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Effect of Obesity on Androgen Levels Among Diabetic Patients

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Abstract **Original Research Article**

Aims: To study BMI and testosterone levels in men with type 2 diabetes mellitus. ***Material and Methods:*** An observational, cross sectional study was performed in 193 male type 2 diabetic patients. Height and weight were evaluated in all subjects. BMI was calculated as weight (kg) divided by square of height (m^2) and was expressed in kg/m^2. Classification of BMI was done according to western pacific regional office (WPRO) (2000) guidelines for BMI for Asian population. Total Testosterone Levels and Free Testosterone Levels were measured based on chemilumiscence on Beckman coulter access 2 immunoassay system (time for collection of samples was between 7am to 11am). ***Observations:*** The average age of study population was 43.32 ± 5.10 years. A total of 142 (73.57%) patients were known cases of diabetes mellitus. A total of 51 (26.42%) patients were newly diagnosed Type 2 Diabetes Mellitus. Average Body Mass Index (BMI) of the patients was 25.73±3.33 kg/m.$^{2.}$ out of 193 patients, total number of Obese II (BMI ≥30) patients were 33 (17.09%), Obese I (BMI 25-29.9) were 62 (32.12%), overweight at risk (BMI 23-24.9) were 60 (31.08%) and normal (BMI 18.5-22.9) were 37 (19.17%). OUT of 33 Obese II (BMI ≥30) patients, 21(63.63%) patients were having low total testosterone levels and 12 (36.36%) were having normal total testosterone levels. ***Conclusion:*** 63.63% of obese diabetic men aged between 30 to 50 years have low total testosterone levels and 48.48 % of obese patients have low free testosterone levels. Obese diabetic patients have low total testosterone levels as compared to non-obese diabetic patients which conclude that obesity also leads to low testosterone levels in addition to diabetes, which associated with additional increase in low testosterone levels.

Keywords: Body mass index (bmi), testosterone levels, type 2 diabetes mellitus (dm), obesity.

INTRODUCTION

Diabetes mellitus (DM) affects an estimated 285 million people worldwide. This number is expected to reach 438 million by the year 2030, with two-thirds of all cases occurring in low- to middle-income countries [1]. Asians develop diabetes at a younger age, at lower degrees of obesity, and at much higher rates given the same amount of weight gain compared with Western populations [2]. Researchers have highlighted the potential metabolic consequences of testosterone decline on age-associated metabolic changes such as abdominal obesity, diabetes, and markers of prediabetes [3-5]. The relationship between obesity and low testosterone levels appears to be complex and multifactorial. Obese men may present with abnormal levels of reproductive hormones due to changes in their secretion and metabolism, alterations in their transport and/or action at target tissues. Insulin resistance with compensatory hyperinsulinemia with the increased release from adipose tissue of several adipokines and cytokines, and higher estradiol promotion rate due to increase aromatase activity, which in turn alters both directly or indirectly the hypothalamic pituitary gonadal axis, have been suggested to be a major responsibility for low testosterone levels in obese subjects[6]. Adipose tissue functions primarily to store energy. It also plays an important role in systemic glucose homeostasis. Recent epidemiological studies have shown that both serum total testosterone and free testosterone levels are decreased in obese men [7, 8].

MATERIAL AND METHODS

This was hospital based observational, cross sectional study. This study included 193 Patients with Type 2 Diabetes Mellitus, known cases or diagnosed for the first time. Patients have given written consent to participate in the study. Patients with Type 1 diabetics, Secondary diabetes. (Chronic Pancreatitis, Drugs, Cushing's, Pituitary and thyroid disorder), Prior or Present treatment for hypogonadism with testosterone

replacement, with anti-androgens, chronic diseases. (HIV infection, COPD, ESRD), Critical illness Hyperprolactinemia, Medications. (E.g. opiates, anabolic steroids) were not included in this study.

INVESTIGATIONS

Serum Testosterone Levels were measured. Total Testosterone Levels and Free Testosterone Levels were measured based on chemilumiscence on Beckman coulter access 2 immunoassay system (time for collection of samples was between 7am to 11am). Reference ranges for testosterone levels according to age were given in Table 1 and Table 2. In addition to this Fasting plasma glucose, 2 hours Post Prandial Plasma glucose, Lipid Profile, Serum urea, Serum creatinine tests were done. All these biochemical tests were done at IGMC Shimla on KONELAB-30 automatic analyser. HbA1c was measured in all patients by using high-performance liquid chromatography.Urine examination for Micro albuminuria was done. Height and weight were evaluated in all subjects. BMI was calculated as weight (kg) divided by square of height (m^2) and was expressed in kg/m^2. Classification of BMI was done according to western pacific regional office (WPRO) (2000) guidelines for BMI for Asian population (table 3).

Table-1: Reference Ranges for Chemical Variables Testosterone Levels in 30 to 40 Years of Age

Testosterone	Normal Range	Low
Total	241 - 827ng/dl	<241 ng/dl
Free	9.1 - 32.7pg/ml	< 9.1pg/ml

Table-2: Testosterone Levels in 41to50 Years of Age

Testosterone	Normal Range	Low
Total	241 - 827ng/dl	<241 ng/dl
Free	5.7- 30.7pg/dl	<5.7pg/ml

Table-3: Western pacific regional office (wpro) (2000) guidelines for bmi for asian population

Classification	BMI (kg/m^2)
Underweight	<18.5
Normal range	18.5 - 22.9
Overweight at risk	23 - 24.9
Obese I	25 - 29.9
Obese II	≥ 30

STATISTICAL ANALYSIS

Data was recorded on a Microsoft Excel spreadsheet. All discrete variables were expressed as percentages. Statistical analysis was performed using Epi Info2000 and SPS student version 16.0(SPSS Inc, Chicago, USA).

