

Evaluation of Male Reproductive Hormone Profiles Among Diabetes Patients, With a Focus on Testosterone and Luteinizing Hormone

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<https://dx.doi.org/10.4314/sokjmls.v10i3.35>

Abstract

Diabetes mellitus (DM) is a common metabolic disorder associated with multiple complications, including sexual dysfunction. Hypogonadism, characterized by low serum testosterone, is increasingly recognized among diabetic men but remains under-investigated in Nigeria. This is a cross-sectional study conducted among 70 diabetic men and 70 age-matched apparently healthy controls attending Specialist Hospital Sokoto, Nigeria. Venous blood samples were collected for fasting glucose, testosterone, and luteinizing hormone (LH) assays using ELISA. Anthropometric measurements were obtained. Hypogonadism was defined as serum testosterone < 4.0 ng/ml. Data were analyzed using SPSS version 22 with $p < 0.05$ considered significant. The prevalence of biochemical hypogonadism was significantly higher in diabetic men (56.9%). Diabetic participants had lower mean testosterone levels (3.46 ± 0.37 ng/ml vs. 6.71 ± 0.27 ng/ml, $p < 0.001$) and higher LH concentrations (9.52 ± 1.34 mIU/ml vs. 6.73 ± 0.34 mIU/ml, $p = 0.05$). No significant differences were found between type 1 and type 2 diabetic patients. Testosterone correlated negatively with age, BMI, and duration of diabetes, though not significantly, while LH showed a significant positive correlation with BMI ($p = 0.029$). More than half of diabetic men in this study had biochemical hypogonadism, predominantly of the primary type, as evidenced by low testosterone and elevated LH. Routine hormonal evaluation should be incorporated into diabetes management to improve reproductive and metabolic health outcomes.

Keywords: Diabetes mellitus, Hypogonadism, Testosterone, Luteinizing hormone.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycaemia due to impaired insulin secretion, action, or both. Globally, over 500 million people live with diabetes, a number projected to rise sharply by 2045 (IDF, 2021). Nigeria has the highest burden of DM in sub-Saharan Africa, with an estimated 3.6 million cases as of 2021 (Adeloye *et al.*, 2017). Beyond its classical complications such as retinopathy, nephropathy, and neuropathy, diabetes predisposes men to sexual dysfunction, including erectile dysfunction (ED) and hypogonadism (Giugliano *et al.*, 2010; Salonia *et al.*, 2021). Erectile dysfunction affects more than 50% of diabetic men worldwide and contributes to poor quality of life (Thorve *et al.*, 2011). Pathophysiological mechanisms include vasculopathy, insulin resistance, neuropathy, visceral adiposity, and testosterone deficiency (Yao *et al.*, 2022). Hypogonadism in men with diabetes may manifest as reduced libido, infertility, fatigue, and loss of muscle mass. Biochemically, it is characterized by low serum testosterone, with or without compensatory increases in gonadotropins (Agarwal *et al.*, 2017). Studies have shown that men with type 2 diabetes have significantly lower testosterone compared with non-diabetic counterparts (Corona *et al.*, 2011; Beatrice *et al.*, 2016). However, findings on the relationship between testosterone, body mass index (BMI), and

diabetes duration remain inconsistent, with some studies suggesting a direct inverse relationship and others reporting no significant association (Tomar *et al.*, 2006; Birkebaek *et al.*, 2010). Despite increasing attention to the overlap between DM and hypogonadism in Western countries, there is limited data from Nigeria, particularly in northern populations where cultural factors may obscure reporting of sexual dysfunction. This study therefore aimed to evaluate testosterone and LH levels in male diabetic patients in Sokoto, Nigeria, and to determine the prevalence and correlates of hypogonadism in comparison with apparently healthy controls.

Materials and Methods

Study design and area

This study was carried out on male diabetic patients attending Specialist Hospital Sokoto, Nigeria. Sokoto is located in the North-Western part of Nigeria and shares borders with Niger Republic to the North, Kebbi State to the South-West and Zamfara State to the East (SSBD, 2007). The city lies between longitude 05° 42' to 22' East and latitude 12° 15' to 29' North and covers a total land area of about 32,000 square kilometers and a population of 4,602,298 million based on 2013 projection (SSBS, 2013; UNFPA, 2013).

