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FREQUENCY AND CORRELATES OF HYPOGONADISM AMONG A COHORT OF NIGERIAN MEN WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT

Background: **Low serum testosterone is reported to be common in men with type 2 diabetes mellitus (type 2 DM). However, the Endocrine society has recommended that the diagnosis of male hypogonadism be based on the presence of symptoms of testosterone deficiency in combination with low serum testosterone.**

Objective: **The aim of this study was to determine the frequency and correlates of hypogonadism in a cohort of Nigerian men with type 2 DM**

Methods: **We studied 100 men with type 2 DM and 100 age matched non-diabetic men in a cross-sectional study. The Androgen Deficiency in the Aging Male (ADAM) questionnaire was administered to all study subjects. Anthropometric parameters, total testosterone, sex hormone binding globulin (SHBG), serum Gonadotrophins, glycated haemoglobin and lipid profile were measured. Serum free testosterone was calculated using Vermeulen's equation. Hypogonadism was considered present in men with symptoms of hypogonadism in combination with a low calculated free testosterone (cFT) < 0.255nmol/l. Data was analysed using SPSS 20 package with level of significance set at p value ≤ 0.05.**

Results: **41% of men with type 2 DM had hypogonadism, compared to 10% of non-diabetic men. Secondary hypogonadism was found in 22% of men with type 2 DM, while primary hypogonadism was present in 19%. Amongst hypogonadal men with type 2 DM, secondary hypogonadism was the underlying cause in 53.7%. Truncal obesity was identified as a significant independent predictor of hypogonadism.**

Conclusion: **This study demonstrated that hypogonadism was a common condition among men with type 2 DM. Truncal obesity emerged as a significant independent predictor of hypogonadism.**

Keywords: Frequency, Hypogonadism, Type 2 DM, Nigerian, Testosterone

INTRODUCTION

Low serum testosterone level is reported to be common amongst men with type 2 diabetes mellitus (type 2 DM).[1-3] Male hypogonadism is however defined by the Endocrine society as the presence of symptoms of testosterone deficiency in combination with low serum testosterone.[4] The Endocrine society guidelines also recommend that testosterone replacement therapy be given only to men who fulfil this criterion.[4] Total testosterone (TT) concentration is influenced by alterations in SHBG concentrations[5] and type 2 DM is associated with altered SHBG concentration.[4,5] It is therefore recommended that free or bioavailable testosterone be measured in patients with diabetes.[4]

Only few studies amongst Nigerian men with type 2 DM have utilized both symptoms of hypogonadism along with the presence of low serum testosterone to establish the diagnosis of hypogonadism. The aim of this study was to determine the frequency of hypogonadism among Nigerian men with type 2 DM based on the presence of symptoms of testosterone deficiency in combination with low serum free testosterone.

MATERIALS AND METHODS:

Study center and study subjects

The study was conducted at the Diabetes outpatient clinic of the University College Hospital (UCH), Ibadan, a tertiary health care institution located in the Southwest of Nigeria. It was a cross-sectional study in which 100 men with type 2 DM who fulfilled the inclusion and exclusion criteria were consecutively

recruited. 100 apparently healthy age- matched non-diabetic controls were also recruited.

Inclusion criteria for Study subjects

1. Adult males with ages ≥30 years and diagnosed to have type 2 DM according to the American Diabetes Association (ADA) criteria.
2. Patients who gave consent to participate in the study

Inclusion criteria for controls

1. Adult males with ages ≥30 years of age.
2. Persons with no history of symptoms suggestive of diabetes mellitus, and in whom fasting plasma glucose concentration (FPG) and glycated haemoglobin (HbA1c) were normal. (FPG< 100 mg/dl) and HbA1c of < 5.7% respectively.
3. Persons who gave consent to participate in the study.

Exclusion criteria

1. Persons who refused to participate in the study.
2. Persons with history of benign prostate enlargement or prostate cancer or treatment for prostate cancer.
3. Persons previously diagnosed with primary or secondary hypogonadism.
4. Persons with a previous history of penile or prostate surgery.
5. Persons with known or suspected chronic illnesses including cardiovascular disease, chronic liver disease, chronic renal failure, and chronic obstructive pulmonary disease,
6. Persons on hormonal replacement therapy with androgens or glucocorticoids.
7. Persons with any evidence of acute illness, severe infection or inflammatory diseases
8. Persons on testosterone replacement therapy

All persons recruited into the study were requested to present to the outpatient clinic by 8 a.m. after an overnight fast of 8-12 hours on designated days. Demographic data were obtained for all persons recruited into the study using a questionnaire. The presence or absence of symptoms of hypogonadism was elicited using a validated Androgen Deficiency in Aging Male (ADAM) Questionnaire which consists of 10 questions.[6] All participants recruited into the study underwent a physical examination as well as measurement of anthropometric indices (Weight, Height, Waist circumference, Hip circumference).