RESULTS

OUT of 193 patients who fulfilled the eligibility criteria,67(34.71%) patients were having low total testosterone levels and 57 (29.53%) were having low free testosterone levels& total of 45 (23.31%) patients were having low both total and free testosterone levels. While comparing BMI with low total and free testosterone levels with normal total and free testosterone levels following observations were found. Table 4: Relation of BMI with prevalence of low total testosterone in Type 2 Diabetes Mellitus: BMI ≥ 30, total number of patients were 33 out of which 21 (63.63%) were having low total testosterone level. BMI 25 to 29.9 total numbers of patients were 62, out of which 29(15.03%) were having low total testosterone level. BMI 23 to 24.9, total numbers of patients were 60, out of which 12(20%) were having low total testosterone level. BMI 18.5 to 22.9, total numbers of patients were 37, out of which 4 (10.81%) were having low total testosterone level. This shows significant association between BMI and low total testosterone levels (p value < .0001)

Table-4: BMI with normal and low total testosterone levels

Body Mass Index* (BMI)	Number of patients with normal total testosterone levels (n=126)	Number of patients with low total testosterone levels (n=67)	Total number of patients (n=193)	p Value
≥30	12 (36.36%)	21 (63.63%)	33(17.09%)	<0.0001
25 - 29.9	33(17.1%)	29(15.03%)	62(32.12%)	
23 - 24.9	48(80%)	12(20.0%)	60(31.08%)	
18.5- 22.9	33(89.18%)	4(10.81%)	37(19.17%)	
<18.5	0(0%)	1(0.52%)	1(.51%)	

Table 5: Relation of BMI with prevalence of low free testosterone in Type 2 Diabetes Mellitus: BMI≥30, total numbers of patients were 33 out of which 16 (48.48%) were having low free testosterone level. BMI 25 to 29.9 total numbers of patients were 62, out of which 24(12.44%) were having low free testosterone level. BMI 23 to 24.9, total numbers of patients were 60, out of which 14(23.33%) were having low free testosterone level. BMI 18.5 to 22.9, total numbers of patients were 37, out of which 3(8.1%) were having low free testosterone levels. This shows significant association between BMI and low free testosterone levels (p value .0001).

Table-5: BMI with normal and low free testosterone levels

Body Mass Index*	Number of patients with normal free testosterone levels(n=136)	Number of patients with low free testosterone levels (n=57)	Total number of patients (n=193)	p Value
≥30	17(51.51%)	16(48.48%)	33(17.09%)	<0.0001
25 - 29.9	38(19.69%)	24(12.44%)	62(32.12%)	
23 - 24.9	46(76.66%)	14(23.33%)	60(31.08%)	
18.5 - 22.9	34(91.93%)	3(8.1%)	37(19.17%)	
<18.5	1(100%)	0(0%)	1(.51%)	

DISCUSSION

The study has demonstrated that there is a high prevalence low total testosterone levels in patients with BMI ≥30 (Obese II). OUT of 33 Obese II (BMI ≥30) patients, 21(63.63%) patients were having low total testosterone levels and 12 (36.36%) were having normal total testosterone levels. This study demonstrated that OUT of 33 Obese II (BMI ≥30) patients, 16 (48.48%) were having low free testosterone level. This study is limited by the absence of a non-diabetic group. Our study showed a higher average BMI in men with low total and free testosterone levels (p value <.0001) (Table 4 and 5). The finding that testosterone levels are negatively correlated to BMI is in agreement with work done elsewhere [9, 10]. High BMI, central adiposity, and the metabolic syndrome are associated with and predict low serum total and to a lesser extent free testosterone and SHBG levels [11-13]. These studies were in consistent with our study which showed high prevalence of low total testosterone levels with high BMI as compared to low free testosterone levels. Because obesity suppresses SHBG and as a result total testosterone concentrations. Many studies have addressed the relationship between BMI and LST of patients with T2DM. The outcomes of these studies are controversial. Some studies have shown a significant association between BMI and LST level [5, 14] it is well known that testosterone replacement reduces body fat mass and waist circumference in hypogonadal men with and without obesity [15, 16]. Testosterone treatment has also been shown reduce insulin resistance in obese men and type 2 diabetic subjects. Two studies in type 2 diabetic men have shown an improvement in glycemic control with testosterone replacement therapy [17]. However we have not done any intervention in the form of testosterone replacement therapy in our patients. Hence it is important to measure bioavailable or free testosterone in men with diabetes and obese patients.

CONCLUSION

This study demonstrates that diabetics' patients with high BMI have high prevalence of low total testosterone levels than with normal BMI**:** 63.63% of obese diabetic men aged between 30 to 50 years have low total testosterone levels and 48.48 % of obese patients have low free testosterone levels. Obese diabetic patients have low total testosterone levels as compared to non-obese diabetic patients which conclude that obesity also leads to low testosterone levels in addition to diabetes, which associated with additional increase in low testosterone levels.

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