Testosterone Correlation with Low and High Density Lipoprotein in Male Type 2 Diabetics

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Authors’ contributions

This work was carried out in collaboration among all authors. Authors ML and ZT designed the study, Authors AA and MH performed the statistical analysis, Authors SM and ML wrote the protocol, and wrote the first draft of the manuscript. Authors FA, MH and AA managed the analyses of the study. Author SM managed the literature searches. All authors read and approved the final manuscript.

ABSTRACT

Aim: To determine correlation of serum testosterone with low and high density lipoprotein in male type 2 Diabetics presenting at a tertiary care hospital of Sindh.

Methodology: A cross sectional study, Department of Biochemistry and Department of Medicine, Liaquat University Hospital from January 2018 to February 2019. One hundred male type 2 diabetics (cases) and one hundred age matched male (control) were selected through non – probability purposive sampling. Male diagnosed cases of DM belonging to 4th to 6th decade of life was included. Blood samples were collected by venesection and sera were squeezed by centrifugation and stored at – 20 °C in refrigerators. Testosterone was estimated by the ELISA (competitive immuno- assay) assay method and blood lipids - cholesterol, triglycerides (TAGs),
1. INTRODUCTION

Dysfunctioning of Islet β-cells of pancreas causes reduced insulin secretion resulting in type 2 Diabetes mellitus (T2DM). DM mellitus is a metabolic disorder of blood glucose caused by insulin deficiency that either caused by absolute β-cells dysfunction or target cell insulin resistance [1-2]. Currently, low testosterone is reported in male type 2 diabetics causing hypogonadism [3]. Low testosterone has been associated with poor glycemic control, hyperlipidemia and dyslipidemia in diabetics. Testosterone producing Leydig cells of testes are negatively impacted by the hyperglycemia and dyslipidemia of diabetes mellitus. Dysfunction and decreased testosterone secretion is observed in male type diabetes [1]. Normally, testosterone plays important physiological functions in body and its low concentration adversely affects the male body. Testosterone circulates through blood and reaches target organs such as the brain, skeletal muscle, primary and secondary sex organs, adipose tissue where it regulates a number of biological functions. Thus testosterone performs vital biochemical functions essential for the general well-being and health of male [1-3]. Some studies have shown negative correlation of testosterone levels with the hyperglycemia and insulin resistance [2-4]. (This information was already written at the beginning of the introduction.) Diabetes and hypogonadism are two endocrinopathies that influence each other adversely. Reduced testosterone secretion is probably caused through a number of metabolic insults such as hyperglycemia, hyperlipidemia, and dyslipidemia, oxidative injury, Leydig cell disturbances, steroid hormone enzymopathy and androgen receptor defects, inflammatory cytokines TNF-α (tumor necrosis factor – α) and Interleukins (IL-1β, IL-6) suppress the hypothalamo – pituitary axis. Aromatase enzyme dysfunction causes estrogen excess resulting in low testosterone and male sexual dysfunction [4-5].

Low serum testosterone is associated with a cluster of clinical disorders of dyslipidemia, insulin resistance, impaired glycemic control, visceral obesity, hypertension, etc [4-6]. Several studies had investigated the low testosterone associated with LDLc, HDLc, Cholesterol, TAGs and increased risk of coronary artery disease [5-6]. In recent years, research on androgen (testosterone) deficiency has captured the interest in the diabetic population and its association with circulating blood lipids. Leading cell dysfunction in type 2 diabetics is reported in resulting in androgen (testosterone) deficiency [4-6-7]. As the prevalence of diabetes mellitus is increasing in the country, there is need of conducting more research on the health issue of male diabetics [8-9]. There is dearth of research on the testosterone levels in male type 2 diabetics in the country, and more so in the Sindh. Hence there is dire need of conducting more research highlighting the problem of testosterone deficiency in male type 2 diabetic. The present study was conducted to determine serum testosterone and correlation of serum testosterone with low and high density lipoprotein in male type 2 Diabetics presenting at a tertiary care hospital of Sindh.

