients (2.53 ± 1.13 mg /dL). Similarly, HbA_{1c} levels were significantly higher ($p < 0.0001$) in diabetic subjects as compared to control subjects (8.40 ± 1.27 vs $5.75 \pm 0.24\%$). Testosterone levels showed negative correlation with blood HbA_{1c} levels and positive with duration of disease.

CONCLUSION: In type 2 diabetic male patients serum testosterone levels demonstrated negative correlation with blood HbA_{1c} levels and positive with duration of DM.

KEYWORDS: Serum testosterone, Type 2 diabetes mellitus, Glycated HbA_{1c}

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INTRODUCTION

Diabetes Mellitus (DM) is significant cause of morbidity and mortality¹. In the world approximately 285 million people are affected by DM and hypothesized that in 2030 its prevalence will rise up to 438 million². It considered that in most developed countries, DM is the 4th leading cause of death³. With the burden of Diabetes, Pakistan is at seventh position and it is estimated that if this situation is continuing it will move to the fourth position⁴. Fortunately, therapeutic regimens improvement and early diagnosis permit diabetic patients to spend healthy lives. Clinical biochemistry plays a crucial role in monitoring, diagnosis and treatment of diabetes. Glycemic control, the routine measurement of glycosylated haemoglobin (HbA_{1c}), is generally recommended to limit end organ damage including increase in blood cholesterol and decrease in serum testosterone levels and mortality⁵⁻⁷. Researchers revealed the metabolic effect of testosterone reduction with age-associated metabolic changes such as markers of pre-diabetes, diabetes and abdominal obesity⁸⁻¹⁰. In 2010, Endocrine Society's

Clinical Practice Guideline was recorded the low serum testosterone level in patients in advanced type 2 diabetes. The prevalence rate of said condition was high and it was investigated in the perspective of androgen deficiency syndrome in adult men. The Endocrine society recommends the proper measurement of morning serum total testosterone for those patients already suffered with type 2 diabetes mellitus (T2DM) and having the prominent symptoms of sexual dysfunction, weakness or weight loss¹¹. This study will help to improve the fertility status of patients having type-II diabetes mellitus.

METHODOLOGY

This cross sectional study was conducted at the Biochemistry Department, Liaquat University Hospital Jamshoro from December 2015 to May 2016. One hundred subjects (n=100) were distributed in two groups; Group A (n=50): Diagnosed type 2 Diabetic patients (Case), Group B (n=50): Non-Diabetics and healthy normal subjects (Control). Study population included diagnosed T2DM patients with age 30-60 years and excluded those patients diagnosed as

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diabetic erectile dysfunction, diabetic nephropathy, diabetic renal failure, metformin therapy, familial dyslipidemia, and hypercholesterolemia.

Research bias was overcome by selecting the study population according to inclusion and exclusion criteria. Diagnosed cases of T2DM (defined as per American Diabetes Association criteria) with age 30-60 years. Diabetic erectile dysfunction, Diabetic nephropathy, Diabetic Renal failure, Metformin therapy, Familial dyslipidemia, hypercholesterolemia, etc; were excluded from the study. Disposable syringe (BD, USA) was used for vein prick to collect 5 ml of venous blood, 2.5ml was shifted to EDTA containing glass tube for HbA1c estimation, remaining was centrifuged at 3000 rpm (10 minutes) to get the sera. The sera were used for the Biochemical analysis and the Analysis of parameters performed on Roche, Hitachi chemistry analyser at the Research and Diagnostic Laboratory, Liaquat University Hospital Jamshoro/Hyderabad. Readings of Testosterone were recorded at 500nm on spectrophotometer for all samples. The HbA1c was estimated from the clotted Blood. The clotted Blood was analysed on the Chemistry analyser Hitachi, Roche, Cobas systems (501) based on the turbid metric inhibition immunoassay for the Haemolysed whole blood. Consent form was printed in trilingual format. A volunteer was eligible to enter in the research protocol once he signed the consent form or by his legal heir. Data analysis including paired and correlation analysis were computed using SPSS software version 21.0 (IBM, Incorporation, and USA) for windows. Paired t-test was used to determine the significance of changes. P-value ≤ 0.05 was considered to indicate statistical significance.

RESULTS

Total 100 male subjects with age between 30-60 years were evaluated to find correlation (Association) of glycated haemoglobin with serum cholesterol and testosterone levels in T2DM patients. The mean age of study subjects of Group A was 58.24 ± 11.13 years with range 24(36-60) years. The mean age of Group B subjects was 54.56 ± 10.44 years with range 28(31-59) years. The mean age distribution of Group A and Group B is presented in Graph I. The detailed descriptive statistics of age of both groups are presented in Table I. The mean glycated haemoglobin (HbA1c) of study subjects of Group A was 8.40 ± 1.27 while the mean HbA1c of study subjects of Group B was 5.75 ± 0.24 (%). The mean serum testosterone of study subjects of Group A was 2.53 ± 1.13 mg/dL while the mean serum testosterone of study subjects of Group B was 3.53 ± 0.74 mg/dL.

