

Correlation of testosterone with glycemic indices and lipid profile of the male patients with type 2 diabetes mellitus

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Abstract— Type 2 diabetes mellitus (T2DM) is one of the most common metabolic disorder associated with defects in hormonal control at the cellular level. Testosterone had been identified as a marker of stress in many cases, and has been found to influence the age related diseases like cardio vascular diseases (CVD), hypertension etc. Studies on the role of testosterone, if any, in glycemic control and lipid profile in normal and diabetic subjects are scanty. The present study was under taken to correlate the effects of total testosterone (TT) on glycemic control and lipid profile. The fasting blood glucose (FBG), glycated haemoglobin (HbA1c) and lipid profile of 97 patients and 30 age matched controls were correlated with their respective TT levels. There was a negative correlation in FBG, HbA1c and all lipid fractions except HDL-cholesterol (HDL-C) with TT in the study and control subjects ($p < 0.001$). HDL-C was found to be positively correlated ($p < 0.001$) with TT levels. It was observed that there is a significant correlation of serum TT with glycemic indices and lipid profile in the patients with T2DM.

Index Terms— Diabetes mellitus, Glycemic indices, Lipid profile, Total testosterone.

1 INTRODUCTION

Over the past 30 years, status of diabetes had changed from being considered as a mild disorder of the elderly, to one of the major causes of morbidity and mortality affecting youth and middle aged people [1]. T2DM is the most common condition affecting majority of the population and is usually marked with insulin resistance (IR) [2]. Since it is asymptomatic in early stages, late detection is an obstacle in treatment of this disease. IR has various causes, of which the effect of gonadal hormones needs more clinical evaluation. The impact of testosterone in this context is becoming important at the level of disease progression and its treatment. As men age, their ability to produce testosterone declines. Also, some men's production of leutinising hormone decreases with aging, which lowers testosterone production. Moreover, a protein that binds up and holds onto testosterone called sex hormone binding globulin (SHBG) increases in older men. This reduces the amount of free (unbound) testosterone in the blood that is available to tissues, such as muscles.

From studies on muscle biopsies it was observed that low testosterone impairs mitochondrial oxidative phosphorylation. As up to 70% of the body's insulin sensitivity can be accounted for by muscle action, this tissue may develop reduced insulin sensitivity in the low testosterone state sufficient to contribute in overall state of IR [3]. Similarly diabetic men treated with androgen ablation therapy for prostate cancer were found to have worsening diabetic control and need for a significant increase in their diabetic medication [4]. The research on animals shows that, those animals with low testosterone expressed high IR and metabolic impairments when compared with the control groups in which the role of testosterone was not inhibited [5].

At present, the association between testosterone and T2DM has not been fully elucidated. The purpose of this study was therefore to investigate the effects of TT on glycemic status of an individual along with the lipid profile. The glycemic status of individuals under study were analysed by measuring their FBG and their HbA1c levels. The total cholesterol, triglycerides (TG), HDL-C and LDL-C levels were measured to assess the lipid composition. The serum TT levels were estimated, in the same patient samples and were compared with the glycemic indices and lipid profile.

2 MATERIALS & METHODS

The study was conducted in 97 male T2DM subjects in the age group of 40 - 60 years referred from the University Health Centre. Thirty age matched healthy males constituted the control group. None of the subjects were suffering from any acute or chronic illness, systemic diseases or auto immune diseases. Seven mL of fasting venous blood sample was collected from all the subjects after getting informed consent. Two mL blood was taken in fluoride/oxalate bottle for FBG estimation, three mL was collected in vacutainers containing clot activators for lipid profile and serum total testosterone estimation and remaining two mL blood was collected in EDTA vacutainers for HbA1c.