Laboratory testing

Blood samples (total of 15mls) were drawn between 8.00 and 9.00am from the participants after they had been seated for 10 minutes. Samples were obtained for assay of serum total testosterone (TT), SHBG and gonadotropins (FSH& LH) assays, fasting plasma glucose, glycated haemoglobin (HbA1c) and serum lipid profile. All samples, except that for HbA1c estimation, were centrifuged at 15,000rpm for 10 min to obtain the and serum and plasma and stored at –20°C until analysis. Total testosterone was measured by enzyme linked immune-sorbent assay. (ELISA). Intra-assay and inter-assay coefficients of variations (CV) were 5.3% and 3.1% respectively. SHBG was also measured using a direct microplate ELISA assay kit. The intra-assay and inter-assay coefficients of variations for the SHBG assay were 5.03% and 5.32% respectively. Calculated free testosterone (cFT) was calculated from TT and SHBG using the Vermeulen's equation.[4,7-9] cFT has been shown to correlate very well with free testosterone measured by equilibrium dialysis.[8] A cFT level of less than 0.255 nmol/L was considered to be low.[9] Serum FSH & LH were measured using ELISA assays. Glycated haemoglobin (HbA1c) was analyzed using high performance liquid chromatography method (Bio-Rad 220-0212, Hercules, California, USA). Fasting plasma glucose was determined by glucose oxidase enzymatic method. Hypogonadism was defined as the presence of symptoms of testosterone insufficiency along with low calculated free testosterone(cFT) level < 0.255nmol/l.

Data management and statistical analysis

Data analysis was carried out using the Statistical Package for Social Sciences software, (SPSS) version 20. The frequency of hypogonadism in subjects with type 2 DM and non-diabetic controls was determined. Clinical and laboratory parameters of subjects with type 2 DM and controls were compared. A comparative analysis of clinical and laboratory parameters between type 2 DM subjects with hypogonadism and those who were eugonadal (no hypogonadism) was also performed. Quantitative variables were presented as mean ± standard deviation, while categorical variables were presented as frequencies (proportions). Data was presented with text and frequency tables as appropriate. The Shapiro-Wilk's test was used to test for normality of continuous variables. The differences in continuous variables between groups were compared with T-test where normally distributed. Non-parametric analysis was done for data that were not normally distributed. Categorical variables were compared with Chi-square, and Fischer's exact tests where necessary. The strength of associations was determined using correlation analysis. Pearson's correlation analysis was used for normally distributed data, while Spearman's correlation analysis was used for data with skewed distribution. A logistic regression model was explored with hypogonadism as the dependent variable while age, truncal obesity and HbA1c were the independent

variables. Calculated P-values d" 0.05 were considered statistically significant.

RESULTS

Socio-demographic, anthropometric and clinical characteristics

The socio-demographic and anthropometric characteristics of the men with type 2 DM and non-diabetic controls are shown in Table 1. Men with type 2 DM had a significantly lower frequency of alcohol and cigarette smoking. Otherwise, the two groups were similar.

Table 2 presents the clinical characteristics of men with type 2 DM and non-diabetic controls. Key findings noted were that men with type 2 DM had a significantly higher frequency of family history of diabetes and systemic hypertension compared to non-diabetic controls: $p < 0.001$.

