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ORIGINAL ARTICLE

Testosterone Deficiency in Young Diabetic Males

Chaurasia A[a], Valame S[b], Jain MK[c]

a Corresponding Author: Associate Professor, Department of Medicine, SSMC,Rewa, Madhya Pradesh, India.<dr.acrewa@rediffmail.com>
b Senior Resident, Department of Medicine, SSMC,Rewa, Madhya Pradesh, India.<shaunak_valame@hotmail.com>
c Ex-Professor & HOD, Department of Medicine, SSMC,Rewa, Madhya Pradesh, India.<drjainmk@yahoo.co.in>

Abstract:

Testosterone deficiency and diabetes mellitus have been found to share an intimate bond. Studies have found the prevalence of hypogonadism to be 24.5% in diabetes mellitus (DM) patients presenting with erectile dysfunction versus 12.6% in non-diabetic erectile dysfunction patients. It has negative correlation with waist circumference and body mass index and predicts insulin resistance. In line with these thoughts, we aimed to assess the prevalence of testosterone deficiency in male diabetes mellitus patients of ≤40 years of age and the impact of hypogonadism on their clinical parameters. Thirty male DM patients, below 40 years of age were assessed between October 2008 and September 2010 for symptoms of sexual dysfunction. All necessary routine biochemical tests were also carried out. For statistical analysis, the p-value was calculated using Fisher's exact test. Out of 30 male diabetics ≤40 years of age, 13 (43.33%) had low Serum Free Testosterone levels. The mean serum fT was 11.08±6.79 ng/dl. Type of Diabetes Mellitus, its duration, inadequate glycemic control, high waisthip ratio and loss of early morning penile tumescence significantly correlated with low fT. Thus, there is an intricate relation between Diabetes and Testosterone level as elucidated by the current study. As clinicians, we need to evaluate sexual dysfunction in young male diabetics, as its potential implications have physiological and psychological aftermaths.

Keywords: ***diabetes mellitus, testosterone, hypogonadism, sexual dysfunction***

INTRODUCTION

In today's age of non-communicable diseases, it is pertinent to assess the interactions between the two endocrinological complexes of diabetes mellitus (DM) and testosterone deficiency. Their relationship was initially brought to the forefront only after the turn of the millennium. With the ability to afflict almost any age group, the association of diabetes on serum testosterone level would have more profound effect in younger patients. Studies have found the prevalence of hypogonadism to be 24.5% in DM patients presenting with erectile dysfunction versus 12.6% in non-diabetic erectile dysfunction patients.[1]Hypogonadism in diabetes has also been shown to have a negative correlation with body mass index (BMI) and waist circumference.[2] Oh et al.

concluded that low testosterone levels are predictors of insulin resistance (IR) and incident type 2 DM in older adults.[3] Similarly, low testosterone levels are commonly observed in men with IR and type 2 DM.[4] Haidar et al. suggested that androgen deprivation has a negative impact on IR and glycaemic control in their study on diabetic prostate cancer patients.[5] This goes hand in hand with Morimoto's conclusion that steroid hormones exerted some natural protective effects in their study on rat pancreas.[6] In 2004, Corona demonstrated that metabolic syndrome (MetS), and in particular visceral adiposity (as assessed by increased waistline and hypertriglyceridemia), was specifically associated with hypogonadism in subjects consulting for sexual dysfunction.[7]In line with these thoughts, we aim at assessing the impact of hypogonadism in young patients of DM, and the co-morbidities which are an integral part of this vicious cycle.

AIMS

1. To study the prevalence of testosterone deficiency in male DM patients of ≤40 years of age.
2. To assess the impact of low testosterone on demographic and clinical parameters of the patients.