FBG was estimated by Hexokinase Glucose-6-phosphate dehydrogenase method [6], serum total cholesterol by Cholesterol oxidase peroxidase method [7], triglycerides by Glycerol-3-phosphate oxidase- para amino antipyrine method [8], HDL-C and LDL-C by accelerator selective detergent method [9], HbA1c by Ion-exchange HPLC [10] and TT by competitive solid phase ELISA [11]. All the reagents, standards, chemicals, calibrators and quality control serum for FBG and lipid profile analysis were supplied by M/s Beckman Coulter Inc, USA. All the reagents, standards, chemicals, calibrators and quality control serum for HbA1c analysis were supplied by M/s BIO-RAD laboratories and for that of total testosterone analysis were supplied by M/s United Bioresearch Inc, Sunnyvale.

3 STATISTICS

All the obtained data were analysed statistically using SPSS 16.0. Each of the parameters were analysed for correlation with testosterone values of respective classes using the Karl Pearson correlation analysis and students 't' test was performed to check the statistical significance.

4 RESULTS

Ninety seven males with clinically proved T2DM patients were included in the study. Thirty healthy age matched male individuals were included as control. The subjects were divided in to three age group as less than 50 years, 51-55 years and 56-60 years (table 1). The mean age group was 50 ± 10.12 years. Patients above age of 60 were not included in the study. The corresponding values for control subjects are also given in table 1. The same age group, as of that of the study subjects were only included as control. There were 9 subjects with age < 50 years, 10 subjects with age between 51-55 years and 11 subjects with age 56-60 years. The mean age group of control subjects was 51 ± 6.4 years (Table 1). Comparison of the mean values of each parameter of study subjects with

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that of control subjects is given in table 2, fig 4.1 and fig 4.2. All parameters except HDL-C and TT were significantly elevated in the study subjects compared to that of the control population. HDL-C and TT was found to be significantly lower in the test subjects than that of controls (Table 2). From the results it was observed that the alterations in serum TT level

correlated negatively with the FBG, HbA1c, total cholesterol, serum TG and LDL-C concentrations, where as HDL-C is positively correlated with serum TT level variations. Fig 4.3 indicates the correlation scatter plot of variation in the glycemic indices and lipid profile with decreasing TT levels.

Table 1: Age wise distribution of the test and control subjects

MEASURED PARAMETER	AGE IN YEARS						Total	
	<50		51-55		56-60			
	Test (n= 27)	Control (n= 9)	Test (n= 33)	Control (n= 10)	Test (n= 37)	Control (n= 11)	Test (n= 97)	Control (n= 30)
FBG(mg/dL)	168.7±62.4	98.2±9.4	159.7± 71.5	99.3±9.1	178.4± 98.6	90.7±9.9	168 ± 77.5	95.8±9.9
HbA1c(%)	8.0±1.8	5.6±0.40	7.9±1.9	5.7±0.40	8.6±2.3	5.5±0.37	8.1±2.0	5.6±0.3
Total Cholesterol (mg/dL)	207.9±43.4	181.8± 12.4	196.8± 54.1	183 ± 12.03	195.8± 57.5	176± 14.3	200.1± 51.9	180±14.2
Triglyceride (mg/dL)	131.6±66.3	111.6± 24.4	141.5± 66.4	115.4± 23.09	145.7± 46.8	108± 27.2	139± 61.3	90.8±6.7
HDL- C(mg/dL)	41.8±13.7	54.1±8.6	41.5± 12.6	54.7±8.67	43.8±12.3	51.8±8.4	43.3± 12.9	53.4±8.4
LDL-C(mg/dL)	138.2±43.3	89.44±6.5	123.8± 48.9	92±6.35	128.6± 55.7	88.2±6.8	129.8± 49.2	111.2±27. 2
Total Testosterone (ng/mL)	9.2±6.5	10.3±1.57	9.0±5.7	9.68±1.64	8.5±6.0	10.7± 1.75	7.9±5.8	10.2±1.7

