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Hypergonadotropic hypogonadism in Nigerian men with type 2 diabetes mellitus

ABSTRACT

Background. Studies have reported a higher prevalence of hypogonadism in men with type 2 diabetes mellitus (T2DM) than non-diabetic men. The pattern of hypogonadism in men with T2DM using gonadotropin-releasing hormone (GnRH) stimulation test in Sub-Saharan Africa is unknown.

Objective. This study was conducted to determine the prevalence and pattern of hypogonadism in Nigerian men with T2DM.

Methods. A cross-sectional study involving 358 men with T2DM and 179 non-diabetic men as controls. Androgen Deficiency in the Ageing Male (ADAM) questionnaire was administered. Luteinizing hormone (LH) and follicle-stimulating hormone (FSH) both at 0 hours and 4 hours after subcutaneous buserelin injection, fasting total testosterone (TT), fasting plasma glucose and glycated haemoglobin were measured. Ninety-nine men with T2DM selected by randomization using a computer underwent GnRH stimulation test, with subcutaneous injection of 100 micrograms of buserelin.

Results. The mean TT of T2DM men was significantly lower compared to the controls (8.79 ± 3.35 nmol/L *vs* 15.41 ± 3.79 nmol/L, p < 0.001). The prevalence of hypogonadism in T2DM men was 80.4%, comprising 38.5% of severe hypogonadism and 41.9% mild hypogonadism. The mean LH and FSH levels were significantly higher in T2DM men than the controls (9.62 ± 6.82 IU/L *vs* 8.24 ± 5.91 IU/L, p = 0.022 and 8.50 ± 8.17 IU/L *vs* 5.17 ± 3.89 IU/L, p < 0.001 respectively). There was a statistically significant exaggerated response in mean (±SD) LH and FSH levels at 4 hours after buserelin injection compared to the 0-hour levels (58.58 ± 40.72 IU/L *vs* 8.38 ± 6.10 IU/L, p < 0.001 and 23.03 ± 18.02 IU/L *vs* 8.41 ± 7.45 IU/L, p < 0.001 respectively) in men with T2DM who had GnRH stimulation tests.

Conclusion. This study shows that the prevalence of hypogonadism in men with T2DM is significantly higher than in non-diabetic men with mild hypogonadism accounting for most cases. Hypergonadotropic hypogonadism occurs more frequently in men with T2DM in Nigeria. (Clin Diabetol 2021; 10, 1: 129–137)

Key words: hypergonadotropic hypogonadism, hypogonadism, type 2 diabetes mellitus, GnRH stimulation, total testosterone

Introduction

Diabetes mellitus is a major non-communicable disease encountered worldwide with a more significant burden in developing countries. International Diabetes Federation reported that 80% of people affected by diabetes mellitus (DM) globally are from low and middle-income countries [1]. Sub-Saharan Africa and other African countries are experiencing a rise in the prevalence of diabetes due to increasing life expectancy of the population, urbanization and adoption of the western lifestyle [2, 3]. Several cross-sectional studies have shown an increasing trend in DM prevalence in Nigeria [4–6].

Hypogonadism is a clinical syndrome of symptoms, with or without signs, in conjunction with biochemical

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evidence of testosterone deficiency [7, 8]. It is associated with several metabolic consequences, including T2DM, insulin resistance, metabolic syndrome, osteoporosis and carotid atherosclerosis [9–12].

Several studies have reported hypogonadism to be associated with T2DM [13–17]. In cross-sectional studies conducted in Nigeria, Ogbera *et al.* reported the prevalence of hypogonadism to be 36% among type 2 diabetic men attending Gbagada General Hospital Lagos. Meanwhile, Onung *et al.* and Ugwu *et al.* reported the prevalence of hypogonadism to be 38.9% and 52.5% in men with T2DM in Lagos and Ile-Ife, respectively [15–17]. In South Africa, Kemp et al reported the prevalence of androgen deficiency symptoms to be 94.7% among male diabetics aged 50 years and above [18]. The mechanisms underpinning hypogonadism in T2DM have been postulated to include obesity, adipocytokine mediated inhibition of gonadotropins and leydig cell dysfunction, testicular steroidogenesis inhibition, hyperoestrogenaemia due to exaggerated aromatase activity and decreased sex hormone-binding globulin levels [7, 10, 13, 19].