METHODS

The study was conducted on 30 male DM patients, below 40 years of age, in the out-patient clinic and in-patients of the Department of Medicine, Shyam Shah Medical College & associated Sanjay Gandhi Memorial Hospital, Rewa (MP), between October 2008 and September 2010. Besides demographic and anthropologic analysis, all patients were evaluated for symptoms of sexual dysfunction. Biochemical tests of complete blood count, lipid profile, HbA_1c, and serum free testosterone were carried out in all patients. Serum free testosterone was measured through a morning blood sample by radioimmunoassay and reference values used for diagnosis are in accordance to Vermeulen.[8] Thus, low testosterone (T) level was defined as a serum free testosterone (fT) <12.3 ng/dl and <10.3 ng/dl in patients between 25–34 years and 35–44 years respectively. To evaluate sexual intercourse related symptoms, patients' own subjective assessment of early morning penile tumescence and desire for intercourse was relied upon. For statistical analysis, the p-value was calculated using Fisher's exact test.

Table 1: Demographic and anthropologic profile.

	Low fT (%)	Normal fT (%)	Total(Mean fT-ng/dl)
Age (p=0.221)			
<30 years	02 (25%)	06 (75%)	08 (10.56±6.80)
>30 years	11 (50%)	11 (50%)	22 (11.26±6.78)
Mean: 33.37±5.72 yrs	Mean: 33.61±5.76 yrs	Mean 33.17±5.71 yrs	
DM Type (p=0.030)			
Type 1	04 (25%)	12 (75%)	16 (13.14±6.78)
Type 2	09 (64.29%)	05 (35.71%)	14 (8.71±6.76)
Duration of DM (p=0.037)			
<10 years	06 (30%)	14 (70%)	20(12.36±6.74)
>10 years	07 (70%)	03 (30%)	10(8.51±6.67)
Mean: 8.07±5.48 yrs	Mean: 8.46±5.57 yrs	Mean: 7.76±5.54 yrs	
Waist hip ratio9 (p=0.024)			
<0.9	03 (21.43%)	11 (78.57%)	14 (13.41±6.78)
≥0.9	10 (62.5%)	06 (37.5%)	16 (9.04±6.82)
Mean: 0.913±0.031	Mean: 0.918±0.029	Mean: 0.909±0.031	

OBSERVATIONS

Out of 30 male diabetics ≤40 years of age, 13 (43.33%) had low serum free testosterone levels. The mean serum fT was 11.08±6.79 ng/dl.

Table 1: Demographic and anthropologic profile. The current study revealed that subjects with low fT had a higher mean age (33.37±5.72 yrs) than those with normal fT (33.17±5.71 yrs). Although this difference was not significant, the finding proves that the age-related drop in serum fT, in our study group, could be attributed to the diabetic status of the patients. In accordance with this, we found a significantly lower fT among our patients of type 2 DM (8.71±6.76 ng/dl) compared to type 1 DM (13.14±6.78 ng/dl). While the mean duration of diabetes among the study group was 8.07±5.48 yrs, it was found that the group with low fT had a significantly higher duration of disease (8.46±5.57 yrs) than those with a normal fT (7.76±5.54yrs). Patients with a waist hip ratio (WHR) of ≥0.9 had a significantly lower fT (9.04±6.82 ng/dl) compared to those with a normal central adiposity (13.41±6.78 ng/dl).

Table 2 reveals the subjective findings of sexual desire and early morning penile tumescence in the current study group. Although all patients of low fT perceived a reduced sexual desire, this finding was not significant. However, such patients also reported a reduced frequency of early morning tumescence compared to a time before their diagnosis of DM. Thus, the mean serum fT was 8.02±6.78ng/dl among this group, while those who appreciated no change in early morning tumescence had a mean serum fT of 16.34±6.95 ng/dl. This association was highly significant (p=0.0002).

Table 2: Sexual symptoms

	Low fT (%)	Normal fT (%)	Total (Mean fT-ng/dl)
Sexual desire (p=0.37)			
No Change	00 (0%)	01 (100%)	01 (9.16)
Reduced	13 (44.83%)	16 (55.17%)	29 (11.14±6.79)
Early morning tumescence (p=0.0002)			
No change	00 (0%)	11 (100%)	11 (16.34±6.95)
Reduced	13 (68.42%)	06 (31.58%)	19 (8.02±6.78)

Table 3: Biochemical parameters.