Biochemical and Hormonal parameters of men with type 2 DM compared with non-diabetic controls

Biochemical and hormonal parameters of the men with type 2 DM are presented in Table 3. Mean FBG,

Table 1: Socio-demographic and Anthropometric characteristics of men with type 2 DM and the non-diabetic controls

Characteristic	Cases, N = 100	Controls, N = 100	p-value
Age (years)	56 (6)	56 (7)	0.732
Age range (years)			0.987
40-49	17 (17%)	17 (17%)	
50-59	52 (52%)	53 (53%)	
60-69	31 (31%)	30 (30%)	
Smoking history			0.003
Nonsmoker, never smoked	80 (80%)	90 (90%)	
Ex-smoker, stopped for at least 1 year after smoking regularly	18 (18%)	4 (4.0%)	
Smokers	2 (2.0%)	6(6.0%)	
Alcohol Ingestion			<0.001
Does not drink alcohol	64 (64%)	75 (75%)	
Drank alcohol regularly in the past, but has stopped for at least 1 year	23 (23%)	3 (3.0%)	
Dinks alcohol	13 (13%)	22 (22%)	
WT (kg)	74 (13)	75 (15)	0.803
HT (m)	1.68 (0.10)	1.70 (0.09)	0.051
BMI (kg/m^2)	26.1 (4.1)	25.9 (5.1)	0.534
BMI category			~~0.035~~
Normal	35 (35%)	37 (37%)	
Obese	20 (20%)	11 (11%)	
Overweight	42 (42%)	38 (38%)	
Severely Obese	1 (1.0%)	8 (8.0%)	
Underweight	2 (2.0%)	6 (6.0%)	
WC (cm)	87 (18)	86 (14)	0.131
HC (cm)	90 (15)	91 (13)	0.690
Abdominal obesity	36 (36%)	29 (29%)	0.291

WT - weight; HT - height; BMI - body mass index; WC – waist circumference; HC – hip circumference

Table 2: Clinical Characteristics of men with type 2 DM compared with non-diabetic controls

Characteristic	Cases, N = 100	Controls, N = 100	p-value
Diabetes duration (months)	114 (83)	NA (NA)	
Family history of diabetes	26 (26%)	12 (12%)	0.012
Diabetes duration			>0.999
< 10 years	55 (55%)	0 (NA%)	
≥ 10 years	45 (45%)	0 (NA%)	
Have you been diagnosed to have hypertension?	64 (64%)	17 (17%)	<0.001
SBP (mmHg)	135 (18)	124 (21)	<0.001
DBP (mmHg)	79 (10)	78 (11)	0.393

SBP – systolic blood pressure; DBP -diastolic blood pressure

Table 3: Biochemical and hormonal parameters of men with type 2 DM compared with non-diabetic controls

Characteristic	Cases, N = 100	Controls, N = 100	p-value
FPG (mg/dl)	114.2 (59.52)	73.3 (13.44)	<0.001
HbA1c (%)	6.85 (1.63)	4.89 (0.35)	<0.001
Total Cholesterol (mg/dl)	130.8 (53.82)	107.1 (34.95)	0.002
HDL-C (mg/dl)	43.0 (7.19)	47.0 (9.85)	0.001
LDL-C (mg/dl)	67.0 (55.71)	43.1 (36.21)	0.002
Triglyceride (mg/dl)	103.8 (30.17)	84.9 (17.73)	<0.001
TT (nmol/L)	11.4 (5.16)	15.6 (5.11)	<0.001
SHBG (nmol/L)	47.9 (54.74)	51.2 (30.25)	<0.001
LH (mIU/ml)	4.12 (3.13)	5.64 (2.68)	<0.001
FSH (mIU/ml)	15.3 (8.17)	12.7 (8.20)	0.006
cFT (nmol/L)	0.22 (0.14)	0.28 (0.11)	<0.001
Low Testosterone	68 (68%)	39 (39%)	<0.001

FPG – fasting plasma glucose; HbA1c – glycated hemoglobin; HDL-C – high density lipoprotein-cholesterol; LDL-C -low density lipoprotein cholesterol; TT- total testosterone; SHBG – sex hormone binding globulin; LH – luteinizing hormone; FSH – follicular stimulating hormone; cFT– calculated free testosterone

Table 4: Demographic and clinical characteristics of hypogonadal and eugonadal men with Type 2 DM