There is under-diagnosis of hypogonadism in the general population, possibly due to non-specificity of symptoms, shame and embarrassment in talking about sexual matters and inadequate information about the condition among some health care workers [7]. Among these many symptoms of hypogonadism are reduced/loss of libido, reduced quality and frequency of erections, fatigue, decreased physical strength and endurance, change in mood with depression and irritability, hot flushes and sweats, central adiposity, sarcopenia and gynaecomastia [7].

Several studies have reported that hypogonadotropic hypogonadism accounts for the majority of the cases of hypogonadism in T2DM [16, 20, 21]. However, primary hypogonadism (hypergonadotropic hypogonadism) has been reported with higher frequency in people with diabetes compared to non-diabetics [22].

Specific specialized tests are useful in evaluating borderline gonadotropin (LH and FSH) levels in the setting of hypogonadism. They include gonadotropin-releasing hormone (GnRH) stimulation test, clomiphene stimulation test, and human chorionic gonadotropin (hCG) stimulation test [23]. Gonadotropin-releasing hormone stimulation test involves an intravenous injection of 100 μg of GnRH to cause a rise in serum LH levels by 3-6-fold and FSH between 20% and 50% after 30 minutes in a normal pituitary response. Alternatively, pituitary stimulation with GnRH agonists such as buserelin has been suggested to have a better discriminating effect between testicular and pituitary disorders [24]. In GnRH agonists (Buserelin) stimulation test, 100 μg of buserelin is administered subcutaneously. Blood samples are collected at 0- and 4-hours post-injection for analysing LH and FSH levels [24]. Primary testicular failure causes an exaggeration in LH and FSH peak levels while hypothalamic or pituitary disorders show a decreased or normal response [23].

Currently, few studies have reported on the pattern of hypogonadism in men with T2DM in Sub-Saharan Africa using basal gonadotropins (LH and FSH) [16, 22]. There is currently no available data reporting the pattern of hypogonadism in men with type 2 diabetes mellitus using a GnRH stimulation test in Sub-Saharan Africa, particularly of importance in those with borderline gonadotropin levels. Furthermore, our study had the largest sample size among other studies that have earlier reported on hypogonadism or low testosterone in men with T2DM in Sub-Saharan Africa [15–18, 22, 25]. This study assessed the prevalence and pattern of hypogonadism in Nigerian Men with T2DM.

Material and methods

This study was a cross-sectional comparative study involving 358 men with T2DM and 179 healthy non-diabetic men who served as controls. The study was conducted at the Endocrine clinic of Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria. A cohort of 99 men was selected from the pool of 358 type 2 diabetic subjects by randomization using a computer for the GnRH stimulation test. Ethical clearance for the study was obtained from ABUTH ethical committee (ABUTHZ/HREC/NP18/2015), and participants gave written informed consent.

Exclusion criteria were refusal to participate in the study, male patients on previous or present treatment of hypogonadism with testosterone and anti-androgen or related drugs, patients with chronic liver disease, chronic kidney disease, panhypopituitarism and HIV, patients on admission, patients with type 1 diabetes, age less than 21 years and patients with suspected prostate or testicular cancer.

A structured questionnaire was administered to study participants to obtain information on biodata, medical history, smoking history, alcohol history and medication. The Androgen Deficiency in the Ageing Male (ADAM) questionnaire was also administered to obtain information about features of hypogonadism [26].

Fasting samples (10 mL) were collected in the morning between 8:00 AM and 10:00 AM into plain tubes by venipuncture of an antecubital vein. The sera were collected after centrifugation into sample bottles and frozen at -20 °C. These were used for the analysis of total testosterone, LH, FSH, fasting plasma glucose. Additional 4 ml of blood was collected into EDTA bottle for HbA_{1c} assay.

To perform a GnRH stimulation test, GnRH agonist (buserelin) was injected subcutaneously at a dose of 100 micrograms using an insulin syringe. Blood sampling at 0 and 4 hours for LH and FSH, in 99 selected men with T2DM was performed. Buserelin was available as injection suprefact in 1 mg/1 mL (5.5 mL/vial), manufactured by Sanofi-Aventis Deutschland GmbH, Industriepark Hoschst, 65926 Frankfurt am Main, Germany.

