Journal of Pharmaceutical Research International

33(40B): 200-206, 2021; Article no.JPRI.71483
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

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

Mubeena Laghari[1], Shazia Murtaza[2], Zuha Talpur[3], Mohsina Hamid[4], Faryal Adnan[5*] and Arslan Ahmed[6]

[1]Department of Biochemistry, LUMHS, Pakistan.
[2]Prince Naif Health Research Center, King Saud University Medical City, Riyadh, KSA.
[3]Isra University Hyderabad, Pakistan.
[4]Department of Biochemistry, Independent Medical Collage, Faisalabad, Pakistan.
[5]Department of Biochmistry, Peoples University of medical and Health Sciences for Women Nawabshah, Pakistan.
[6] Peoples University of Medical and Health Sciences for Women Pakistan.

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.

Article Information

DOI: 10.9734/JPRI/2021/v33i40B32279
Editor(s):
(1) Prof. Q. Ping Dou, Wayne State University, USA.
Reviewers:
(1) Eline Meulenberg, ELTI Support, Netherlands.
(2) Camila Lehnhardt Pires, Estadual Paulista University, Brazil.
Complete Peer review History: https://www.sdiarticle4.com/review-history/71483

Original Research Article

Received 16 May 2021
Accepted 22 July 2021
Published 11 August 2021

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 4^{th} to 6^{th} decade of life was included. Blood samples were collected by venesection and sera were squeezed by centrifugation and stored at – 20 ^{0}C in refrigerators. Testosterone was estimated by the ELISA (competitive immuno- assay) assay method and blood lipids - cholesterol, triglycerides (TAGs),

**Corresponding author: E-mail: faryal_adnan@hotmail.com;*

LDLc and HDLc by colorimetric method. Pearson`s correlation was generated on Statistical software SPSS 21.0 version (IBM, Incorp, USA) for correlation of serum testosterone with lipids fractions (P≤0.05).

Results: Age shows majority of male type 2 diabetics were in their 5th decade. We found low serum testosterone level (10.85±4.7 mmol/L) in cases compared to normal testosterone level (13.39±3.8 mmol/L) in control (P=0.0001). Pearson`s correlation shows inverse association with HDLc (r= -0.70) (P=0.0001) and positive association with LDLc (r= 0.670) (P=0.0001).

Conclusion: We found low serum testosterone in male type 2 diabetics that showed negative correlation with high density lipoprotein (HDLc) and positive correlation with low density lipoprotein (LDLc).

Keywords: Testosterone; HDLc; LDLc; Type 2 diabetics.

1. INTRODUCTION

Dysfunctioning of Islet β-cells of pancreas causes reduced insulin secretion resulting in type 2 Diabetes mellitus (T2DM).[1] 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 diabetics [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 [9] 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 ^{0}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 <3ng/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±3.3mg/dl and 32.9±7.3 vs. 42.9±5.3 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*

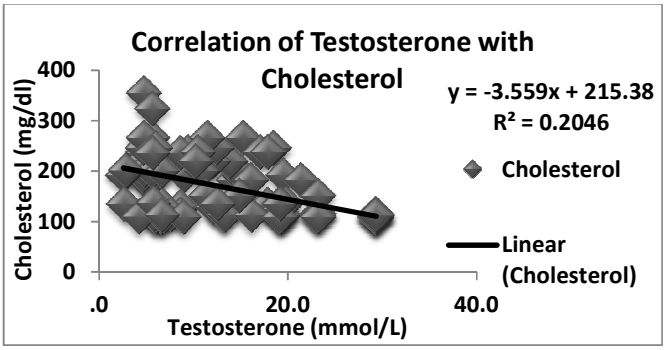

Fig. 1. Scatter plot showing negative correlation of Testosterone with Cholesterol