Characteristic	Cases		p-value
	Eugonadal N = 59	Hypogonadal N = 41	
Age(years)	56 (7)	56 (6)	0.565
Age range (years)			0.233
40-49	10 (17%)	7 (17%)	
50-59	27 (46%)	25 (61%)	
60-69	22 (37%)	9 (22%)	
Smoking history			0.654
Nonsmoker, never smoked	48 (81%)	32 (78%)	
Ex-smoker, stopped for at least 1 year after smoking regularly	10 (17%)	8 (20%)	
Smokes cigarettes	1 (1.7%)	1 (2.4%)	
Alcohol Ingestion			0.289
Does not drink alcohol	40 (68%)	24 (59%)	
Drank alcohol regularly in the past, but has stopped for at least 1 year	14 (24%)	9 (22%)	
Dinks alcohol	5 (8.5%)	8 (19.5%)	
Diabetes duration (months)	118 (82)	108 (87)	0.446
Family history of diabetes	10 (17%)	16 (39%)	0.013
Diabetes duration			0.854
< 10 years	32 (54%)	23 (56%)	
≥ 10 years	27 (46%)	18 (44%)	
History of hypertension	36 (61%)	28 (68%)	0.456
SBP (mmHg)	134 (15)	137 (22)	0.688
DBP (mmHg)	78 (9)	80 (11)	0.247
WT(Kg)	72 (12)	76 (13)	0.162
HT (m)	1.66 (0.10)	1.71 (0.08)	0.020
BMI (Kg/m^2)	26.2 (4.0)	26.1 (4.4)	0.771
BMI category			0.639
Normal	20 (34%)	15 (37%)	
Obese	13 (22%)	7 (17%)	
Overweight	24 (41%)	18 (44%)	
Severely Obese	0 (0%)	1 (2.4%)	
Underweight	2 (3.4%)	0 (0%)	
WC (cm)	82 (20)	93 (13)	0.002
HC (cm)	87 (15)	94 (13)	0.008
Abdominal obesity	14 (24%)	22 (54%)	0.002

WT - weight; HT - height; BMI - body mass index; WC – waist circumference; HC – hip circumference SBP – systolic blood pressure; DBP -diastolic blood pressure

HbA1c, total cholesterol, LDL-C and triglycerides were all significantly higher in men with type 2 DM when compared with the non-diabetic controls. In contrast, mean HDL-C and SHBG were significantly lower in men with type 2 DM.

Furthermore, men with type 2 DM had a significantly lower total testosterone and cFT, when compared with the non-diabetic controls (p = < 0.001). Notably, 68% of men with type 2 DM had low calculated serum free testosterone, which was significantly higher than the 39% observed in non-diabetic controls; p < 0.001.

Frequency and Pattern of hypogonadism in men with type 2 DM

A significant difference was observed in the frequency of hypogonadism between men with type 2 DM and non-diabetic controls. Specifically, 41.0% of men with type 2 DM had hypogonadism, compared to 10.0% of non-diabetic controls; p < 0.001. Among the men with type 2 DM, 22% had secondary hypogonadism, 19% had primary hypogonadism, while the remaining 59% were eugonadal.

In the subgroup of men with type 2 DM and hypogonadism (n = 41), 53.7% of them had secondary hypogonadism, while 46.3% had primary hypogonadism.

In contrast, among non-diabetic controls, 5% had secondary hypogonadism, 5% had primary hypogonadism, while the remaining 90% were eugonadal

Demographic and clinical characteristics of hypogonadal and eugonadal men with Type 2 DM

On comparison of demographic characteristics of hypogonadal and eugonadal men with type 2 DM as shown in Table 4, there was no signification difference between these 2 groups.

39% of men with type 2 DM who were hypogonadal had a family history of diabetes and this was significantly higher that observed in eugonadal men (39% versus 17%); p =0.013.

However, notable significant differences were observed on comparison of their clinical characteristics (Table 4). Mean waist circumference was significantly higher in hypogonadal men with type 2 DM when compared with eugonadal men; p< 0.05. Truncal obesity was also more prevalent in hypogonadal men (54%) compared to eugonadal men (24.0%); p < 0.005.

Comparison of biochemical indices in type 2 DM patients with and without hypogonadism

Table 5 presents the biochemical indices of men with type 2 DM and hypogonadism, compared to eugonadal men. The key findings were: Significantly lower mean total testosterone and calculated free testosterone (cFT) in hypogonadal men compared to eugonadal men; p < 0.001. Long-term (HbA1c) and short-term (FPG) glycaemic control was similar in both groups.

No significant differences were observed in serum gonadotrophins and lipid profile parameters between the hypogonadal and eugonadal men with type 2 DM.