* All the values are mean ± SD

Table 2: Comparison between test and control

Variables	Test (n=97)	Control (n=30)	p value
FBG(mg/dL)	168±77.5	95.8±9.9	<0.001
HbA1c (%)	8.1±2.0	5.6±0.3	<0.001
TOTAL CHOLESTEROL (mg/dL)	200.1± 51.9	180±14.2	<0.001
TRIGLYCERIDE (mg/dL)	139±61.3	90.8±6.7	<0.001
HDL-C(mg/dL)	43.3±12.9	53.4±8.4	<0.001
LDL-C(mg/dL)	129.8± 49.2	111.2±27.2	<0.001
TOTAL TESTOSTERONE (ng/mL)	7.9±5.8	10.2±1.7	<0.001

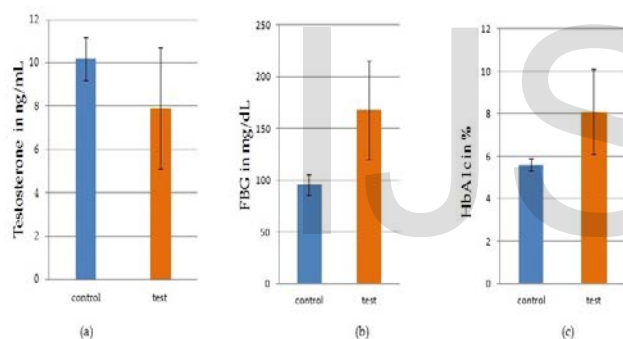


Fig 4.1 Glycemic indices and testosterone in control and test population

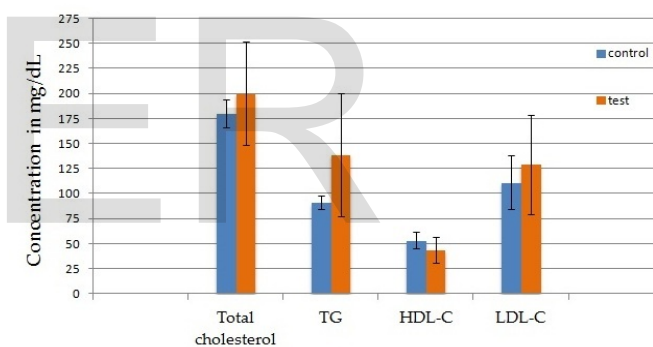


Fig 4.2 Lipid profile in control and test population

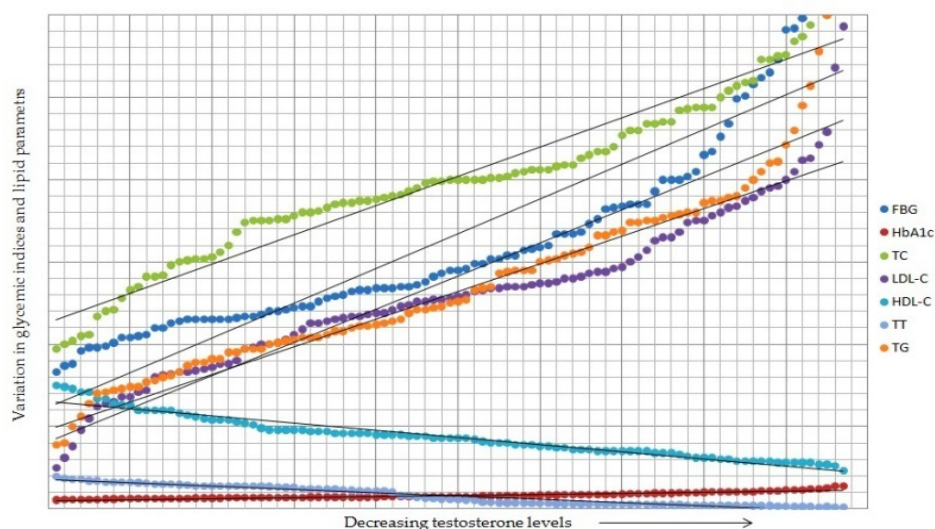


Fig 4.3. Correlation of testosterone with glycemic indices and lipid profile

7 DISCUSSION

Testosterone is one of the most important hormones that regulate the physiological functions of the body. Many reports are available on the literature suggesting that testosterone deficiency contributes to the onset and progression of T2DM, IR, MetS, CVD, and erectile dysfunction [12]. The increased prevalence of T2DM together with lower testosterone levels in adult males above 40 years have been demonstrated in many studies [13]. In the present study the mean age group of subjects is 50.5 ± 10 years. There were no patients below the age of 40 years. In this respect the present study is well in agreement with the previous reports.