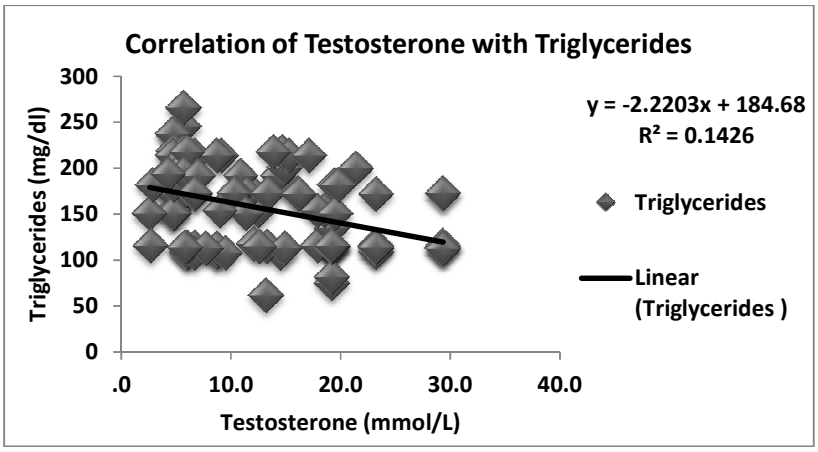

Fig. 2. Scatter plot showing negative correlation of Testosterone with Triglycerides

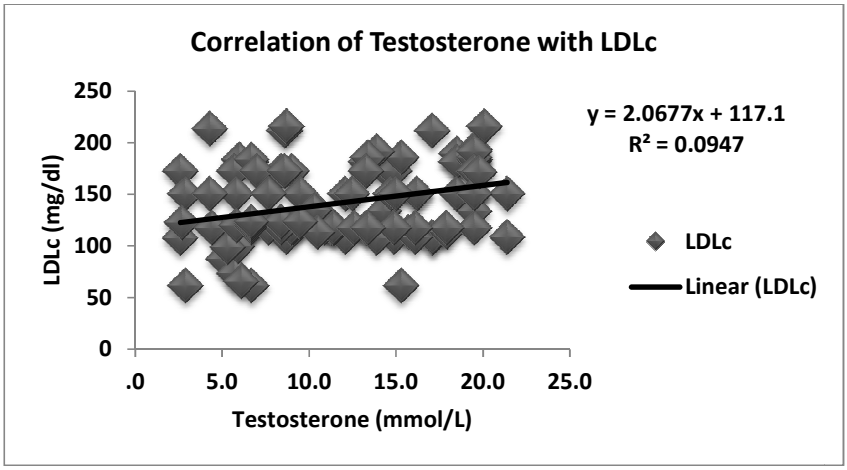

Fig. 3. Scatter plot showing positive correlation of Testosterone with Low Density Lipoprotein Cholesterol (LDLc)

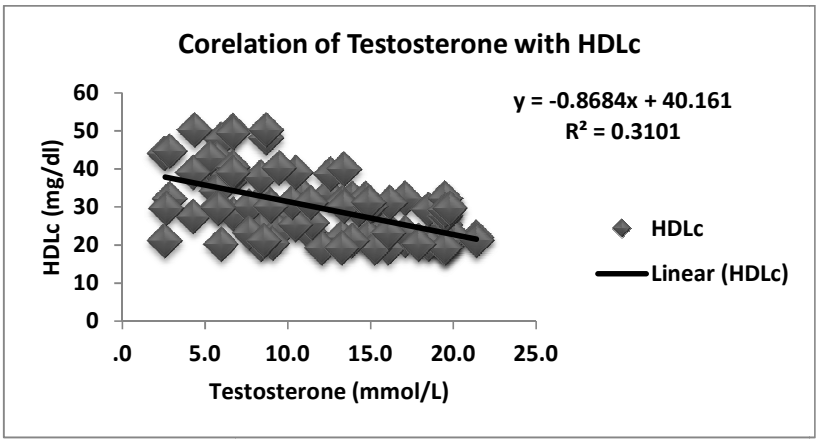

Fig. 4. Scatter plot showing negative correlation of Testosterone with High Density Lipoprotein Cholesterol (HDLc)

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 ± 3.8 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.