Serum total testosterone was measured by an enzyme immunoassay technique using Testosterone AccuBind ELISA kits from Monobind Inc, CA, USA, serum LH and FSH were measured by an enzyme immunoassay technique using LH and FSH AccuBind ELISA kits respectively from Monobind Inc, CA, USA. Glycated haemoglobin was measured using the Clover A1C TM self/test cartridge (South Korea). Hypogonadism was diagnosed using total testosterone levels < 8 nmol/L with or without symptoms or total testosterone levels of 8–12 nmol/L with the presence of symptoms [27].

Data were analyzed using Statistical Package for Social Sciences (SPSS) version 21 after validation to detect and correct errors before entry into SPSS. Descriptive analysis of data was performed for means and standard deviations, frequencies, and percentages. Quantitative variables such as age, FPG, HbA_{1c}, testosterone levels, LH and FSH levels were presented as means and standard deviations. Student's t-test was used to determine the difference in FPG, HbA_{1c}, testosterone levels, LH and FSH levels between type 2 diabetic men and controls. Correlations between hormones and obesity and glycaemia in men with T2DM was assessed using univariate linear regression. P values < 0.05 were considered statistically significant.

Results

Socio-demographic characteristics of the men with type 2 diabetes mellitus and controls

The primary study population comprised of 358 men with T2DM and 179 controls who were recruited following fulfilment of the inclusion criteria. The participants' socio-demographic characteristics are summarized in Table 1. The mean age (SD) of the men with T2DM was 46.34 ± 5.66 years, while that of the controls was 44.09 ± 12.39 years. There was no statistically significant difference between the mean age of men with T2DM and the controls (p = 0.570). Majority of both men with T2DM (98.9%) and controls (79.9%) were married (Table 1).

Clinical characteristics of men with type 2 diabetes mellitus

One hundred and seventy-seven (49.4%) of men with T2DM had diabetes for a period of 0-5years, 91 (25.4%) ones for a period ranging between 6-10 years, while 15.4%, 3.6% and 6.2% of men had diabetes for 11–15, 16–20 and more than 20 years respectively. Among men with T2DM, the majority took a combination of metformin and glimepiride therapy, as shown in Figure 1. The prevalence of hypertension among men with T2DM was 75%, and the prevalence of obesity in type 2 diabetic men using body mass index (BMI) and waist circumference was 14.5% and 43.6% respectively. However, among the controls, 10.1% had abdominal obesity. Among men with T2DM, 39.1% achieved target fasting plasma glucose, 46.9% had poor glycaemic control, and 14% had tight glycaemic control. Meanwhile, 85.8% of men with T2DM did not achieve target glycated haemoglobin.

Table 1. Socio-demographic characteristics of the men with type 2 diabetes mellitus and controls

Characteristics	T2DM men	Controls	P values
Age (mean ± SD)	46.34 ± 5.66	44.09 ± 12.39	**0.570**
Marital status			**< 0.001**
Married	354 (98.9%)	143 (79.9%)	
Single	3 (0.8%)	35 (19.5%)	
Divorced	0 (0%)	1 (0.6%)	
Widowed	1 (0.3%)	0 (0%)	
Total	358 (100%)	179 (100%)	
Occupation			**< 0.001**
Business	106 (29.7%)	11 (6.2%)	
Civil servant	116 (32.4%)	134 (74.8%)	
Farming	63 (17.5%)	22 (12.2%)	
Students	2 (0.6%)	6 (3.5%)	
Unemployed	2 (0.6%)	2 (1.1%)	
Others*	69 (19.2%)	4 (2.2%)	
Total	358 (100%)	179 (100%)	
Highest educational level			**< 0.001**
Primary	65 (18.2%)	34 (19.0%)	
Secondary	53 (14.8%)	98 (54.7%)	
Tertiary	143 (39.9%)	27 (15.1%)	
No formal education	97 (27.1%)	20 (11.2%)	
Total	**358 (100%)**	**179 (100%)**	

* Retirees, clergy

Prevalence of hypogonadism

The prevalence of hypogonadism in men with T2DM was 80.4% while in the controls, the prevalence was 10%. Hypogonadism was defined as serum total testosterone < 8 nmol/L with or without symptoms or serum total testosterone 8-12 nmol/L with the presence of symptoms. Among the hypogonadal type 2 diabetic men, 38.5% had severe hypogonadism (total testosterone levels less than 8 nmol/L) and 41.9% had mild hypogonadism (total testosterone levels between 8–12 nmol/L). The

