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Inhibin B Levels in Relation to Obesity Measures and Lipids in Males with Different Numbers of Metabolic Syndrome Components

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Authors' contributions

This work was carried out in collaboration between all authors who designed the study, wrote the protocol, read and approved the final manuscript. Author DOL wrote the first draft of the manuscript, managed the literature searches and performed the statistical analysis. Authors MACD, SUO and EOA interpreted the data and critically reviewed the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Defective spermatogenesis and metabolic syndrome affect 2-4% and 12.4% of males respectively. Deficient testosterone levels due to increased conversion of testosterone to oestradiol have been demonstrated in males with the metabolic syndrome (MS) with limited pituitary and leptin contribution. Defective spermatogenesis is thus implicated in males with MS but is controversial. Inhibin B is a marker of spermatogenesis. This study aims at evaluating inhibin B levels and their relationship with obesity measures and lipids in males with different number of MS components.

Materials and Methods: This is a preliminary prospective study in which a total of 106 apparently healthy males (30, 30, 30 and 16 males with 0, 1, 2 and ≥3 components of metabolic syndrome (NMSC) respectively) aged 19-64 years were purposely selected. Blood pressure (BP) and obesity measures (including visceral adiposity index (VAI) and body mass index (BMI)) were obtained by standard methods. Fasting plasma glucose (FPG), total cholesterol (TC), triglycerides and high density lipoprotein cholesterol (HDLC) were determined by enzymatic methods while low density lipoprotein cholesterol (LDLC) and the lipid ratios (TG/HDLC, TC/HDLC, LDLC/HDLC) were calculated. Inhibin B was analysed by enzyme linked immunosorbent assay (RayBiotech, Inc. USA). Data analysed using analysis of variance (ANOVA) and multiple regressions were significant at P <.05.

Results: Inhibin B decreased significantly in males with 0 to 2 NMSC (P <.05). However, inhibin levels between males with 0 and ≥3 NMSC were similar. Age and inhibin B levels were also similar among the different classes of BMI (***P***>0.05). Inhibin B related positively with HDLC and TC but negatively with VAI, LDLC and TC/HDLC.

Conclusion: Reproductive function appears protected in Nigerian males with MS. However, improvement in HDLC, LDLC, TC levels, VAI and TC/HDLC may enhance fertility potential especially in males with one or two MS components, probably through dietary modulation and physical activity.

Keywords: Metabolic syndrome; hormones; inhibins; hypogonadism; obesity.

1. INTRODUCTION

Infertility is the inability of a couple to achieve pregnancy after having unprotected sexual intercourse for one year [1]. Male factor infertility affects 20–50% of couples in their reproductive age, either independently or in conjunction with female factor infertility [2,3]. Defective spermatogenesis due to chronic infections, anti-sperm anti-bodies, socio-environmental and genetic factors was reported in 2-4% of infertility cases [4].

The epidemic of overweight and sedentary lifestyles is thought to have increased the prevalence of metabolic syndrome (MS), reported as 12.4% in males [5]. The MS is a complex of interrelated risk factors for the development of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Assuming great prominence in clinical discourse in the past decade, the MS has undergone different diagnostic modifications by various organisations over the years [6,7,8]. In 2009, the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity proposed a Joint Interim Statement (JIS) with a view to harmonizing the various criteria used for the diagnosis of MS [9].

The Joint Interim Statement criteria include any three of the following five risk factors: Elevated waist circumference (≥ 94 cm for males and ≥ 80 cm for females), elevated serum triglycerides (≥1.7 mmol/L or ≥150 mg/dL), reduced serum high density lipoprotein cholesterol (HDLC) (<1.0 mmol/L or <40 mg/dL for males and <1.3 mmol/l or <50 mg/dL for females), elevated blood pressure (systolic blood pressure of ≥130 mmHg and/or diastolic blood pressure of ≥85 mmHg) and elevated fasting blood glucose (FPG) (≥5.6 mmol/l or ≥100 mg/dL).

Sexual dysfunction and hypotestosteronaemia were demonstrated in males with MS and T2DM [10,11]. A large proportion of male infertility cases are associated with systemic defects such as dyslipidaemia, diabetes and obesity, which are components of the MS, with unclear mechanisms [12]. However, hormonal

imbalances have been suggested as possible mechanisms of obesity-related subfertility [13]. The hypofunction of the pituitary was implicated as reduced glucose utilization by the anterior pituitary cells and a decreased response of follicle stimulating hormone (FSH) and luteinizing hormone (LH) to gonadotrophin releasing hormone administration was demonstrated in rats [10]. Leptin is an adipocyte-derived, satiety-regulating hormone that acts within the hypothalamus and other brain sites. Elevated leptin levels might reflect adiposity in individuals with MS and T2DM. It may also be a compensatory mechanism for the maintenance of weight/fat loss and blood pressure [14]. Chou et al. [15] reported that energy imbalance could lead to leptin associated reproductive dysfunction.

