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Evaluation of Serum Testosterone Level among Diabetic and Non-Diabetic Men Diagnosed with Benign Prostatic Hyperplasia

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Abstract **Original Research Article**

Background: Type 2 diabetes mellitus (T2DM) and low serum testosterone level had been reported in many studies. Both conditions are endocrinologically related. Many researchers have suggested a causal link claiming that low serum testosterone may be a risk factor for the development of T2DM, while others assert that it may well be a consequence of T2DM and age in the background. ***Materials and Methods:*** A total of seventy six (76) men were included in this study. Information from their case-notes were retrieved including biodata, history and physical examination findings, laboratory and imaging results. These information were obtained during their clinic visits and such folders were coded to avoid duplication of information. Variables such as age and body mass index (BMI) were grouped. Patients were also categorized as diabetic and non-diabetic according to their medical history and laboratory results (diabetic when FBG >126mg/dl). Collated data were displayed on SPSS software version 20.0 and analysed. ***Results*:** Seventy six patients aged between 41 and 86 years with a mean age of 64.07± 18.84 years were studied. Diabetic group were older (68.39± 7.6 years) than the non-diabetic arm (62.19 ± 8.7 years), however, with lower serum testosterone level (4.45 ±2.7ng/ml) than non-diabetics (5.39 ± 2.17ng/ml). ***Conclusion:*** Diabetic men in this study had a lower serum level of testosterone and we suggest a routine laboratory test of this hormone in the elderly to diagnose hypogonadism and prevent its complications.

Keywords: Type 2 diabetes, serum testosterone, benign prostatic hyperplasia.

INTRODUCTION

Serum testosterone is a major hormone secreted by the male gonads and serves to regulate important physiological functions in males. Its function has been associated with the development and growth of the prostatic cells both in benign and malignant conditions. Testosterone metabolism and T2DM are both endocrinologically related. Numerous studies had reported low levels of testosterone in men diagnosed with T2DM compared with healthy age-matched controls [1-3]. Other researchers propose that low testosterone may be a strong risk factor for the development of T2DM and may even predict its onset [4, 5]. In a recent study among Caucasian and Asian men diagnosed with hypogonadism, there was a strong association with metabolic syndrome in this population [6]. In another study, men with low serum testosterone were associated with insulin resistance and incident T2DM in older adults [3]. However, the nature of this association remains unclear. Attempts have been made to substantiate this relationship. One of such is the reduction in insulin resistance and fasting blood glucose (FBG) after treatment of hypogonadic diabetic men with testosterone replacement therapy (TRT) and improvement in glycated hemoglobin (HbAIc) levels [7, 8]. Yialamas *et al*., suggested that optimal levels of serum testosterone may regulate insulin sensitivity affecting cellular glucose metabolism and improvement in insulin resistance and T2DM [9]. Others think that low serum levels of testosterone may be a consequence of T2DM and advancing age [10, 11]. T2DM is associated with insulin resistance and this has been shown to have an inverse relationship with sex hormone binding globulin (SHBG) and low circulating levels of testosterone [12]. As a follow up to this, Ding et al working on newly diagnosed T2DM reported that higher testosterone levels correlated negatively with incident T2DM [2]. These then suggest that optimal serum levels of testosterone may partially offer protection against the development of metabolic syndrome including T2DM.

In this study, we set out to evaluate and compare serum levels of testosterone in T2DM and non-diabetic

patients diagnosed with benign prostatic hyperplasia (BPH).

MATERIALS AND METHODS

This study was conducted in the urology clinic of University of Uyo Teaching Hospital between September 2021 and August 2022. Information from patients' case- notes were retrieved on their clinic visits and such folders were coded to avoid duplication of information. Diabetic men were diagnosed based on elevated fasting blood glucose (FBG) (>126mg/dl) and a medical history of diabetes mellitus. Non-diabetic patients were indicated by absence of such information. Other clinical details such as biodata, history and physical examination, laboratory and imaging reports were retrieved. Exclusion criteria were men with incomplete clinical information, patients with history of hypogonadism, hyperthyroidism, patients taking exogenous testosterone, anti-androgen and antifungal medications. Others were patients suffering from chronic debilitating illnesses such as cardiac failure, liver cirrhosis, testicular and pituitary diseases. Variables such as age, BMI, diabetic status were grouped. Collated data were analysed using SPSS software version 20.0. The mean and standard deviation for continuous variables was obtained. Frequency table was constructed for categorical variables such as age, BMI and diabetic status. Comparison of measured variables between testosterone and designated variables was done. Results were displayed and used for discussion.

RESULTS

A total of 76 BPH patients were used for this study. Twenty three (30.3%) were diabetic while 53(69.7%) men were non-diabetic. The mean age of all patients was 64.07± 8.84 years ranging from 41 to 86 years. Non-diabetic men were younger than diabetic men (62.19±8.7 years versus 68.39±7.6 years). Overall mean BMI was 26.06 ± 4.36, diabetic men had a higher BMI than non-diabetic counterparts (26.92±4.00 versus 25.68±4.52). Mean overall serum testosterone was 5.10±2.37ng/ml while T2DM men had a lower serum level (4.45±2.71ng/ml), non-diabetics had a slightly higher serum testosterone (5.39±2.17ng/ml). Men in their 7th decade of life formed the majority (Table 2) and 49% of them were in the over-weight and obese categories (Table 2). Mean age of diabetic men was statistically different from mean age of non-diabetics (Pvalue = 0.04). Again, age and BMI correlated negatively with serum testosterone eventhough it lacked statistical significance (Pvalue>0.5).

