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Original research article

Testosterone levels and body mass index in diabetic patients: clinical descriptive study

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Abstract

For decades, the diagnosis of diabetes was based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h value in the 75-g oral glucose tolerance test (OGTT). In 2009, an International Expert Committee that included representatives of the ADA, the International Diabetes Federation (IDF), and the European Association for the Study of Diabetes (EASD) recommended the use of the A1C test to diagnose diabetes, with a threshold of ≥ 6.5%, and the ADA adopted this criterion in 2010. 83 male patients of age 35-70 years attending Medicine OPD or admitted and as diagnosed cases of T2DM according to American Diabetes Association, 2014 guidelines would constitute the study population. The low Te subjects in BMI grouped cases and controls were tabulated and the difference between them was found to be statistically insignificant ($\chi 2$= 2.16 df=2 P=0.3396). Among cases there was statistical difference between low and normal Te values when BMI matched ($\chi 2$= 8.25 df=2 P=0.0162). It was significant among controls as well ($\chi 2$= 7.55 df=3 P=0.0229) which showed that the difference in Te levels in controls might have been because of the difference in their BMI.

Keywords: Testosterone, body mass index, diabetes

Introduction

India stands second only to China in having the largest number of diabetic subjects. According to the Diabetes Atlas 2013 published by the IDF, the number of people with diabetes in India currently around 65.1 million.Diabetes currently affects more than 62 million Indians, which is more than 7.1% of the adult population. According to the Indian Heart Association, India is projected to be home to 109 million individuals with diabetes by 2035[1, 2].

Although there is an increase in the prevalence of T1DM also, the major driver of the epidemic is the more common form of diabetes, namely T2DM, which accounts for more than 90% of all diabetes cases. The so called "Asian Indian Phenotype" refers to certain unique clinical and biochemical abnormalities in Indians which include increased insulin resistance, greater abdominal adiposity i.e., higher waist circumference despite lower body mass index, lower adiponectin and higher high sensitive C-reactive protein (hs-CRP) levels. This phenotype makes Asian Indians more prone to diabetes[3].

For decades, the diagnosis of diabetes was based on plasma glucose criteria, either the fasting plasma glucose (FPG) or the 2-h value in the 75-g oral glucose tolerance test (OGTT).

In 2009, an International Expert Committee that included representatives of the ADA, the International Diabetes Federation (IDF), and the European Association for the Study of Diabetes (EASD) recommended the use of the A1C test to diagnose diabetes, with a threshold of ≥ 6.5%, and the ADA adopted this criterion in 2010 [4]. The diagnostic test should be performed using a method that is certified by the NGSP and standardized or traceable to the Diabetes Control and Complications Trial (DCCT) reference assay. Although point-of-care (POC) A1C assays may be NGSP certified, proficiency testing is not mandated for performing the test, so use of these assays for diagnostic purposes could be problematic.

Methodology

Sample size

83 cases and 85 controls.

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Case selection
83 male patients of age 35-70 years attending Medicine OPD or admitted and as diagnosed cases of T2DM according to American Diabetes Association, 2014 guidelines would constitute the study population.

Control selection
85 age and BMI matched normal non-diabetic healthy male volunteersattending for blood donation in blood bank would serve as control group.

Study design
A hospital based Observational cross sectional study.

Inclusion criteria
1. Male patients attending Medicine OPD in the age group 35-75 years.
2. Patients who are willing to give informed consent.

Exclusion criteria
1. Type 1 Diabetes.
2. On hormone replacement therapy, steroids or testosterone use.
3. Chronic renal or hepatic disease.
4. HIV infection.
5. Surgically uncorrected cryptorchidism.
6. Malignancy and use of cancer chemotherapeutic agents or radiation therapy.
7. Prior infectious orchitis.
8. Surgical orchiectomy.

A detailed history, clinical examination and investigations will be done in each patient to assess disease severity and its complications giving main emphasis on serum Te levels. History taking will include symptoms of neuropathy, past history of hypertension and use of anti-hypertensive medications and Androgen Deprivation in Ageing Male (ADAM) questionnaire to calculate ADAM score which correlated with evidence of hypogonadism.

Results

Table 1: Age distribution of cases

Age in years	Cases n (%)	Controls n(%)
35-40	17(20%)	21(24.7%)
41-50	40(48%)	37(43.5%)
51-60	26(31%)	27(31.7%)
TOTAL	83	85

Cases were divided into 3 groups based upon age. 17(20%) were in 35-40 yr age group. 40 patients (48%) were in 41-50 yrs age group & 26 (31%) were in 51-60 yrs age group. Controls comprised of 21 (24.7%) in 35-40age group, 37 (43.5%) in 41-50age group and 27 (31.7%) in 51-60 age group.
On applying chi square test the value of $\chi 2$ is 1.15 with df=3 & p value =0.765 which is insignificant suggesting both groups are perfectly matched regarding age distribution.

Table 2: Mean age of subjects under study

Age in Years	Cases(n=83)	Controls(n=85)
Mean	47.31	45.44
SD	7.52	8.86

Mean age of cases was 47.31±7.52 yrs as compared to 45.44±8.86 yrs of controls (CI 95% t=1.4733, df =166 with P value =0.1426 which is insignificant). Thus both cases & controls are matched regarding their age wise distribution.