Our recent studies showed limited contribution of the pituitary and leptin to hypogonadism in males with MS and T2DM. Rather the observed hypotestosteronaemia was attributed to increased conversion of testosterone to oestradiol by aromatase enzyme found in increased adipose tissue in these men [14]. Oestrogen plays a key role in the development and maintenance of fertility. However, its increased levels are known to inhibit differentiation and proliferation of leydig cells and occupation of testosterone receptor sites, block the ability of serum testosterone to induce healthy hormonal signal, increase the production of sex hormone binding globulin that binds to testosterone and decrease fertility. Thus decreased testosterone oestradiol ratio may disrupt spermatogenesis as testosterone is required for spermatogenesis [16].

FSH, released from the anterior pituitary, was used as a marker of spermatogenesis but is influenced by the hypothalamus, testicular factors and steroid hormones. However, serum inhibin B reflects the functional state of the seminiferous epithelium and has been reported as a more direct serum marker of spermatogenesis produced by sertoli cells during germ cell differentiation and spermatogenesis [17,18,19,20]. Inhibin B is a dimeric gonadal glycoprotein (αβ subunit) secreted by the testes consisting of two disulfide-linked subunits [21]. It is involved in the feedback of the pituitary gonadal axis and negatively correlates with the pulsatile release of FSH [18].

Studies show obesity related deterioration in semen quality [22,23]. Inhibin B strongly and positively correlates with testicular volume and sperm counts [17,19]. Men with impaired spermatogenesis have low to undetectable level of inhibin B in the presence of elevated FSH concentration [24]. As a marker of exocrine testicular function, it offers improved diagnosis and treatment modalities for male infertility [21].

Adequate endocrine environment is necessary for spermatogenesis. Thus the reduction of testosterone in favour of oestrogen demonstrated in males with MS suggests defective spermatogenesis in them. However, adequate spermatogenesis has been reported as Inhibin B was previously shown to be unrelated to testosterone [25]. We therefore evaluated inhibin B levels and their relationship with obesity measures and lipids in men with different number of MS components in Ibadan, South West Nigeria.

2. MATERIALS AND METHODS

2.1 Study Design

A total of 106 apparently healthy male participants aged 19-64 years were purposely selected for this preliminary prospective study after written informed consent from a cohort study of 788 participants on risk assessment of type 2 diabetes mellitus in individuals with MS recruited from Bodija and environs in Ibadan. 30, 30, 30 and 16 participants had 0 (controls), 1, 2 and ≥3 MS components respectively. Although the men were not aware of their metabolic status, they were non-diabetics with no known cardiovascular disease and were not on any treatment for any component of MS. The study was approved by the University of Ibadan/University College Hospital (UI/UCH) Joint Ethical Committee.

2.2 Metabolic Syndrome Components

Identification of the MS components was made using the Joint Interim Statement criteria (JIS, 2009). The criteria include central obesity measured as WC (≥94 cm), raised triglyceride (TG): ≥150 mg/dl (1.7 mmol/L), reduced HDLC: <40 mg/dl (<1.0 mmol/L), raised BP: ≥130/85 mmHg, and raised fasting plasma glucose (FPG) ≥100 mg/dl (>5.6 mmol/L). Individuals with MS had ≥3 MS components.

2.3 Sample Collection

Ten ml of venous blood sample was asceptically obtained by venepuncture from the participants after an overnight fast (10-14 hrs). 4 ml of blood

was dispensed into potassium ethylene diamine tetra acetic acid (K_3EDTA) bottle for the determination of lipid profile (TC, TG and HDLC). Two ml of blood was dispensed into fluoride oxalate bottle for FPG estimation while 4 ml of blood was dispensed into plain serum tubes and kept for 1 – 2 hours to clot to obtain serum used for hormonal indices. All samples were centrifuged at 3000 rpm for five minutes after which serum and plasma were extracted and stored in small aliquots at –20℃ until analyses was carried out.

2.4 Obesity and Blood Pressure Measures

General obesity measures was body mass index (BMI) calculated from body weight and height. Central obesity measures were waist circumference (WC), percentage body fat (PBF), waist to hip ratio (WHR), waist to height ratio (WHtR), lipid accumulation product (LAP), conicity index (CI) and visceral adiposity index (VAI) while subcutaneous obesity measure was hip circumference (HC). Blood Pressure (systolic and diastolic) was also obtained from participants. Waist to height ratio was calculated as waist circumference (cm)/Height (cm). Lipid accumulation product was calculated as WC - 58 × TG (mg/dL). Conicity Index was calculated as WC (0.109×√weight/height) while VAI was calculated as WC/36.58 + (1.89 × BMI) × TG/0.81 × 1.52/HDLC. The other measures were obtained by standard methods described elsewhere [10,26].

2.5 Lipids, Fasting Plasma Glucose and Inhibin B Estimations

Triglycerides (TG), Total cholesterol (TC), HDLC and FPG were estimated by enzymatic methods while low density lipoprotein cholesterol (LDLC) was calculated using Friedwald's formula as described by [26]. Inhibin B was estimated by enzyme linked immunosorbent assay (RayBiotech, Inc. USA).