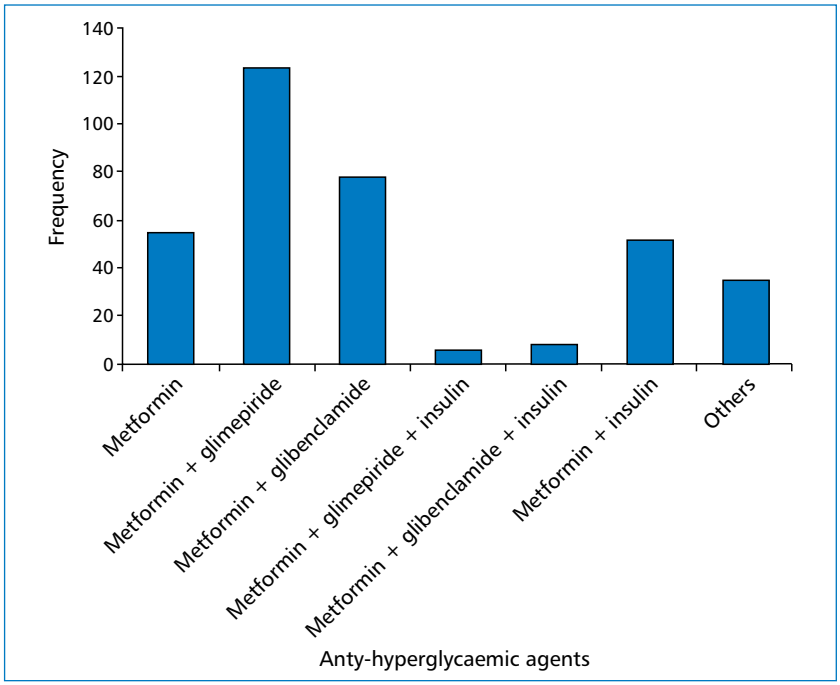

Figure 1. Anti-hyperglycaemic agents used by men with type 2 diabetes mellitus

Table 2. Mean (± SD) clinical and biochemical profile of the men with type 2 diabetes mellitus and controls

	Type 2 diabetic men Mean±SD	Controls Mean±SD	Significance (P-values)
Weight [kg]	72.84 ± 14.13	67.79 ± 12.23	< 0.001
BMI [kg/m^2]	25.26 ± 4.45	24.31 ± 3.79	0.010
WC [cm]	92.40 ± 11.96	79.49 ± 9.84	< 0.001
FPG [mmol/L]	8.30 ± 4.77	4.43 ± 1.79	< 0.001
HbA_{1c} [%]	9.13 ± 2.12	5.07 ± 0.74	< 0.001
Total testosterone [nmol/L]	8.79±3.35	15.41 ± 3.79	< 0.001
LH [IU/L] [0-hours]	9.62 ± 6.82	8.24 ± 5.91	0.022
FSH [IU/L] [0-hours]	8.50 ± 8.17	5.17 ± 3.89	< 0.001

P < 0.05 is statistically significant. BMI — body mass index; FSH — follicle-stimulating hormone; FPG — fasting plasma glucose; HbA_{1c} — glycated haemoglobin; LH — luteinizing hormone; WC — waist circumference

mean (±SD) total testosterone levels of men with T2DM and controls were 8.79 ± 3.35 nmol/L and 15.41 ± 3.79 nmol/L, respectively. The mean total testosterone level in men with T2DM was statistically significantly lower compared to the controls (p < 0.001) as shown in Table 2.

Comparison of clinical features of hypogonadism using ADAM questionnaire in men with type 2 diabetes mellitus and controls

The most commonly documented features of hypogonadism (low testosterone) among men with T2DM were erectile dysfunction, loss of libido, decreased in strength/endurance and lack of energy. Majority of the eugonadal controls had no symptoms of androgen deficiency syndrome. Decreased strength/endurance was the most statistically significant feature of androgen deficiency syndrome among men with T2DM with hypogonadism compared with the eugonadal men (p = 0.033, Table 3).

