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Article

Impact of Type 2 Diabetes on Men's Testosterone, BMI, and Lipid Profiles

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Abstract: Type 2 diabetes mellitus (T2DM) is the most prevalent type of diabetes globally, with well-understood pathophysiology. Recent research suggests testosterone may influence metabolic disorders like T2DM. This study aimed to examine the association between lipid profiles, testosterone levels, and body mass index (BMI) in 60 male Iraqi patients aged 40-50 with T2DM. A case-control study was conducted, including 60 diabetic men divided into two subgroups based on testosterone levels and a control group of 20 non-diabetic men. Measurements included testosterone, fasting blood glucose (FBG), HbA1c, lipid profiles, and BMI. Results indicated that diabetic men with low testosterone had significantly higher lipid profiles (TC, triglycerides, LDL, VLDL, HDL) and BMI compared to those with normal testosterone and the control group. FBG correlated positively with triglycerides and VLDL but negatively with HDL in the low testosterone group. Additionally, HbA1c negatively correlated with LDL, and the duration of diabetes correlated positively with cholesterol and LDL. The study concludes that low testosterone levels are common in T2DM patients and are associated with adverse lipid profiles and increased BMI, suggesting a potential role of androgens in lipid metabolism in diabetic patients.

Keywords: Type 2 Diabetes, Diabetes Mellitus, Testosterone, Body mass index, FBG, HBA1C.

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1. Introduction

A chronic hyperglycemic state brought on by abnormalities in insulin secretion, action, or both characterizes diabetes mellitus (DM), a group of metabolic disorders [1]. Chronic hyperglycemia brought on by either type 1 diabetes (insufficient insulin production) or type 2 diabetes (insufficient cell capacity to properly utilize insulin) [2]. Through a highly coordinated series of actions, such as stimulating glucose uptake in peripheral tissues like muscle and fat, inhibiting hepatic glucose output, and controlling lipid metabolism, insulin plays a monumental role in maintaining glucose homeostasis [3]. Apart from insulin, other hormones that contribute to glucose homeostasis maintenance include glucagon, growth hormone, cortisol, catecholamines, and insulin like growth factor-1 [4].

Recent years have seen a surge in interest in androgen deficiency among medical researchers, who have linked testosterone to a number of common systemic illnesses, including type 2 diabetes in addition, to men's general health. Most cross-sectional studies have generally found a correlation between higher endogenous testosterone concentrations and a more favorable cardiovascular profile, which includes higher HDL cholesterol and lower triglyceride concentrations, blood glucose, blood pressure, and body mass index [4].

However, exogenous testosterone or other anabolic steroid overdoses have been linked to negative health effects, such as hepatic disease and sudden cardiac death [5]. There have been numerous discussions about whether low testosterone is a biomarker for diabetes or if it plays a role in the pathophysiology of the disease. As a result, the current study's objective is to assess the serum testosterone levels of men with type 2 diabetes and discover whether there is any statistically significant correlation between different parameters.

2. Materials and Methods

The study was conducted on (60) Iraqi men with diabetes who were divided into two subgroups according to testosterone level in serum : (1) Diabetic with normal testosterone group (11 people) (2) Diabetic with low testosterone group (49 people) aged between (40- 50) years of age who were diagnosed based on the level of fasting blood glucose (FBG) and glycated hemoglobin (HBA1C) and who visited the Specialized Center for Endocrinology and Diabetes in Baghdad Governorate, in addition to a control group whose total number is (20) of those aged between (40-50) years old and were subjected to the same tests for the purpose of comparison between the two groups. Blood was collected from each individual intravenously after (12-14) hours of fasting using a 10 ml disposable syringe between (8:00 - 10:30 am) and centrifuged by a centrifuge at 3000 rpm for 10 minutes. Serum was used to measure fasting blood glucose by using Reflotron test strips according to [6], determine HBAIC by the i-CHROMA TM system according to [7], Determine the concentration of testosterone by ichroma™ reader in sample based on the competitive immunofluorescence assay [8], total Bioconcentration of cholesterol (TC), TG and HDL by enzymatic chromatography using linear chemical reagents and tools.

Statistical Analysis

Utilizing Snedcor and Cochran's [9], analysis of variance one way (ANOVA), the Statistical Analysis System-SAS (2012) was utilized to examine the impact of the groups (patients and controls) on the study parameters. In this study, a significant comparison between means was made using the Least Significant Difference (LSD) test.