	Low fT (%)	Normal fT (%)	Total (Mean fT-ng/dl)
Haemoglobin (p=0.039)			
>13 g/dl	01 (12.5%)	07 (87.5%)	08 (17.64±6.94)
<13 g/dl	12 (54.54%)	10 (45.45%)	22 (8.68±6.82)
Mean: 11.97±1.83g/dl	Mean: 11.33±1.81g/dl	Mean: 12.45±1.91g/dl	
HbA1c (p=0.034)			
<7%	02 (18.18%)	09 (81.82%)	11 (12.21±5.82)
>7%	11 (57.89%)	08 (42.11%)	19 (9.34±5.73)
Mean: 9.38±3.32	Mean: 11.02±3.55	Mean: 8.13±3.26	
Serum Cholesterol (p=0.772)			
<200 mg%	11 (42.31%)	15 (57.69%)	26 (11.26±6.78)
>200 mg%	02 (50%)	02 (50%)	04 (9.85±6.83)
Mean: 150.95±47.25	Mean: 157.08±45.51	Mean: 146.26±49.24	
Serum Triglycerides (p=0.030)			
<150 mg%	02 (14.29%)	12 (85.71%)	14 (13.75±6.78)
>150 mg%	11 (68.75%)	05 (31.25%)	16 (8.73±6.79)
Mean: 146.37±39.92	Mean: 169.23±40.11	Mean: 128.89±41.17	
Serum HDL-C (p=0.009)			
<40 mg%	10 (66.67%)	05 (33.33%)	15 (8.56±6.67)
>40 mg%	03 (20%)	12 (80%)	15 (13.58±6.80)
Mean: 37.99±10.03	Mean: 33.06±9.21	Mean: 41.76±9.04	

Through the current study, we also correlated the effects low fT would have on the biochemical parameters of diabetics. The low fT subgroup of patients had significantly lower mean haemoglobin concentration (11.33±1.81g/dl) and mean serum HDL-C (33.06±9.21) compared to their normal fT diabetic counterparts (mean Hb: 12.45±1.91g/dl and mean HDL-C 41.76±9.04). On the other hand, these patients had significantly higher mean value of HbA_1c (11.02±3.55 %) and serum triglycerides (169.23±40.11 mg/dl). Although mean serum total cholesterol was higher in the low fT subgroup, it was not found to be significant.

DISCUSSION

The current study conducted on ype 1 and 2 diabetics ≤40 yrs of age showed that 84.62% of low fT patients were ≥30 years of age. This result is similar to Chandel et al.,[10] who found a negative correlation of fT with age while Kapoor et al.[2] found an increasing trend in the prevalence of hypogonadism across all age groups. Ageing is associated with a decline in testosterone levels in men.[11] But, this decline, although present in the current study, was not found to be significant. Hence, there must be other factors in play which affect the decline in testosterone level. Thus, we hypothesise that one such factor is diabetes itself, as well as metabolic disturbances associated with it.

On comparing the type of diabetes, it was found that significantly higher number of type 2 DM patients had low fT levels (64.29%) as well as having a significantly lower mean fT level (8.71±6.76 ng/dl) compared to type 1 diabetics (35.71%; 13.14±6.78 ng/dl). Tomar et al.[12] also showed that patients of type 2 DM had frequent occurrence of hypogonadotrophic hypogonadism while fT concentrations in type 1 diabetes tended to be normal. In Dandona's study in 2009,[13] duration of diabetes was not found to affect testosterone levels. However, current study found that 70% of patients with a low fT level had duration of diabetes of ≥10 years. Mean fT value was also significantly lower in this subgroup (12.36±6.74 ng/dl) compared to patients with duration of diabetes <10 years (8.51±6.67 ng/dl). The complex interplay between diabetes and testosterone thus requires further evaluation if we are to ascertain the exact relationship between the two.

Studies have shown that free testosterone levels are low in obese men and inversely correlate with the degree of obesity.[14,15] Thus, if diabetes is added to this equation, it would not be surprising that the current study found that 10 of 16 obese patients had low fT; significantly higher than the 3 of 14 non-obese patients as evaluated by their WHR. Mean fT in patients of WHR ≥0.9 was thus significantly lower (9.04±6.82 ng/dl) than those with WHR <0.9 (13.41±6.78 ng/dl). Kapoor et al.[2] also found waist circumference to be negatively correlated with testosterone levels in their study on diabetic men. Thus, diabetes itself contributes to low testosterone levels associated with obesity.