Table 1: Mean and standard deviation of variables

Variable	Mean std deviation	Min	Max
Age (years)	64.07±8.84	41	86
BMI (kg/m^2)	26.06±4.36	18.50	36.08
PSA (ng/ml)	4.34±4.40	0.20	26.60
Testosterone (ng/ml)	5.10±2.37	0.10	11.30
Prostate volume (mls)	58.01±49.98	12.80	305.97

Table 2: Frequency of categorical variables:

Age	Frequency	Valid %	Cum %
40 – 49	6	7.9	7.9
50 – 59	12	15.8	23.7
60 – 69	39	51.3	75.0
70 – 79	15	19.7	94.7
80 – 89	4	5.3	100.0
Total	**76**	**100.0**	
Diabetics status:			
Diabetic	23	30.3	30.3
Non-Diabetic	59	69.7	100.0
Total	76	100.0	
BMI Status:			
Normal	25	51.0	51.0
Overweight	16	32.7	83.7
Obese	8	16.3	100.0
Total	**49**	**100.0**	

Table 3: Comparison of Measured variables between study groups by students T-test

Variables	Diabetic	Non-Diabetic	Pvalue
Age (years)	68.39±7.6	62.19±8.7	.004*
BMI (kg/m2)	26.92±.4.0	25.68±4.52	.366
Testosterone (ng/ml)	4.45±2.71	5.39±.2.17	.115

*Statistical significance set at P<.05

Table 4: Correlation table for testosterone and other variables

Variables	Correlation	Pvalue
Age	ɤ= -.113	.329
BMI	ɤ= -.251	.082
PSA	ɤ= .072	.538

Statistical significance set at P<.05

DISCUSSION

Testosterone is an important hormone secreted from the male gonads and regulates important physiological functions in males. Its serum level has been reportedly lower in T2DM than age-matched control healthy men [1-3]. The subnormal serum level of testosterone has been suggested as a strong risk factor for the development of T2DM [4, 5]. In one study, non-diabetics had twice as high serum testosterone level as diabetic men and same result was also documented in a meta-analysis of 3,825 men [1, 2]. In a more recent meta-analysis involving 11,831 men consisting of 1,822 T2DM and 10,009 non-diabetic men found a significantly lower level of testosterone in diabetic men [13].

In this study, serum testosterone level was lower in diabetic men compared to non-diabetics, although not statistically significant (Pvalue> 0.05) but confers a relevant clinical information in line with other studies in same subject area. Clinical questions have arisen as to why T2DM patients are associated with lower testosterone levels. Some levels may not be overtly hypogonadic (<3.ong/ml) as in this index study but seen to be consistently lower as in many series. It has been documented that insulin resistance (hyperinsulinaemia) directly impairs testosterone secretion by the Leydig cells of the testes since these cells also contain insulin receptors [14]. In another study, obese men had attenuated pulse amplitude of luteinizing hormone (LH) production leading to reduction in Leydig cell stimulation and testosterone production [15]. In our study, T2DM men had higher BMI than non-diabetics. High BMI is associated with visceral adiposity which is an important cause of insulin resistance and it is involved in the conversion of testosterone to estradiol by enzyme aromatase thus lowering serum testosterone levels [16]. This in part may be responsible for reduced serum level of testosterone in our cohort of men.

We studied men in their 7th decade of life who were being evaluated for BPH. It has been documented that fat mass increases with age and this contributes to high BMI associated with increased peripheral conversion of testosterone in the fat [17]. Adrekami *et al*., reported an inverse association between total and free testosterone in aging males [18]. The mean age of our patients was 64.07± 8.84 years. A peculiar mean age in BPH patients [19]. BPH is a disease of the middle aged and elderly population of men. There seems to be an additive effect of high BMI and advancing age that contributed to low testosterone level in our study population. In several studies, men with T2DM who were younger (ages between 45 and 57 years) than our patients had statistically significant lower testosterone values than their age–matched controls [1, 20-23]. This may suggest that before advancing age contributes to low testosterone, processes leading to this abnormality would have been ongoing due to those factors discussed earlier [14-16]. In this study, there was an inverse correlation between age and testosterone level (Table 4), even though it did not reach a statistically significant level (Pvalue>.05), but agreed with other studies in this subject [18]. BMI was also negatively associated with serum testosterone. This infers that the higher the BMI the lower the serum testosterone level. This was also reported by Kapoor *et al*., [16].

This work appeals to clinicians to evaluate all men with T2DM for testosterone level as TRT had been reported to improve diabetic symptoms and complications in hypogonadic men, although long term safety is uncertain [24, 25]. Again several longitudinal epidemiological studies have revealed that low testosterone is an independent risk factor for the development of T2DM and metabolic syndrome in later life [26, 27]. Testosterone should be added in the list of ancillary tests for aging males.

Limitations of this study were as follows: being a retrospective study, it may contain inherent flaws involved in data generation. It was a single centre study so that information obtained may not be generalized even though other studies both locally and internationally have documented same. We could not altogether rule out type one diabetes mellitus (T1DM) although same results had been made in T1DM men. We could not also ascertain whether the underlying pathology of BPH had any influence on testosterone level.

CONCLUSION

This study confirms the high prevalence of low serum testosterone levels in T2DM than in non-diabetic men. We advocate routine testing of serum testosterone in T2DM patients as a means of diagnosing hypogonadism and taking measures to prevent its complications to offer good quality of life (QoL). Active exercises and optimal diabetic control can also reduce BMI and attenuate the process of adipocyte pro-inflammatory cytokine production in order to optimize serum testosterone level.

Authors Contribution:

EAU: Substantial contributions to conception and design, Acquisition of data, Drafting the article, revising it critically for important intellectual

content, data analysis and Final approval of the version to be published.

OEA: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

AEU: Substantial contributions to conception and design, revising it critically for important intellectual content and final approval of the version to be published.

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