REFERENCES

1. Cohrs CM, Panzer JK, Drotar DM, Enos SJ, Kipke N, Chen C, et al. Dysfunction of Persisting β Cells Is a Key Feature of Early Type 2 Diabetes Pathogenesis. Cell Reports. 2020;31(1):107469:1-13.
2. Khoharo HK, Shaikh DM, Nizamani GS, Shaikh TZ, Ujjan I, Uqaili AA et al. Effects of Berberine on Blood Glucose, Glycated Hemoglobin A1, Serum Insulin, C–Peptide, Insulin Resistance and β– Cell Physiology. J Pharma Res Int`l. 2020;32(36):36-41.
3. Xu W, Morford J, Mauvais-Jarvis F. Emerging role of testosterone in pancreatic β-cell function and insulin secretion. J Endocrinol. 2019;240(3):R97-R105.
4. Holmboe SA, Jensen TK, Linneberg A, Scheike T, Thuesen BH, Skakkebaek NE, et al. Low Testosterone: A Risk Marker Rather Than a Risk Factor for Type 2 Diabetes. J Clin Endocrinol Metab. 2016; 101(8):3180–90.
5. Oskui PM, French WJ, Herring MJ, Mayeda GS, Burstein S, Kloner RA. Testosterone and the cardiovascular system: a comprehensive review of the clinical literature. J Am Heart Assoc. 2013; 2:e000272.
6. Araujo AB, Dixon JM, Suarez EA, Murad MH, Guey LT, Wittert GA. Clinical review: endogenous testosterone and mortality in men: a systematic review and meta-Analysis. J Clin Endocrinol Metab. 2011;96:3007–3019.
7. Kundu D, Ghosh E, Roy SS, Basu S. Serum testosterone levels in type 2 diabetes mellitus. Int J Med Res Rev. 2018;6(08):409-413.
8. Ijaz M, Ali I, Hussain A. Diabetes mellitus in Pakistan: the past, present and the future. Intl J Diabetes Dev Ctries. 2020;40:153-4.
9. Adnan M, Aasim M. Prevalence of Type 2 Diabetes Mellitus in Adult Population of Pakistan: A Meta-Analysis of Prospective Cross-Sectional Surveys. Annals Global Health. 2020; 86(1):1–8.
10. Mattack N, Devi R, Kutum T, Patgiri D. The Evaluation of Serum Levels of Testosterone in Type 2 Diabetic Men and Its Relation with Lipid Profile. J Clin Diagn Res. 2015;9(1):BC04-BC07.
11. Farooq R, Bhat MH, Majid S, Mir MM. Association between T2DM and the lowering of testosterone levels among Kashmiri males. Arch Endocrinol Metab. 2020;64(5):528-32.
12. Tiwari A, Srivastava A. Serum testosterone in males with newly diagnosed type 2 diabetes and its association with glycemic status and other metabolic indices. J Evid Based Med Health. 2016; 3(85):4621-6.
13. Kim JS, Kim BS, Jeon JY, Choi YJ, Chung YS. Testosterone Deficiency Associated with Poor Glycemic Control in Korean Male Diabetics. Endocrinol Metab. 2014;29:300-306.
14. Yeap BB, Alfonso H, Chubb SA, et al. Reference ranges and determinants of testosterone, dihydrotestosterone, and estradiol levels measured using liquid chromatography-tande mass spectrometry in a population-based cohort of older men. J Clin Endocrinol Metab. 2012;97(11): 4030-9.
15. Yao QM, Wang B, An XF, Zhang J, Ding L. Testosterone level and risk of type 2 diabetes in men: a systematic review and meta-analysis. Endocrine Connections. 2018;7:220–231.
16. Ding EL, Song Y, Malik VS. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. JAMA. 2006;295(11):1288-99.
17. Kupelian V, Page ST, Araujo AB. Low sex hormone-binding globulin, total testosterone, and symptomatic androgen deficiency are associated with development of the metabolic syndrome in nonobese men. J Clin Endocrinol Metab. 2006;91(3):843-50.
18. Fabian UA, Charles-Davies MA, Fasamade AA, Olaniyi JA, Oyewole OE, Owolabi MO, et al. Male Sexual Dysfunction, Leptin, Pituitary and Gonadal Hormones in Nigerian Males with Metabolic Syndrome and Type 2 Diabetes Mellitus. J Reprod Infertil. 2016;17(1): 17-25.
19. Ogbera AO. Relationship between Serum Testosterone Levels and Features of the

Metabolic Syndrome Defining Criteria in Patients with Type 2 Diabetes Mellitus. West African J Med. 2011;30(4):277-81.

20. Haider KS, Haider A, Saad F, Doros G, Hanefeld M, Dhindsa S, et al. Remission of type 2 diabetes following long-term treatment with injectable testosterone undecanoate in patients with hypogonadism and type 2 diabetes:11-year data from a real-world registry study. Diabetes Obes Metab. 2020;22: 2055–68.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/71483