Gonadotropins of men with type 2 diabetes mellitus

The mean (±SD) luteinizing hormone (LH) levels of the men with T2DM and controls were 9.62 ± 6.82 IU/L

Table 3. Comparison of clinical features of hypogonadism (using ADAM Questionnaire) in men with type 2 diabetes mellitus and controls

	Type 2 diabetic subjects				Control			
	Hypogonadal	Eugonadal	Total	P value	Hypogonadal	Eugonadal	Total	P value
Decrease in libido								
Yes	237 (84.6%)	43 (15.4%)	280	0.178	10 (16.7%)	50 (83.3%)	60	0.564
No	61 (78.2%)	17 (21.8%)	78		16 (13.4%)	103 (86.6%)	119	
Lack of energy								
Yes	210 (83.3%)	42 (16.7%)	252	0.942	3 (6.7%)	42 (93.3%)	45	0.084
No	88 (83%)	18 (17%)	106		23 (17.2%)	111 (82.8%)	134	
Decrease in strength/endurance								
Yes	215 (86%)	35 (14%)	250	0.033	6 (14.3%)	36 (85.7%)	42	0.960
No	83 (76.9%)	25 (23.1%)	108		20 (14.6%)	117 (85.4%)	137	
Loss of height								
Yes	23 (85.2%)	4 (14.8%)	27	0.778	2 (18.2%)	9 (81.8%)	11	0.722
No	275 (83.1%)	56 (16.9%)	331		24 (14.3%)	144 (85.7%)	168	
Decrease enjoyment of life								
Yes	178 (85.2%)	31 (14.8%)	209	0.248	3 (12%)	22 (88%)	25	0.699
No	120 (80.5%)	29 (19.5%)	149		23 (14.9%)	131 (85.1%)	154	
Sad/grumpy								
Yes	46 (80.7%)	11 (19.3%)	57	0.576	5 (21.7%)	18 (78.3%)	23	0.293
No	252 (83.7%)	49 (16.3%)	301		21 (13.5%)	135 (86.5%)	156	
Erection less strong								
Yes	262 (84.2%)	49 (15.8%)	311	0.197	6 (14.6%)	35 (85.5%)	41	0.982
No	36 (76.6%)	11 (23.4%)	47		20 (14.5%)	118 (85.5%)	138	
Deterioration in playing sports								
Yes	126 (87.5%)	18 (12.5%)	144	0.077	3 (11.1%)	24 (88.9%)	27	0.585
No	172 (80.4%)	42 (19.6%)	214		23 (15.1%)	129 (84.9%)	152	
Falling asleep after dinner								
Yes	74 (81.3%)	17 (18.7%)	91	0.570	4 (15.4%)	22 (84.6%)	26	0.983
No	224 (83.9%)	43 (16.1%)	267		22 (14.4%)	131 (85.6%)	153	
Deterioration in work performance								
Yes	152 (85.9%)	25 (14.1%)	177	0.187	0 (0%)	23 (100%)	23	0.028
No	146 (80.5%)	35 (19.3%)	181		26 (16.7%)	130 (83.3%)	156	

and 8.24±5.91 IU/L, respectively. The mean serum LH level was statistically significantly higher in men with T2DM compared to the controls ($p = 0.022$, Table 2). Similarly, the mean (± SD) follicle-stimulating hormone level was 8.50 ± 8.17 IU/L for type 2 diabetic men and 5.17 ± 3.89 IU/L for the controls. The mean FSH level was statistically significantly higher in men with T2DM compared to the controls ($p < 0.001$, Table 2).

Hormonal profile of men with type 2 diabetes mellitus before and after GnRH (Buserelin) stimulation test

Following GnRH stimulation test using subcutaneous buserelin in 99 men with T2DM, the mean (±SD) LH and FSH at baseline (0 hours) were 8.38 ± 6.10 IU/L and 8.41 ± 7.45 IU/L respectively while the mean (±SD) values for LH and FSH at 4 hours post buserelin administration were 58.58 ± 40.72 IU/L and 23.03 ± 18.02 IU/L respectively. The levels of LH and FSH at 4 hours after buserelin injection were higher than the levels of LH and FSH at 0 hours, and these were statistically significant ($p < 0.001$, Table 4). An exaggerated response was found in most of the GnRH stimulated type 2 diabetic men with hypogonadism constituting 65% and 91.2% for LH and FSH, respectively (Table 4). This finding was consistent with hypergonadotropic hypogonadism.