3. Results

Table (1) shows The levels of lipid profile and BMI included Cholesterol level (TC), triglyceride, LDL, VLDL, HDL mg/dl increased significantly ($P<0.01$) in Diabetic with low Testosterone group (170.34 ± 5.37, 161.89 ± 11.79, 115.26 ± 5.29, 32.10 ± 2.27, 23.02 ± 1.27, 28.70 ± 0.46, respectively) in comparison with Diabetic with normal Testosterone group (144.82 ± 7.44, 118.91 ± 24.15, 82.00 ± 10.06, 23.91 ± 4.82, 29.82 ± 3.48, 29.21 ± 0.55 respectively) and control group (145.40 ± 5.87, 98.20 ± 7.11, 93.15 ± 6.05, 19.85 ± 1.41, 24.05 ± 1.63, 22.87 ± 0.27, respectively) but the level was within normal range in Diabetic with low testosterone group while BMI were significantly increase in Diabetic with normal testosterone group and testosterone low group compared to control groups.

Table 1. The levels of lipid profile and BMI in Diabetic with (Normal and Low) Testosterone group

The group	Mean ± SE					
	Total cholesterol (mg/dl)	Triglyceride (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)	HDL (mg/dl)	BMI
Control	145.4 ±5.9 b	98.2±7.1 b	93.2±6.1 ab	19.9±1.4 b	24.1±1.6 ab	22.9±0.3 b
Diabetic with Normal Testosterone group	144.8 ±7.4 b	118.9±24.2 ab	82.0±10.1 b	23.9±4.8 ab	29.8 ± 3.5 a	29.2 ± 0.6 a
Diabetic with Low Testosterone group	170.3 ±5.4 a	161.9 ±11.8 a	115.3 ±5.3 a	32.1±2.3 a	23.0 ± 1.3 b	28.7 ± 0.5 a
Normal value	150-200	40-150	69-166	8-30	35-60	18.5-24.9
LSD value	21.984 **	47.676 **	22.430 **	9.261 **	5.849 *	1.776 **
P-value	0.0070	0.0040	0.0043	0.0045	0.0499	0.0001
* (P<0.05), ** (P<0.01). Means having with the different letters in same column differed significantly.						

In table (2) the Diabetic with Normal Testosterone group shows no correlation between FBG and HBA1C with TC, triglyceride, VLDL, LDH, and HDL while in Diabetic with Low Testosterone group, FBG shows positive correlation with the triglyceride, VLDL, and negative correlation with HDL, and HBA1C shows significantly (P<0.05) negative correlation (-0.29) with the LDL. BMI has significantly (P<0.05) negative correlation (-0.62) only with FBG in Diabetic with Normal Testosterone group.

Table 2. Correlation of FBG and HBA1C with lipid profile and BMI.

Lipids Profile	FBG		HBA1C%	
	Diabetic with Normal Testosterone group	Diabetic with Low Testosterone group	Diabetic with Normal Testosterone group	Diabetic with Low Testosterone group
Total cholesterol	-0.27 NS	-0.11 NS	-0.23 NS	-0.21 NS
Triglyceride	-0.03 NS	0.33 *	0.18 NS	0.20 NS
LDL	0.09 NS	-0.20 NS	-0.10 NS	-0.29 *
VLDL	-0.04 NS	0.36 **	0.18 NS	0.22 NS
HDL	0.25 NS	-0.28 *	0.34 NS	-0.06 NS
BMI	-0.62 *	0.11 NS	-0.33 NS	0.02 NS
* (P<0.05) , **(P<0.01) NS: Non-significant				

In table (3), the age has negative correlation (-0.66) with testosterone in Diabetic with Normal Testosterone group while the duration of illness has positive correlation with the cholesterol (0.29) and LDL (0.29) in Diabetic with Low Testosterone group.

Table 3. Correlation coefficient of Age, Duration of illness with Testosterone and lipid profile

Parameters	Diabetic with Normal Testosterone group		Diabetic with Low Testosterone group	
	Age	**Duration of illness**	**Age**	**Duration of illness**
Testosterone	-0.66 *	-0.26 NS	0.02 NS	-0.19 NS
TC	0.42 NS	-0.16 NS	0.29 *	-0.14 NS
Triglyceride	-0.15 NS	-0.07 NS	0.004NS	-0.09 NS
LDL	0.07 NS	-0.34 NS	0.29 *	-0.13 NS
VLDL	-0.15 NS	-0.08 NS	-0.02 NS	-0.10 NS
HDL	0.28 NS	-0.06 NS	0.10 NS	0.10 NS
* (P<0.05) ,(P<0.01), NS: Non-significant				

Figure (1) showed the frequency of normal and low testosterone in diabetic group according to normal value of testosterone (2.5-10.0 ng/ml) [10]. The frequency of low Testosterone was significantly difference than normal testosterone (81.66% and 18.33%, respectively).