Ethical Approval

The ethical approval for the study was obtained from the Ethics and Research Committee of Specialist Hospital, Sokoto.

Study population: The study enrolled 70 confirmed diabetic men aged 28–60 years and 70 apparently healthy, age-matched non-diabetic controls. Participants with chronic liver disease, renal failure, pituitary disorders, or testosterone therapy were excluded.

Sample collection and analysis: Five milliliters of venous blood were collected from each participant. Two and a half milliliters (2.5 ml) were placed in fluoride oxalate tubes for glucose assay, while the remainder was placed in plain tubes for serum separation. Samples were centrifuged at 3000 rpm for 5 minutes, and serum aliquots stored at –20 °C until analysis.

Hormonal assays: Serum testosterone and luteinizing hormone (LH) concentrations were measured using commercial ELISA kits (Shanghai BlueGene Biotech, China) according to manufacturer's instructions.

Definition of hypogonadism: Biochemical hypogonadism was defined as serum testosterone < 4.0 ng/ml, consistent with clinical guidelines (Bhasin *et al.*, 2018).

Sample Analysis

Serum sample was assayed for Testosterone and Luteinizing hormone (LH) using ELISA kits (Shanghai BlueGene Biotech, China).

Assay Procedure

Testosterone (Competitive Elisa)

The desired number of coated wells were arranged in the holder. 10 µl of standards, specimens and controls were dispensed into appropriate wells. 100 µl of Testosterone-HRP conjugate reagent was dispensed into each well. 50 µl of rabbit anti-testosterone reagent to each well. Thoroughly mixed completely for 30 seconds. Incubated at 37°C for 90 minutes. The microwells were rinsed and flicked 5 times with distilled or deionized water (tap water was not used). 100 µl of TMB reagent was dispensed into each well. Gently mixed for 10 seconds. Incubated at room temperature (18–25°C) for 20 minutes. The reaction was stopped by adding 100 µl of Stop Solution to each well. The solution was gently mixed for 30 seconds, ensuring that all the blue color changes to yellow color completely. Absorbance was read at 450 nm with a microtiter well reader within 15 minutes.

Luteinizing Hormone (LH) (Sandwich Elisa)

The desired number of coated wells were arranged in the holder. 50 µl of standard, specimens, and controls were dispensed into appropriate wells. 100 µl of Enzyme Conjugate Reagent was dispensed into each well. It was gently mixed completely for 30 seconds. Incubated at room temperature (18–25°C) for 45 minutes. Remove the incubation mixture by flicking plate contents into a waste container. The microtiter wells were rinsed and flicked 5 times with distilled. The wells were stroked

sharply onto absorbent paper to remove all residual water droplets. 100µl of TMB Reagent was dispensed into each well and gently mixed for 10 seconds. The mixture was incubated at room temperature in the dark for 20 minutes. The reaction was stopped by adding 100µl of Stop Solution to each well. Gently mix for 30 seconds. It was ensured that all the blue color changes to yellow color completely. The optical density was read at 450nm with a microtiter plate reader within 15 minutes.

Glucose Estimation (glucose oxidase–peroxidase (GOD–POD))

1.0 ml of glucose reagent was dispensed into each of the test, standard, and blank tubes. To the test tube, 10 µl of the sample was added, while 10 µl of standard glucose solution was added to the standard tube; no addition was made to the blank.

All tubes were mixed thoroughly and incubated at 37 °C for 10 minutes. The absorbance of the test and standard solutions was then measured against the blank at 500 nm using a spectrophotometer.

Statistical analysis: Data were analyzed using SPSS version 22 (IBM Corp., NY, USA). Continuous variables were expressed as mean ± standard error of mean (SEM). Comparisons between groups were made using Student's t-test. Correlation analyses were performed using Pearson's correlation. A p-value < 0.05 was considered statistically significant.