2. MATERIALS AND METHODS

It was conducted over the duration from January 2018 to February 2019. Male diagnosed cases of DM belonging to 4th to 6th decade of life was included. One hundred male type 2 diabetics (cases) and one hundred age matched male (control) were selected through non – probability purposive sampling. Diagnosis of type 2 DM was confirmed by a consultant physician. Medical records of male type 2 diabetics were checked.
for segregation of patient to fulfill the inclusion criteria. Control was defined as an age matched male without DM with good health. Volunteer male type 2 diabetics were asked the consent to participate for study protocol is on voluntary basis, were informed to sign the consent form on voluntary basis and that this study will not cause any physical or economic loss to them and informed of blood sampling. All participants were informed that the participation will cause not harm except of blood sampling that is on volunteer – consent basis and there was no need to pay charges of laboratory investigations. Patient findings were entered in a pre – structured proforma and confidentiality secured by keeping in the lockers. Data was taken in custody by the principal investigator/researcher. Handling of patients was according to the human research conductance as suggested by “Helsinki’s Declaration”. Rules were followed strictly to facilitate the research in smooth way. 5 ml of blood was drawn from peripheral vein using a disposable syringe (BD, USA). 3 ml blood was centrifuged at x3000 rpm for 15 minutes. Centrifuged serum was stored at –20 °C for biochemical analysis. Research variables of glucose and lipids fractions were estimated by standard methods. Cobas analyzer (Roche) was used for estimation of glucose, A1C, and cholesterol, triglycerides (TAGs), LDLc and HDLc. ELISA assay method utilized for determining the serum testosterone. Testosterone lower range was taken as <3 ng/ml [7]. Pearson’s correlation was analyzed on Statistical software SPSS 21.0 (IBM, Incorp, USA) for determining the association/correlation of serum testosterone with blood lipids. 95% Level of significance calculation was taken as clinically significant result (P=0.05).

3. RESULTS
Mean±SD age of cases was 53.2 ± 11.1 years and control was 54.5±10.4 years (P=0.056). Serum testosterone in cases was 10.85 ± 4.7 mmol/L compared to 13.39 ± 3.8 mmol/L (P=0.0001). Fasting blood glucose (FBG) and Random blood glucose (RBG) in cases and control was noted as 162.7 ± 25.3 vs. 82.5 ± 10.3 mg/dl, and 299.3 ± 5.7 vs. 142.5 ±31.3 mg/dl respectively. Glycemic status of male type 2 diabetics reveals A1C 8.4 ± 1.7% compared to 5.5 ± 0.24% in control. Cholesterol, TAGs, LDLc and HDLc in cases and controls was noted as 198.402 ± 1.2 vs. 115.75 ± 0.24 mg/dl, 702.5±11.3 vs. 602.5±12.3 mg/dl, 137.6±10.9 vs. 99.6±3.3 mg/dl and 299.3 ± 5.7 vs. 142.5 ±31.3 mg/dl respectively (P=0.0001). Table 1 shows the negative correlation of testosterone with FBG, RBG, A1C, Cholesterol, TAGs and HDLc. While LDLc shows strong positive correlation with testosterone. (P=0.0001).

Table 1. Correlation of Testosterone with study variable

| Particulars | R-value | P-value |
|-------------|---------|---------|
| FBG         | -0.197  | 0.03    |
| RBG         | -0.312  | 0.003   |
| A1C         | -0.231  | 0.014   |
| Cholesterol | -0.243  | 0.014   |
| Triglycerides | -0.781 | 0.0001  |
| LDLc        | 0.672   | 0.0001  |
| HDLc        | -0.701  | 0.0001  |

*: r-value - Correlation co-efficient

![Fig. 1. Scatter plot showing negative correlation of Testosterone with Cholesterol](image-url)

\[ y = -3.559x + 215.38 \]
\[ R^2 = 0.2046 \]
Fig. 2. Scatter plot showing negative correlation of Testosterone with Triglycerides

![Correlation of Testosterone with Triglycerides](image)

\[ y = -2.2203x + 184.68 \]
\[ R^2 = 0.1426 \]

Triglycerides
Linear (Triglycerides)

Fig. 3. Scatter plot showing positive correlation of Testosterone with Low Density Lipoprotein Cholesterol (LDLc)

![Correlation of Testosterone with LDLc](image)

\[ y = 2.0677x + 117.1 \]
\[ R^2 = 0.0947 \]

LDLc
Linear (LDLc)