The detailed descriptive statistics of HbA1c and testosterone of both groups are presented in Table-II. While the Comparison of serum HbA1c is in both Groups A and B is shown in Graph II. Stratification

with respect to diabetes and higher levels of HbA1c was done to observe effect of these modifiers with low serum testosterone levels. These results exhibited that there was a significant association of low serum testosterone level with diabetes ($p < 0.05$) and HbA1c ($p < 0.05$), and it has also been described with the duration of Diabetes Mellitus type 2. It showed that as the duration of Type 2 diabetes mellitus increases there is significantly reduction in serum testosterone levels.

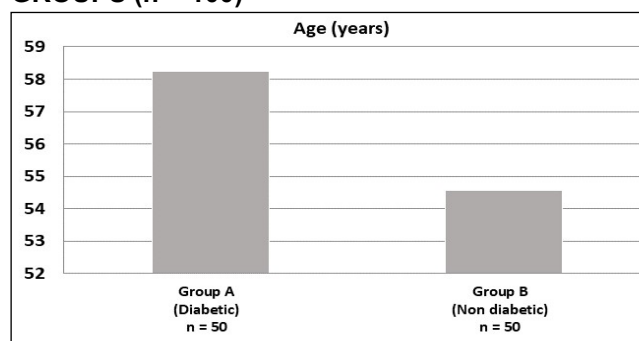
Scatter plots show the correlation of HbA1c with serum testosterone and duration of diabetes mellitus. (Scatter plot I) shows the positive correlation (Association) of HbA1c and duration of DM, as the duration of DM increases so an increase in % of HbA1c noted (Scatter plot I & II). Interpolation curve shows the negative correlation (association) of serum testosterone duration of disease in diabetic population.

TABLE I: AGE DISTRIBUTION OF THE DIABETIC AND NONDIABETIC GROUPS (n=100)

Variable	Group A (Diabetic) (n=50)	Group B (Non-diabetic) (n=50)	P value
Age (in years)	58.24 ± 11.13	54.56 ± 10.44	0.0001

Student t-test was applied for statistical analysis of age and SPSS output was presented as mean SD. P value 0.09 shows that the two study groups are age matched.

GRAPH I: COMPARISON OF AGE (YEARS) BETWEEN DIABETIC AND NON DIABETIC GROUPS (n = 100)



GRAPH II: COMPARISON OF SERUM HbA1c LEVEL BETWEEN DIABETIC AND NONDIABETIC GROUPS (n = 100)

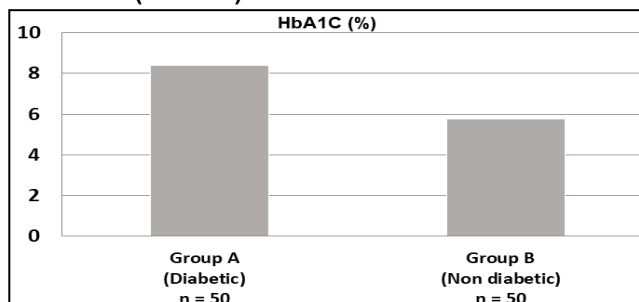
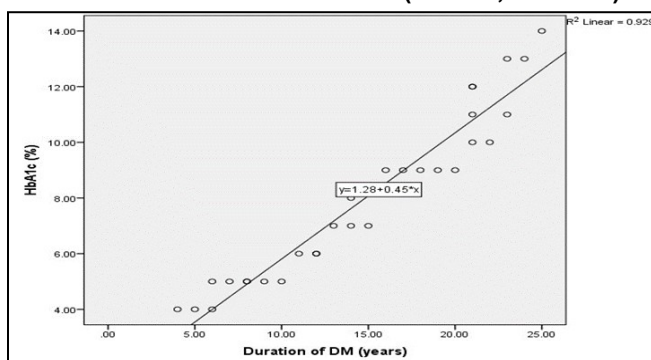


TABLE II: COMPARISON OF SERUM TESTOSTERONE AND HbA1c LEVELS BETWEEN DIABETIC AND NON DIABETIC GROUPS (n = 100)