Results

A total of 140 men were recruited for the study (70 diabetics and 70 controls). Table 1 presents the socio-demographic characteristics.

Table 1. Socio-demographic characteristics of participants

Variable	Diabetics (n = 70)	Controls (n = 70)
Age group (years)		
28–39	28 (40%)	45 (64.3%)
40–60	42 (60%)	25 (35.7%)
Ethnicity		
Hausa/Fulani	55 (78.5%)	51 (72.9%)
Yoruba	4 (5.7%)	6 (8.6%)
Igbo	8 (11.2%)	7 (10.0%)
Others	3 (4.2%)	6 (8.5%)
Duration of diabetes		–
=2 years	33 (47.1%)	–
3–5 years	33 (47.1%)	–
6–10 years	4 (5.8%)	–

Key: n = 70 (number of participants)

Diabetic men had significantly lower serum testosterone levels (3.46 ± 0.37 ng/ml) compared to controls (6.71 ± 0.27 ng/ml, $p < 0.001$). Serum LH was significantly higher in diabetics (9.52 ± 1.34 mIU/ml) than controls (6.73 ± 0.34 mIU/ml, $p = 0.05$). Mean fasting glucose was also significantly elevated in diabetics, while BMI did not differ significantly (Table 2). When stratified by type of diabetes, there were no statistically significant differences in testosterone, LH, or BMI between type 1 and type 2 diabetics (Table 3).

Correlation analysis showed a negative, though non-significant, association between testosterone and age, BMI, and duration of diabetes. Conversely, LH showed a significant positive correlation with BMI ($p = 0.029$) but non-significant negative correlations with age and duration of diabetes (Table 4). The prevalence of biochemical hypogonadism (testosterone < 4 ng/ml) was 56.9% among diabetics.

Table 2. Mean biochemical and anthropometric parameters of diabetics and controls

Parameter	Controls (n = 70)	Diabetics (n = 70)	p-value	Remark
BMI (kg/m ²)	22.10 ± 0.24	20.40 ± 0.90	0.07	NS
Fasting glucose (mmol/L)	5.01 ± 0.22	7.73 ± 0.47	<0.001	SS
Testosterone (ng/ml)	6.71 ± 0.27	3.46 ± 0.37	<0.001	SS
LH (mIU/ml)	6.73 ± 0.34	9.52 ± 1.34	0.05	SS

Key: n = 70 (number of participants), NS = No significant.

Table 3. Comparison of parameters between type 1 and type 2 diabetes

Parameter	Type 1 DM	Type 2 DM	p-value	Remark
Age (years)	1.88 ± 0.23	2.26 ± 0.12	0.25	NS
Duration (years)	1.25 ± 0.64	1.63 ± 0.08	0.09	NS
BMI (kg/m ²)	22.44 ± 0.41	21.06 ± 0.54	0.31	NS
Testosterone (ng/ml)	4.65 ± 0.75	5.16 ± 0.29	0.52	NS
LH (mIU/ml)	11.53 ± 2.83	7.59 ± 0.67	0.53	NS

Key: NS = No significant.

Table 4. Correlation of testosterone and LH with age, duration of diabetes, and BMI

Variable	Testosterone (r, p)	LH (r, p)
Age	-0.098, 0.421	-0.144, 0.235
Duration of diabetes	-0.082, 0.502	-0.015, 0.902
BMI	-0.065, 0.445	+0.185, 0.029*

Discussion

This study demonstrates that more than half (56.9%) of male diabetic patients in Sokoto have biochemical hypogonadism, compared to only 11.5% of non-diabetic controls. The low testosterone and compensatory elevation of LH observed suggest a predominant pattern of primary hypogonadism.