Table 4. The pattern of hypogonadism in men with type 2 diabetes mellitus using GnRH (Buserelin) stimulation test

Mean (± SD) luteinizing hormone and follicle stimulating hormone before and after GnRH stimulation			
	Before stimulation (basal)	After stimulation	P values
LH (IU/L)	8.38 ± 6.10	58.58 ± 40.72	< 0.001
FSH (IU/L)	8.41 ± 7.45	23.03 ± 18.02	< 0.001
Nature of gonadotropins response to buserelin injection among GnRH stimulated type 2 diabetic men with hypogonadism			
	Exaggerated response frequency	Normal response frequency	
LH (IU/L)	52 (65%)	28 (35%)	
FSH (IU/L)	73 (91.2%)	7 (8.8%)	

P < 0.05 is statistically significant. FSH — follicle-stimulating hormone; LH — luteinizing hormone

Table 5. Correlations between hormones and obesity and glycaemia in men with T2DM

	Total testosterone	LH	FSH
Total testosterone		–0.064	–0.137*
LH	–0.064		0.498*
FSH	–0.137*	0.498*	
BMI	–0.059	0.012	–0.023
WC	–0.081	0.074	0.022
FBG	0.017	0.044	0.009
HbA1c	0.001	0.012	–0.035

* Correlation is significant at p < 0.05. BMI — body mass index; FBG — fasting blood glucose; FSH — follicle-stimulating hormone; HbA_{1c} — glycated haemoglobin; LH — luteinizing hormone; WC — waist circumference

Correlations between total testosterone, LH, FSH and obesity and glycaemia in men with T2DM

There was a negative correlation between serum total testosterone and FSH, LH, BMI, and WC, but only FSH reached statistical significance. Furthermore, total testosterone was not significantly correlated with fasting plasma glucose and glycated haemoglobin (Table 5).

Discussion

Several cross-sectional studies have reported a high prevalence of hypogonadism in men with T2DM [13–17]. This study demonstrated that the prevalence of hypogonadism in men with T2DM was 80.4% while in the controls, the prevalence was 10%. The prevalence of hypogonadism in men with T2DM was statistically significantly higher than in the controls. Studies from Nigeria and South Africa, compared to this study, reported a lower prevalence of hypogonadism or low serum total testosterone in men with T2DM [15–17, 25]. In Nigeria, Ogbera *et al.* reported the prevalence of hypogonadism among men with T2DM to be 36% at General Hospital Gbagada, Lagos. In comparison, Onung et al reported a prevalence of 38.9% in Lagos and Ugwu *et al.* reported a prevalence of 52.5% in Ile-Ife [15–17]. Paruk *et al.* reported the prevalence of low serum total testosterone in men with T2DM to be 35.8% [25]. Tan *et al.* reported a prevalence of hypogonadism among elderly diabetics to be 64%; however, the effect of advancing age on testosterone levels could have been a confounding factor [28]. Similarly, some studies have reported the prevalence of hypogonadism to be 30–80% in T2DM [13, 21]. This study demonstrated a similar higher prevalence of hypogonadism among men with T2DM compared to previous studies, and this perhaps may be attributed to the disparity in the diagnostic criteria, laboratory assay methods, central obesity and poor metabolic control. Our study population was from Northern Nigeria where poverty is high compared the Southern Nigeria, from where studies have reported a lower prevalence of hypogonadism [29]. Putatively, low socioeconomic level of the study population may be negatively impacting on metabolic control due to limited health-care access and affordability to medications. Further, a high proportion of men with T2DM had obesity and poor glycaemic control which have been reported to be associated with hypogonadism [21]. In this study, 85.8% of men with T2DM did not achieve the glycated haemoglobin target, which may explain the high frequency of hypogonadism in the men with T2DM. Although in this study, there was no significant correlation between total testosterone and glycated haemoglobin as reported in another study [30], this might have been impacted by the massive number of patients who did not achieve target glycated haemoglobin. Cross-sectional studies have reported a negative correlation between total testosterone and HbA_{1c} [17, 31, 32]. Also, total testosterone inversely correlated with obesity (BMI, WC), although this was not statistically significant. Several studies have reported an association between low testosterone and central obesity [33–36]. Poor glycaemic control is known to induce defective Leydig cells function and alteration

in the hypothalamic-pituitary-testicular axis as a result of high estradiol, cytokines, advanced glycated end products and leptin that are associated with obesity and hyperglycaemia [16, 37]. Majority of the men with T2DM had mild hypogonadism with severe hypogonadism accounting for 38.5%. The prevalence of severe hypogonadism in this study was comparable with the reported incidence by Asare-Anane *et al.* [37]. However, other cross-sectional studies reported a lower prevalence of severe or overt hypogonadism among men with T2DM [15, 17, 21]. Among the controls, the prevalence of hypogonadism was 10%, which was comparable to the reports from Ghanaian, Jordanian and Italian studies [13, 37, 38].