Table 3: BMI of study population

BMI (kg/m^2)	Cases n (%)	Controls n (%)
18.5-22.9	20(24.1%)	28(33%)
23-27.4	56(67.5%)	53(63.5%)
≥27.5	7(8.4%)	4(3.5%)
TOTAL	83	85

The value of $\chi 2$ for BMI distribution is 0.221 with df = 2 and P value = 0.3312 which is insignificant. Thus

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both cases & controls are matched regarding their BMI also.

Table 4: Mean BMI of subjects under study

BMI (kg/m^2)	Cases(n=83)	Controls(n=85)
MEAN	24.56	24.84
SD	1.84	1.91

Mean BMI of cases was 24.56±1.84kg/m^2 as compared to 24.84±1.91kg/m^2 of controls CI 95%, t=0.9673, df=166 with p value =0.3348 which is insignificant. Thus both cases & controls are matched regarding their BMI distribution as well.

Table 5: Te levels in BMI matched cases and controls

BMI(kg/m^2)	Cases		Controls	
	Low Ten (%)	Normal Ten (%)	Low Ten (%)	Normal Ten (%)
18.5-22.9	4(10.8%)	16(34.8%)	1(10%)	27(36%)
23-27.4	31(83.8%)	25(54.3%)	7(70%)	46(61.3%)
≥27.5	2(5.4%)	5(10.9%)	2(20%)	2(2.7%)
Total	37	46	10	75

The low Te subjects in BMI grouped cases and controls were tabulated and the difference between them was found to be statistically insignificant (χ2= 2.16 df=2 P=0.3396). Among cases there was statistical difference between low and normal Te values when BMI matched (χ2= 8.25 df=2 P=0.0162). It was significant among controls as well (χ2= 7.55 df=3 P=0.0229) which showed that the difference in Te levels in controls might have been because of the difference in their BMI.

Table 6: Mean serum Te levels as per BMI distribution

BMI distribution (kg/m^2)	Mean Te in cases (Mean±SD ng/dl)	Mean Te in controls (Mean±SD ng/dl)	P value	T value
18.5-22.9	281.61±107.28	384.76±106.11	0.0018	3.3053
23-27.4	240.14±171.59	354.71±124.52	0.0001	3.9707
≥27.5	237.85±149.84	270.22±145.91	0.7361	0.3477

There was significant difference in the mean Te levels among cases and controls when distributed as per BMI in 18.5-27.7 kg/m^2 category but not in ≥27.5 kg/m^2 which was likely due to small sample size in that category.

Table 7: Mean BMI in cases

BMI (kg/m^2)	Low Te	Normal Te
Mean	24.87	24.32
SD	1.53	2.07

The mean BMI in low Te group among cases was 24.87±1.53 kg/m^2 as compared to 24.32±2.07 kg/m^2 among normal Te group, CI 95%, t=1.3466, df=81 with P value =0.1819 which is insignificant. The higher BMI seen in low Te group was not due to the difference in BMI.

Discussion

Leydig cell function is under regulation by LH and other hormones therefore, it is possible that increased IR or hyperglycemia may result in reduced Te biogenesis because of decreased central stimulation. Interestingly, Pitteloud*et al.*[5] did not observe a correlation between insulin sensitivity and parameters of LH secretion or LH response to exogenous GnRH, suggesting that low Te levels associated with IR are not attributable to a major decrease in hypothalamic or pituitary hormone secretion. The authors have demonstrated a strong positive correlation between hCG-stimulated Te secretion and insulin sensitivity in men using physiological doses of HCG in the presence of experimentally induced hypogonadism. Ballester*et al.*[6] proposed several potential mechanisms that affect Te biogenesis in diabetes. The authors suggested that diminished Leydig cell function and Te production in insulin-dependent diabetes is attributed to reduce or absent stimulatory effect of insulin on Leydig cells. Oltmanns*et al.*[7] presented data suggesting that hypoglycemia but not insulin suppresses Te secretion and that this is mediated by pituitary decrease in LH output. Adipose tissue, which is considered an endocrine organ and produces a host of hormones and cytokines, may modulate insulin action and regulate Leydig cell function. Leptin production is tightly coupled to IR and may play a key role in steroid biogenesis and reduced Te levels. Leptin levels have been shown to be inversely correlated with serum Te levels and increased circulating leptin may be involved in the pathogenesis of Leydig cell dysfunction. The expression of leptin receptors in Leydig cells and the inhibition of HCG stimulated Te secretion from rat Leydig cells by leptin suggest a role of this hormone in

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the biogenesis of Te. Hong *et al.*[8]Proposed that TNF-a inhibits steroid biosynthesis in Leydig cells and proposed a molecular mechanism by which pro-inflammatory factors could contribute to inhibition of androgen biosynthesis. Additional studies are needed to fully delineate the biochemical and physiological mechanisms underlying reduced Te synthesis in diabetes.

Conclusion

There was significant difference in the mean Te levels among cases and controls when distributed as per BMI in 18.5-27.7 kg/m^2 category but not in ≥27.5 kg/m^2 which was likely due to small sample size in that category.

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