Our findings are consistent with previous reports showing increased prevalence of hypogonadism among diabetic men (Corona *et al.*, 2011; Agarwal *et al.*, 2017). A recent meta-analysis estimated that up to

50% of men with type 2 diabetes have low testosterone, contributing to erectile dysfunction and infertility (Ding *et al.*, 2006). From this study, the age of the study participants were between 28-60 for apparently healthy individuals (41.51±0.76) and for diabetics (37.29±1.11). The mean difference of testosterone and LH between control and diabetics was statistically significant. There is a significant decrease (p<0.05) in the level of testosterone, as compared to control. There is significant increase (p <0.05) in the level of LH as compared to control. This shows a primary hypogonadism and agrees with report that there is sufficient evidence to show that

patients with diabetes have a greater tendency to acquire several complications, including hypogonadism (Agarwal *et al.*, 2017). Male hypogonadism is defined as a clinical condition in which the men exhibit the symptoms/signs and biochemical evidence of testosterone deficiency. Furthermore, many studies have shown that the testosterone levels reported in men with diabetes was much lower than those of the apparently healthy individuals (Kapoor, 2007). There mean difference of age, BMI, Testosterone and Luteinizing hormone (LH) between type 1 and 2 diabetes were not significant ($p > 0.05$). There was an increase in testosterone level in type 2 than in type 1 diabetes but not significant, this is contrary to research that documented that one-third of the men with T2DM possess low testosterone as compared to T1DM and causes a considerable public health burden with respect to deficient sexual function and potential infertility (Beatrice *et al.*, 2016). A non-significant decrease in LH was also seen in type 2 as compared to type 1 diabetes agrees with a study that reported LH secretion was impaired in Type 1 than Type 2 diabetic men in a study conducted by Lopez-Alvarenga *et al.* (2002). There was no-significant decrease in BMI of type 2 as compared to type 1 diabetes and is inversely related to testosterone in both type. This is consistent with a report that indicated there is an inverse relationship between BMI and testosterone concentrations in both type 1 and type 2 diabetes (Tomar *et al.*, 2006). We observed a non-significant negative correlation between age with testosterone and LH. There was also a negative correlation between the duration of diabetes with testosterone and LH. We observed that there was a non-significant positive correlation of diabetes with low level of testosterone. There was a significant negative correlation between diabetes with increased level of LH. There was a non-significant negative correlation between BMI and testosterone. This finding is consistent with a previous report by Wang *et al.* (2011) who observed that an increased in BMI is primarily due to overweight and obesity and is directly associated with low total testosterone level. There was a significant positive correlation between BMI and LH. This finding is contrary with a previous report which indicated an inverse relationship exist between LH and BMI (Birkebaek *et al.*, 2010). No significant differences were found between type 1 and type 2 diabetic men in testosterone or LH levels. The negative correlation of testosterone with age and

diabetes duration, though not statistically significant, is in line with evidence that aging and chronic hyperglycaemia contribute to declining gonadal function (Corona *et al.*, 2020; Hackett *et al.*, 2022).

Conclusion

This study reveals a high prevalence (56.9%) of hypogonadism among diabetic men in this study, with testosterone deficiency and elevated LH indicating primary testicular dysfunction. Routine hormonal evaluation in male diabetics should be integrated into clinical care to improve reproductive and metabolic health outcomes.

Recommendation: Given the high prevalence observed, routine screening for hypogonadism in diabetic men should be considered in Nigeria. Early identification and management may improve sexual health, quality of life, and metabolic outcomes.

Limitations: This study was cross-sectional and limited to a single health center, which may restrict generalizability. We also did not assess follicle-stimulating hormone (FSH) or estradiol, which could provide further insights into the hypothalamic-pituitary-gonadal axis.

Conflict of Interest

We wish to declare that there is no conflict of interest or opinion on the preparation and submission of this manuscript.

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Citation: Muhammad Salihu Baba, Bunza Umar Faruq, Ogunkoya Oluseun Funke, Muhammed Isiaka, Ibrahim Umar Alhaji, Sa'idu Hadiya Muhammad. Evaluation of Male Reproductive Hormone Profiles Among Diabetes Patients, With a Focus on Testosterone and Luteinizing Hormone. *Sokoto Journal of Medical Laboratory Science*; **10(3)**: 364–369. <https://dx.doi.org/10.4314/sokjmls.v10i3.35>

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