Table 5: Biochemical characteristics of hypogonadal and eugonadal men with type 2 DM

Characteristic	Eugonadal N = 59	Hypogonadal N = 41	p-value
TT (nmol/L)	13.0 (5.50)	9.1 (3.54)	<0.001
cFT (nmol/L)	0.28 (0.15)	0.15 (0.07)	<0.001
LH (mIU/ml)	3.77 (2.67)	4.62 (3.66)	0.332
FSH (mIU/ml)	15.4 (8.42)	15.2 (7.89)	0.795
FPG (mg/dl	111.0 (57.95)	118.7 (62.15)	0.217
HbA1c (%)	6.98 (1.78)	6.67 (1.38)	0.436
HbA1c			0.958
Good	40 (68%)	28 (68%)	
Poor	19 (32%)	13 (32%)	
Total Cholesterol (mg/dl)	134.4 (55.75)	125.5 (51.14)	0.330
HDL-C (mg/dl)	42.9 (7.37)	43.2 (7.02)	0.757
LDL-C (mg/dl)	69.8 (56.87)	62.9 (54.42)	0.385
Triglyceride (mg/dl)	108.6 (34.39)	96.9 (21.32)	0.184

FPG – fasting plasma glucose; HbA1c – glycated hemoglobin; HDL-C – high density lipoprotein-cholesterol; LDL-C -low density lipoprotein cholesterol; TT- total testosterone; SHBG – sex hormone binding globulin; LH – luteinizing hormone; FSH – follicular stimulating hormone; cFT– calculated free testosterone

Predictors of hypogonadism among men with Type 2 DM

Multivariate logistic regression analysis revealed two significant independent predictors of hypogonadism: Truncal obesity (waist circumference ≥ 94cm): Odds Ratio (OR) = 1.04; Confidence Interval (CI) = 1.01-1.04; p = 0.017 and family history of diabetes: OR = 0.35; CI = 0.12-0.98; p = 0.048.

These findings indicate that truncal obesity and a family history of diabetes are independently associated with an increased risk of hypogonadism.

DISCUSSION

Although low serum testosterone is reported to be common amongst men with Type 2 diabetes,[1,2,10-12] the Endocrine Society recommends that the diagnosis of hypogonadism be made based on the presence of symptoms of testosterone deficiency alongside low serum testosterone.

This study has demonstrated that the frequency of hypogonadism amongst a cohort on Nigerian men with type 2 DM (defined by the presence of symptoms of hypogonadism as well as measurement of calculated free testosterone) is high. 41% of men with type 2 DM in this study had hypogonadism and this was significantly higher than of age matched non-diabetic controls (22%). In our study, 22% of the type 2 DM men had secondary hypogonadism (defined as men with low testosterone levels and normal or low gonadotrophins), while 19% had primary hypogonadism. Of the 41 type 2 DM men with hypogonadism, 53.7% had secondary hypogonadism, while 46.3% had primary hypogonadism. Our study also showed that truncal obesity was a significant predictor of hypogonadism.

A study of men with type 2 DM by Kapoor *et al.*[13] in which hypogonadism was also defined as the combination of symptoms of hypogonadism in combination with low free testosterone level reported that 42% of men with type 2 DM had hypogonadism and this is similar to the frequency of hypogonadism in our study. 26% of the hypogonadal men in the study by Kapoor *et al.* had primary hypogonadism, while 74% had secondary hypogonadism.

Few studies have been conducted to determine the frequency of hypogonadism amongst Nigerian men with type 2 DM with frequencies ranging from 29.5% to 80.4%.[14-17] It is however noted that the studies used varying methodologies. The study by Ugwu *et al.*[15] was the only one that made combination of both symptoms and low serum testosterone mandatory for the diagnosis of hypogonadism. Ogbera *et al.*[14] and Musa[17] *et al.* defined hypogonadism on the basis of a low serum total testosterone of 8-12 nmol/L with symptoms of hypogonadism or levels of less than 8 nmol/L with or without symptoms of hypogonadism, while the study by Onung *et al.* defined hypogonadism as serum-free testosterone level <25 pg/ml with or without the presence of symptoms of hypogonadism.[16]

Total testosterone (TT) concentrations are influenced by alterations in sex hormone binding globulin (SHBG) concentrations. As type 2 DM is associated with altered SHBG concentration, it is recommended that free or bioavailable testosterone be measured in patients with diabetes.[4] The studies by Ogbera *et al.* and Ugwu *et al.* measured total testosterone, while the study by Onung *et al.* measured free testosterone using enzyme linked immunosorbent assay (ELISA). Our study utilized calculated free testosterone (cFT) determined from TT and SHBG using the Vermeulen's equation, which has been shown to correlate well with free testosterone measured by equilibrium dialysis.[7,8]