Dissecting the social component, most of the men with T2DM in this study were married, and they accounted for 98.9%. This finding was comparable with the proportion of married type 2 diabetic men in a similar study in Ethiopia [39]. With this finding and considering the high frequency of hypogonadism in this study, it is hypothesized that large numbers of men with T2DM might be at risk of strain marital relationships which could probably culminate in separation and divorce, hence, impacting negatively on diabetes care and creating a vicious cycle. This is supported by a report that hypogonadism can significantly reduce the quality of life with resultant loss of livelihood, thereby leading to the separation of couples and divorce [40].

This study found that the most reported features of low testosterone among men with T2DM with hypogonadism were erectile dysfunction, loss of libido, decreased in strength/endurance, deterioration in work performance and lack of energy. Among these features, decreased in strength/endurance was the most significant symptom of hypogonadism. However, among the non-diabetic men, deterioration in work performance showed most significance indicating that other symptoms may be nonspecific to both eugonadal and hypogonadal type 2 diabetic men. Ogbera *et al.* reported similar findings where erectile dysfunction, reduced libido and lack of energy were the most frequently documented symptoms of low testosterone but it was in contrast with our finding, in which lack of energy and reduced libido showed statistical significance. In this study, 84.2% of hypogonadal type 2 diabetic men reported weak erection; however, a study by Bodie *et al.* reported that 18.7% of men with erectile dysfunction had low testosterone levels [41]. Erectile dysfunction in men with T2DM is modulated by factors such as serum testosterone, arterial blood flow and vasodilation and centrally regulated-mechanism of sexual activity [42, 43].

The findings in this study showed that hypergonadotropic hypogonadism is the more common form of hypogonadism in men with T2DM using basal and GnRH stimulated LH and FSH. Majority of the stimulated type 2 diabetic men had exaggerated response in LH (65%) and FSH (91.2%) following buserelin injection consistent with primary hypogonadism. However, 35% and 8.8% showed a normal response in LH and FSH, respectively to GnRH stimulation, suggesting a lower proportion of patients with T2DM may have hypogonadotropic hypogonadism. A previous study found a normal GnRH stimulation test in type 2 diabetic patients [44]. Asare-Anane *et al.* reported primary hypogonadism as the main type of hypogonadism in Ghanaian type 2 diabetic men using basal gonadotropins in contrast to this study [22]. Many studies which used only basal gonadotropins have shown that hypogonadotropic hypogonadism is the more frequent type hypogonadism in male patients with T2DM; however, this has some limitation, mainly when gonadotropins levels are borderline [30, 45, 46]. These study findings may be explained by the resultant effect of chronic hyperglycaemia on testicular microvasculature, which leads to alteration in Leydig cells integrity via cytokines release, thereby leading to hypogonadism. Also, insulin resistance which is a hallmark of T2DM may prevent an adequate supply of energy required for the various metabolic processes involved in testosterone synthesis and release [22].

Limitation and strengths of the study

The limitation of this study might be due to its cross-sectional nature with consecutive recruitment. The study was hospital-based and might not have given an actual reflection of hypogonadism in men with T2DM. The gold standard test for measuring total testosterone is mass spectrometry which was not done due to lack of availability in Nigeria.

Conclusion

Hypogonadism was more common in men with T2DM compared to non-diabetic men, with mild hypogonadism accounting for most cases. Hypergonadotropic hypogonadism is the more frequent type of hypogonadism in Nigerian men with T2DM both at basal and GnRH stimulated states. The most reported symptoms of low testosterone in type 2 diabetic men with hypogonadism are erectile dysfunction, loss of libido, decreased in strength/endurance, deterioration in work performance and lack of energy but decreased strength/ endurance appears to be most important. Prospective research is recommended to dissect the

causal relationship between T2DM and hypogonadism, both locally and internationally.

Conflict of interest

None declared.

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