A 13 year follow up study on males within 40-60 years have suggested decline in endogenous testosterone level with increased age [14]. Cross-sectional studies suggest having TT decline with age by 0.8% per year. It was reported that the hypothalamic-pituitary axis feedback mechanism causes the decline in testosterone [15]. Testosterone level showed marked decline in diabetic subjects compared to the normal healthy controls.

Increase in HbA1c of the test subjects were found to be inversely related to TT levels. FBG values in the present study showed significant negative correlation with the TT. This indicates that hyperglycemia may be due to low testosterone levels. Menendez et al [16] reported that lower plasma concentrations of TT even within the normal range have an increased risk of glucose intolerance and diabetes, regardless of age and body mass index. Earlier it was reported that, in male population under androgen deprivation therapy, there was considerable loss of lean body mass, increased percentage of body fat composition, and development of IR [17]. The reports about metabolic effects of testosterone replacement are controversial. Several studies mention that testosterone replacement improves FBG levels, insulin sensitivity [18], while there were contradictory reports also. However most of the studies confirm the positive effect of testosterone on improved glycemic control.

Studies analysing effects of administration of testosterone shares the beneficial effect of the hormone on serum cholesterol and TG levels in patients with coronary artery diseases and ischemic episodes. These effects relates to metabolic and vasoactive properties of the hormone [19]. The appearance of MetS like condition in men with prostate cancer whose plasma TT levels are rendered low, points to the chance that, low levels of testosterone predict the development of the MetS and T2DM [20]. In the present study low testosterone levels were associated with increased TG levels. Elevated FFA and TG have inhibitory effect on gonadal steroidogenesis there by leading to low TT levels.

The negative correlation of LDL-C levels to testosterone obtained in the present study is significant in the aspect of anti atherogenic role of testosterone. HDL-C levels below 60mg/dL correlated positively with TT in the present study. HDL-C values above 60mg/dL are considered as high. The effects of testosterone therapy on HDL-C levels have been investigated in several studies, with differing results. Studies suggested that increased testosterone correlates with decreased HDL-C levels in certain conditions. It has been hypothesized that testosterone leads to trafficking of the cholesterol back from the peripheral tissues to the liver, leading to consumption of HDL-C [21]. The decrease in HDL-C levels due to increase in testosterone is mostly seen in cases of testosterone replacement which is suggested to exert anti-atherogenic effects.

Studies on asymptomatic males of age 40-60 years showed that low TT is associated with high TG and lower HDL-C levels. Further study on men under going statin therapy with persistent dyslipidemia and inflammation were observed to have low TT levels [22]. It was reported that the effects of androgen in cardiovascular system suggests that androgens have beneficial or neutral cardiovascular effects in males and that they exert different

effects at early (plaque formation) and late (rupture, thrombosis, vasospasm) stages of atherosclerosis [23]. Prospective studies had confirmed that lower endogenous androgens predict central adiposity in men and that, these low TT levels are inversely associated with levels of FBG, TG, and BMI but positively correlated with HDL-C [24].

In the present study it was observed that there is a significant correlation of serum TT with glycemic indices and serum lipid profile in the patients with T2DM. Whether this is the cause of the disease or the effect of disease is not been fully understood. Hence further studies are needed, to find out the exact role of this hormone in lipid and carbohydrates metabolism in normal subjects and in patients undergoing treatment.

6 REFERENCES

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