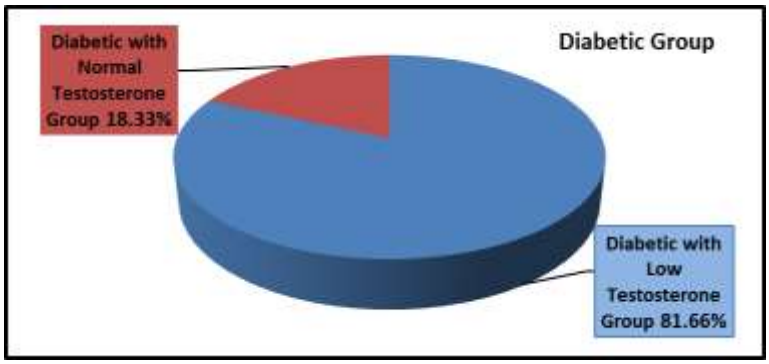

Figure 1. The frequency of (Normal and Low) Testosterone in Diabetic Group

4. Discussion

In our study we found the total cholesterol was significant increase in Diabetic with Low Testosterone group but the elevation was within normal value (150-200 mg /dl), (table 1) the normal level can be elucidate that there is such decrease of TC in control group and Diabetic with Normal Testosterone group that refers to a such hypolipidemia is a reduce in plasma lipoprotein caused by primary (genetic) or secondary (acquired) factors. Physicians are typically unaware of hypolipidemia, its causes, and its effects, in contrast to hyperlipidemia. Interestingly, aggressive treatment of hyperlipidemia rises, especially with the use of potent and more recent hypolipidemic medications. The safest and lowest level of serum cholesterol is difficult to define because even a slightly lower level of cholesterol can signal a serious underlying issue [11]. In the literature, reduced plasma cholesterol is referred to by the terms hypolipidemia, hypocholesterolemia, and hypobetalipoproteinemia, which are used interchangeably. The majority of authors define this condition using total serum cholesterol (TC)[12].

When an acute illness strikes, total cholesterol levels decrease, and they rise back to normal as the body recovers [13]. Hypocholesterolemia in critically ill patients is influenced by multiple mechanisms, such as downregulation of hepatic synthesis [14] which is likely caused by a decrease in the production of precursors to cholesterol, specifically lanosterol and lathosterol [15]. The hypocholesterolemia which seen in Diabetic with Normal Testosterone group and control groups may be associated to the infection during cold

weather as our study began from November to January and are mediated by various cytokines that participate in the acute phase response during infection, such as TNF and IL-1 [16]. Diminished cholesterol levels in critically ill patients indicate the onset of infection. According to some authors, leucocytosis is not as sensitive as hypocholesterolemia as a marker for the onset of infection (13). Furthermore, TG levels are higher in the group of diabetics with low testosterone, suggesting that the hypertriglyceridemia may be caused by increased liver production of triglyceride-rich VLDL and decreased peripheral tissue TG removal, particularly from muscle and adipose tissue (8). Our findings show a decrease in serum HDL concentration as a result of excess catabolism and the previously documented negative correlation between HDL and LDL concentrations [17]. Acute phase responses during sepsis were highly correlated with hypocholesterolemia (measured by the C-reactive protein level) (16).

The results of the table (2) are interpreted as hyperglycemia is related with deranged lipid profile and this may lead to dyslipidemia that [18] reported that elevated fasting blood sugar can significantly increase the serum level of triglycerides ($P<0.01$) in Pre-diabetic and diabetic Patients. In our results, Diabetic with Normal Testosterone group shows negative significant correlation which means adipose tissue in overweight patients has an effect to stimulate insulin secretion to reduce blood glucose level that E2 produced from adipose may take part in the ERα-mediated enrichment of insulin biosynthesis [19] and in the stimulation of insulin secretion by glucose to aid in the pancreatic β-cells' adaptation to the increased insulin demand associated with obesity.