Fig. 4. Scatter plot showing negative correlation of Testosterone with High Density Lipoprotein Cholesterol (HDLc)

![Correlation of Testosterone with HDLc](image)

\[ y = -0.8684x + 40.161 \]
\[ R^2 = 0.3101 \]

HDLc
Linear (HDLc)
4. DISCUSSION

In present research study, we found low serum testosterone level in male type 2 diabetic cases and this revealed negative correlation with Cholesterol \((r = -0.243, P=0.014)\), TAGs \((r = -0.781, P=0.0001)\), HDLc \((r = -0.701, P=0.0001)\) but positive association with LDLc \((r = 0.672, P=0.0001)\). We found negative correlation of testosterone with FBG, RBG and A1C. Our findings are in correlation consistent with previous studies [10-14]. Previous studies [10,11] found similar results of negative correlation of FBG and RBG with testosterone (shown in table –1). A previous study found negative correlation of testosterone with cholesterol \((r=-0.142, P=0.002)\), triglycerides \((r=−0.097, P=0.040)\) in male diabetics similar to present study [13].

Similar finding of negative linear correlation of testosterone with cholesterol, TAGs, HDLc and positive correlation with LDLc was reported by a previous study [11]. Of 100 male types 2 diabetics, 46% cases exhibited low testosterone in present study the finding is agreed by previous studies [7,11-12]. Previous studies found low testosterone in 44.5% and 42% respectively [11-12]. A previous study studied 83 type 2 diabetics and found low testosterone in 44.58% of male diabetics [12]. While Kim et al investigated 464 sample of type 2 male diabetics and found low testosterone in 34.9% [13]. The finding of above study showed low frequency of testosterone deficiency but overall the deficiency points to the health problem. A previous study investigated a sample of 300 male type 2 diabetics of Kashmiri ethnicity and found testosterone deficiency in 42% of male, the finding is parallel to our present study [13]. We found low serum testosterone in cases compared to control. Serum testosterone in cases was 10.85 ± 4.7 mmol/L compared to 13.39 ± 3.6 mmol/L \((P=0.0001)\), the difference being highly significant between cases and controls. This is in agreement with previous studies [7,13]. A pervious study shows the values of 3.51±1.26 ng/ml in male type 2 diabetic cases compared to 5.88±2.34 ng/ml in non-diabetic male that is agreement with our present study [7].

A previous study reported twice low testosterone in male type 2 diabetics in comparison to non – diabetic control male [14]. Previous systemic meta-analyses investigated thousands of studies on the topic of testosterone and male type 2 diabetes mellitus and concluded the low testosterone level is prevalent among the male diabetic populations [15-16]. Yet other studies suggested the male type 2 diabetics with low testosterone may be considered as a marker of insulin resistance [17-18]. Still another study reported the low serum testosterone in male type 2 diabetics is associated with low insulin sensitivity [19]. Very important is a recent study that reported the testosterone supplements in male type 2 diabetics caused remission of diabetes mellitus in their study [20]. Findings of low testosterone in male type 2 diabetics revealing negative correlation with cholesterol, TAGs, and HDLc but positive correlation with LDLc is significantly important clinical findings that need attention in this particular group of diabetic population putting them at increased risk of coronary artery disease. The finding is worth to pay attention within due time to overcome the health issues urgently. The limitations of present study are; first – a small sample size, hence findings are not generalizable, second – cross sectional study designs, hence cause – effect relationship is uncertain, third – study sample belonged to particular ethnicity hence finding cannot be applied to other geographical areas of different ethnicity.

4. CONCLUSION

We found low serum testosterone in male type 2 diabetics that showed negative correlation with Cholesterol, Triglycerides and HDLc and positive correlation with low density lipoprotein (LDLc). It is concluded the altered blood lipids may increase the risk of coronary artery disease in male type 2 diabetes mellitus patients.

5. RECOMMENDATION

Further studies with indigenous male type 2 diabetic population are recommended.

DISCLAIMER

Authors have declared that no competing interests exist. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

All authors declare that ‘written informed consent was obtained from the patient.
ETHICAL APPROVAL
The present study was conducted after the Ethical approval of institute at the Department of Biochemistry and Medicine, Liaquat University Hospital.

COMPETING INTERESTS
Authors have declared that no competing interests exist.

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