Secondary hypogonadism was reported by Ugwu et al to be the most common cause of hypogonadism in men with type 2 DM[15] with a frequency of 76.3%. This was much higher than the 53.7% observed in our study. Age above 60 years and truncal obesity were significant predictors of hypogonadism in the study by Ugwu *et al.*[15] In contrast to the findings of Ugwu *et al.*, age was not a significant predictor of hypogonadism in our study. Results from our study also showed that though mean BMI was similar in hypogonadal and eugonadal men with type 2 DM, mean waist circumference was significantly higher in hypogonadal men when compared with eugonadal men. The proportion of men with truncal obesity was also significantly higher in hypogonadal men with type 2 DM when compared with eugonadal men with type 2 DM. On multiple regression analysis, truncal obesity was a significant predictor of hypogonadism amongst men with type 2 DM, just as earlier reported by Ugwu *et al.*

Obesity has been observed to have a negative correlation with low serum testosterone and hypogonadism in men with type 2 DM.[12,13,18-19] It was hypothesised that an increase in plasma oestradiol resulting from increased activity of aromatase produced by the adipocytes in persons with obesity results in increased conversion of testosterone to oestradiol, and consequently inhibition of the hypothalamic secretion of gonadotropin-releasing hormone (GnRH).[20,21] On the contrary, a study of men with type 2 DM found oestradiol concentrations in patients with subnormal free testosterone

concentrations to be significantly lower than in those with normal free testosterone concentrations,[22] making it plausible that factors other than increased levels of oestradiol are responsible for the secondary hypogonadism reported in men with type 2 DM and obesity.

Secondary hypogonadism in men with type 2 DM has also been proposed to be a manifestation of insulin resistance at the neuronal level, resulting in subnormal secretion of gonadotropin-releasing hormone from the hypothalamus and consequently diminished secretion of LH and FSH from the anterior pituitary and consequently decreased testosterone levels.[23-25] Type 2 DM is also considered to be a chronic systemic inflammatory state, with increased levels of inflammatory markers, which suppress gonadotrophin release and inhibit testosterone biosynthesis in the Leydig cells leading to secondary hypogonadism.[23-25]

Approximately 46% (19 out of 41) of the hypogonadal type 2 DM men in our study had primary hypogonadism. Results from a study by Pitteloud et al demonstrated that low serum testosterone was associated with insulin resistance, (a major pathophysiologic abnormality in type 2 DM) and an alteration in Leydig cell function, though the molecular mechanism was said to be unclear.[26] In another study utilizing rat models of type 2 diabetes, researchers demonstrated decreased proliferation rate, increased apoptotic rate, and decreased secretion of testosterone in Leydig cells of the testes of diabetic rats.[27] These mechanisms have been proposed as possible explanations for primary hypogonadism seen in some men with type 2 DM.

Testosterone replacement therapy (TRT) in men is reported to be effective and safe in hypogonadal men with beneficial effects on sexual function and improved well-being/quality of life.[4,28] Other reported benefits of TRT in hypogonadal men include improvement in body composition, bone mineral density, general well-being, quality of life and amelioration of anemia. Results of randomized controlled trials and meta-analysis have demonstrated that TRT results in significant reductions in waist circumference, visceral adiposity, muscle strength as well as metabolic benefits, namely improvements in HbA1c, insulin sensitivity and lipid profile.[29-33] The institution of lifestyle related measures to achieve weight reduction in the overweight/obese hypogonadal men with type 2 DM would also be beneficial.

CONCLUSION

This study demonstrated that hypogonadism was common among a cohort of men with type 2 DM in South-West Nigeria. Secondary hypogonadism was the underlying cause in slightly more than half of the hypogonadal men. Truncal obesity emerged as a significant independent predictor of hypogonadism. We recommend that men with type 2 DM be routinely screened for symptoms of hypogonadism and those with symptoms should have measurement of serum testosterone, preferably free testosterone.

Statements and Declarations
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Data Availability Statement: The authors declare that all data supporting the findings of this study are available and raw data can be obtained from the corresponding author upon request.

Authors Contributions: JOA, AOS and AE designed the research and conducted the study; AOS supervised the data collection. OOS performed the laboratory analysis. AAA did the data analysis. JOA, AOS and AAA interpreted the data~ JOA and AOS wrote the manuscript for publication. All the authors reviewed the draft of the manuscript. All authors read and approved the final manuscript.

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