Subjective findings of low sexual desire and reduced frequency of early morning tumescence in men was only seen among the subgroup of patients who had low fT. While the association of early morning tumescence was highly significant (p=0.0002), the same could not be said regarding loss of sexual desire (p=0.37). Studies have shown high prevalence of low libido (64%), erectile dysfunction (74%), and fatigue (63%) in hypogonadal men with type 2 diabetes.[2] Erectile dysfunction (ED) is common in diabetic men.[16,17]Etiology may be vascular disease, autonomic neuropathy, hypogonadism, or a combination of these. In addition, lack of testosterone during these reproductively active years has been found to lead to diminished peak bone mass and lack of development or loss of skeletal muscle.[18] Thus, the evaluation of gonadal hormones in patients of diabetes should be a matter of concern, especially among those of a reproductive age, as evaluated by the current study.

Bhatia et al. observed that hypogonadal type 2 diabetic men had a lower hematocrit than those with normal testosterone concentrations as well as a frequent occurrence of mild normocytic normochromic anemia.[19] Similarly, current study found a significantly lower heamoglobin level among

diabetics with a low fT (11.33±1.81g/dl) compared to the subgroup with normal fT (12.45±1.91g/dl). Another study (464 men) also found a direct correlation between free testosterone concentrations and hemoglobin in men with type 2 DM and renal insufficiency.[20] Thus, anaemia in a patient of diabetes may be result of interplay of renal insufficiency as well as low testosterone on erythropoetin.

Current study also showed that diabetics with a low fT had a significantly worse glycaemic control (HbA_1c = 11.02±3.55 %) compared to those with a normal fT (HbA_1c = 8.13±3.26%). Similarly, Fukui et al. have shown a negative correlation between serum bioavailable testosterone concentration with glycated albumin and glycated haemoglobin ratio.[21] A trial in men with new onset type 2 DM of transdermal testosterone also showed a decrease in HbA1c from 7.5% to 6.3% over a period of 1 year.[22]

Corona et al. found that patients presenting with erectile dysfunction with diabetes as co-morbidity, had significantly elevated triglycerides compared with those with impaired or normal fasting glucose.[7] In accordance with this, present study also found significantly elevated serum triglycerides in diabetic males with low fT (169.23±40.11) in comparison to those with normal fT (128.89±41.17). Meanwhile, the low value HDL-C was dramatic when compared between patients of low fT (33.06±9.21 mg/dl) and normal fT (41.76±9.04). Previously, Barret-Connor[23] had found that testosterone level positively correlated with the HDL cholesterol level ($p = 0.009$) and negatively correlated with the triglyceride level ($p = 0.0001$). Fukui et al. also concluded that cholesterol, being a precursor of testosterone, was positively associated with serum bioavailable testosterone concentration.[21] Similarly, 50% of our patients with cholesterol level ≥200 mg/dl had low fT compared to 42.31% of patients with cholesterol <200 mg/dl. This reflects the effect of testosterone on metabolic syndrome. Laaksonen et al. also observed that low testosterone levels were strongly associated not only with components of the metabolic syndrome, but also with the metabolic syndrome itself, independently of BMI.[24] Thus, the effect of testosterone in young diabetic males is widely distributed over the glycaemic and metabolic changes in diabetes.

RECOMMENDATIONS

This study enunciates the vital role of an androgenic hormone – testosterone – in another hormonal disease - DM. With disruption of the insulin axis in diabetes, disarray in testosterone will exponentially worsen biochemical parameters like haemoglobin, glycated haemoglobin, and lipid profile while also contributing to worsening of anthropologic measurements and sexual dysfunction. We recommend a baseline evaluation of testosterone in diabetic males, especially those who report sexual dysfunction. Also, as clinicians, we need to evaluate any degree of sexual dysfunction in young male diabetics, as the potential implications in young diabetic males have physiological as well as psychological aftermaths. As far as testosterone replacement is concerned, trials would be required to ascertain its pros and cons in young diabetic males.

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"A wise man should consider that health is the greatest of human blessings, and learn how by his own thought to derive from his illnesses."

— Hippocrates