In our study, The FBG in Diabetic with Low Testosterone group shows positive correlation with triglyceride and VLDL, and negative correlation with HDL. Free fatty acids have been shown to impair insulin-mediated glucose uptake in humans. The increased glycerol that results from lipolysis tends to trigger gluconeogenesis through mass effect, which increases the liver's production of glucose and exacerbates hyperglycemia. All effects of lipid metabolism on lipid levels occur when the liver is supplied with large amounts of free fatty acids, which it then absorbs, esterifies into phospholipids and triglycerides, and secretes as ketone bodies or very low-density lipoproteins (VLDLs). Triglyceride primary carrier is synthesized by VLDL through endogenous action. Notably elevated VLDL apoprotein B-l00.There are two primary isoforms of the protein found in plasma: ApoB48 and ApoB100. First, it is only produced by the small intestine; second, it is produced by the liver and is associated with obesity, which is a common complication of type 2 diabetes [20]. In order to lyse triglycerides from the VLDL, lipoprotein lipase needs two obligate cofactors: insulin and apo C-II, an apoprotein that is typically found on the VLDL particle. The removal of triglycerides from VLDL may be impacted in the presence of significant insulin insufficiency (IR), which may contribute to the hypertriglyceridemia that is frequently linked to type II diabetes. HDL levels in insulin-resistant patients with type 2 diabetes are frequently lowered in direct proportion to the rise in triglycerides [21].

In our study, There was negative correlation between HBA1C and LDL (-0.29) in Diabetic with Low Testosterone group, that the significant correlation between HBA1C and FBG is in accordance with various previous study done all over the world. Those with diabetes who had poor glycemic control (84% of the total study population with type 2 diabetes) had higher levels of FBG. Diabetes patients should learn how to regularly check their lipid profiles and how to take extremely effective measures to control their blood sugar and cholesterol if anything seems off. Reaching the target for HBA1C will help to improve the lipid profile, which may help Type 2 diabetic patients experience fewer diabetic complications [22], as our results' LDL level was within normal range (115.26 ± 5.29), indicating a negative correlation. Even after controlling for confounders, testosterone is positively correlated with HDL cholesterol levels but negatively correlated with total cholesterol, LDL-C, and TG levels in the majority of population-based studies of men with

and without metabolic disorders, as reviewed by Monore and Dobs [23]. The length of the disease was significantly correlated with higher HbA1c levels, and there was a significant correlation between insulin levels at one year and two to five years of duration (7.9 ± 3.0 and 5.9 ± 2.2, respectively) [24].

The group of diabetic patients with normal testosterone shows in Table (3) that age has a negative relationship with testosterone. This means that the aging of diabetic patients affects the level of testosterone, as the majority of 605 individuals showed low levels of free testosterone, where a negative relationship was recorded between age and free testosterone [25].

In our study there was positive correlation of age in Diabetic with Low Testosterone group with cholesterol and LDL. Triglyceride-rich lipoprotein concentrations have been found to be primarily caused by increased synthesis of VLDL particles in the liver. High levels of serum FFAs in insulin-resistant patients have been suggested as the cause of this excess hepatic production of VLDL and triglycerides. Elevations in VLDL cholesterol have also been reported in T2DM, which may lead to slightly elevated LDL cholesterol levels. These observations are consistent with our study's findings that patients with the metabolic syndrome and obese people have higher levels of cholesterol synthesis. Insulin resistance may account for the increase in cholesterol synthesis in patients with obesity and type 2 diabetes because similar results have been observed in patients with the disease regardless of weight [26]. The duration of disease was non-significant in this group as there was no significant correlation between duration of diabetes and male sex hormones (Testosterone) were in agreement with reported by [27].

5. Conclusion

This study shows that the levels of lipid profile and BMI included Cholesterol level (TC), triglyceride, LDL, VLDL, HDL mg/dl increased significantly in Diabetic with low Testosterone group in comparison with Diabetic with normal Testosterone group and control group while BMI were significantly increase in Diabetic with (Normal and Low) testosterone group compared to control groups. This suggests that androgens in diabetic patients affect the lipid profile through a mechanism that is not well known. FBG shows a positive association with triglycerides and VLDL in diabetic patients with low testosterone range. In addition, our research revealed that among diabetic subject groups, Type 2 diabetes mellitus lowers testosterone levels at (81.66%). Thus, it is suggested that hypoglycemia in men has an evolutionary role in Type 2 diabetes. Also, the duration of the disease has a positive relationship with cholesterol and LDL in the group of diabetic patients with low testosterone..

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