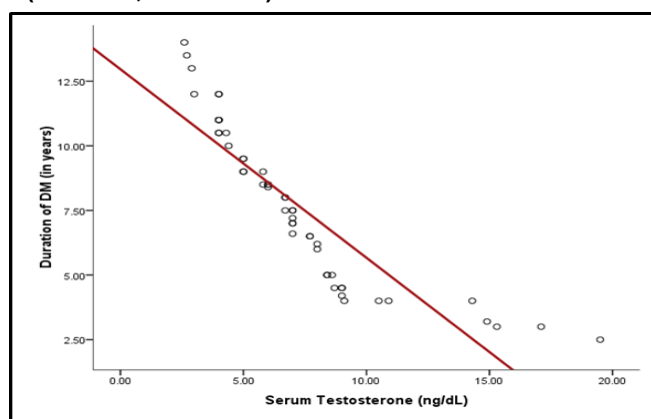
Variable	Group A (Diabetic) (n=50)	Group B (Non-diabetic) (n=50)	P-value
Serum Testosterone (mg/dL)	2.53 ± 1.13	3.53 ± 0.74	<0.05
HbA1c (%)	8.402 ± 1.27	5.752 ± 0.24	<0.05

- Results are presented as Mean ± SD
 - P value calculated by Student "t" test is statistically significant

SCATTER PLOT- I: HbA1c shows positive correlation with Duration of DM type- 2. As Duration of Diabetes mellitus type 2 increases, the Levels of HbA1c also increase (r= 0.67, P=0.001).



SCATTER PLOT-II: Duration of DM shows inverse correlation with Serum Testosterone. As there is rise in duration of DM, the Serum Testosterone concentrations decrease in patients with DM type- 2 (r= - 0.79, P=0.0001)



DISCUSSION

Characteristics hyperglycaemia of type 2 diabetes mellitus damages the various organ systems of human body, in addition to chronic microvascular complications such as diabetic retinopathy, neuropathy, nephropathy and microangiopathy. Type

2DM is reported to be associated with dysfunction of gonads resulting in hypogonadism, osteoporosis, cancer, non-alcoholic fatty liver disease and so forth. Male hypogonadism seriously affects the quality of life in diabetic patients^{12,13}. However, so far, the association between low testosterone levels and T2DM needs more clarification¹⁴. One clinical study found that patients with T2DM are prone to hypogonadism¹⁰. The control of blood glucose in diabetic patient is monitored by the HbA1c. Several studies have been done and they showed that HbA1c positively associated with the duration and complications of DM and its elevation is a high risk factor for cardiovascular diseases^{15,16}.

Retrograde ejaculation, orgasmic dysfunction, erectile dysfunction and reduced libido are recognized complications established with changeable occurrence in men with diabetes. Many researchers have observed that prevalence of hypogonadism in T2DM patients due to low plasma concentration of free testosterone¹⁷, another study associated the low serum testosterone with high aortic atheroma¹⁸. In a study of obese subjects with T2DM, 20(76.9%) had low serum free testosterone while 16 (61.51%) had low level of total testosterone. Mean serum total testosterone was 300.72±33.14 and mean serum free testosterone was 7.65±2.04¹³. Whereas another study reported occurrence of low testosterone in obese diabetics to be 50%¹⁹. Thoma C 2016²⁰ showed that 34% patients of diabetes mellitus had low level of serum total testosterone and Shigehara K et al²¹ showed 25% of low level of serum total testosterone in diabetic patient which is consistent to present and previously reported studies. In present study 20-40% patients were having low serum total testosterone levels while in non-diabetic group 5(10%) had normal serum testosterone levels.

In a study, multivariate analysis did not find a correlation between the serum testosterone concentration and HbA1c level, which was consistent with the results obtained by studies by Soriguer F et al²² and Fukui M 2008²³, while it was in contrast with those by Kapoor D 2007¹⁰ and the present study. Findings from the study by Reinstatler L 2012²⁴ also contradicted from those of the study by Fukui M 2008²³ in which TT levels positively correlated with HbA1c levels. The finding of how serum testosterone decreases is beyond the scope of present study that needs further research.

CONCLUSION

Current study revealed that type 2 diabetic patients shows low serum testosterone levels, while glycated HbA_{1c} shows positive correlation with duration of type 2 DM. Significant negative correlation of Serum Testosterone was observed with glycated haemoglobin A1. Thus it is important to evaluate

diabetic patients for testosterone levels that will ultimately help in early detection and prevention of future complications associated with diabetes mellitus.

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AUTHOR CONTRIBUTIONS

Laghari M: Drafting and final approval, editing, literature review

Shaikh F: Concept, Data collection

Murtaza S: Analysis and interpretation of data

Meraj M: Editing & critical revision of article

Shaikh F: Study survey & literature review

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