2.6 Statistical Analysis

Data obtained were analysed statistically using analysis of variance (ANOVA) for comparison of variables. Post Hoc Test was used for multiple comparisons of variables. Multiple regression was used to find relationships and $P < .05$ was considered statistically significant.

3. RESULTS

Table 1 shows frequency of individual components of MS among the study participants. Reduced HDLC was the most frequent (55.7%) while raised TG was the least frequent (0.9%) MS component.

Table 2 shows comparison of age, blood pressure, fasting plasma glucose and inhibin B in males with different number of MS components (NMSC). There were consistently increasing and significant differences in age, BP (SBP and DBP) and fasting plasma glucose levels with increasing (NMSC). Multiple comparisons (Post Hoc test) showed significant differences in age, BP (SBP and DBP) and FPG between 0 and 2, ≥3, 1 and ≥3 NMSC ($P < .001$). The differences in age and FPG between 2 and ≥3 NMSC were also significant ($P < .003$).

However, Inhibin B levels consistently significantly decreased with increasing NMSC (0-2) but increased in the males with ≥3 NMSC ($P < .001$). Multiple comparison (Post Hoc test) of Inhibin B showed significant decreases when MSC group between males with 0 and 1, and 0 and 2 NMSC ($P < .021$).

Table 1. Frequency of individual components of the metabolic syndrome among the study participants

NMSC	n	WC	BP	TG	HDLC	FPG
0	30 (28.3)	0(0)	0(0)	0(0)	0(0)	0(0)
1	30 (28.3)	2(6.7)	7(23.3)	0(0)	21(70)	1(3.3)
2	30 (28.3)	15(50)	15(50)	1(3.3)	24(80)	6(20)
≥3	16 (15.1)	16(100)	13(81.3)	0(0)	14(87.5)	8(50)
Total	106 (100)	33 (31.1)	35 (33.0)	1 (0.9)	59 (55.7)	15 (14.2)

Values are in frequency with percentages in parentheses, WC = waist circumference, BP = blood pressure, TG = high triglycerides, HDLC = high-density lipoprotein cholesterol, FPG = fasting plasma glucose, n = number of participants, NMSC=number of metabolic syndrome components

There were consistently increases in atherogenic factors (TC/HDLC, TG/HDLC and LDLC/HDLC) while HDLC decreased as NMSC increased from 0 to ≥3 (p<.001). Multiple comparison (Post Hoc test) showed significant differences in HDLC, TG/HDLC, TC/HDLC and LDLC/HDLC when 0 was compared with 2 and ≥3 NMSC (p < .001).

Table 3 shows comparison of obesity measures among the different MS components groups. There were consistently increases in the general obesity measures (body weight and BMI), subcutaneous obesity (HC) and central obesity measures (PBF, WC, WHR, WHTR, LAP, CI and VAI) (***P***<.001***)***. Multiple comparisons (Post Hoc test) showed significant increase in height in males with 2 to ≥3 NMSC (***P*** <.025). All measures of general obesity (weight and BMI), subcutaneous (HC) and central obesity (WC, WHR, WHtR, PBF, LAP, CI and VAI) significantly increased in males with 0 compared with 2 and 3, 1 compared with 2 and 3, and 2 compared with ≥3 NMSC (***P*** <.001).

Table 2. Comparison of age, blood pressure and biochemical parameters in fasting plasma in males with different number of metabolic syndrome components

	Number of MS components				Total	F	*P*
	0	**1**	**2**	≥3			
n	30	30	30	16	106		
Age	34.5±7.8	36.8 ±11.6	40.8±8.9	48.0±8.7	39.0±10.3	8.0	<.001*
SBP	112.0±6.1	121.7±26.5	129.3±22.0	139.4±19.5	123.8±21.9	7.5	<.001*
DBP	72.0±4.8	77.8±11.9	79.3±11.7	86.5 ±12.5	77.9±11.3	7.0	<.001*
FPG	75.8±16.5	80.0±9.6	86.6±15.9	101.8±24.0	84.0±18.1	9.9	<.001*
B	468.1±260.9	311.4±284.4	245.5±232.1	391.3±242.8	354.6±270.0	3.7	.014*
TG(mg/dL)	64.2±32.9	63.3 ±24.5	78.4±42.5	80.4 ±21.5	70.4±33.0	1.9	.126
HDLC(mg/dL)	47.9±6.8	37.2 ±13.5	32.9±11.2	34.6 ±13.6	38.6±12.7	10.1	<.001*
TC (mg/dL)	135.4±39.2	124.3±48.1	143.5±36.7	141.9±37.7	135.5±41.2	1.3	.297
LDLC(mg/dL)	74.8±3	6.574.0±40.1	94.8±30.5	91.0 ±39.8	82.7±37.2	2.4	.071
TC/HDLC	2.8±0.8	3.5±1.3	4.7±1.7	5.0±3.5	3.9±2.0	7.9	<.001*
TG/HDLC	1.3±0.7	1.9±1.0	2.4±1.5	2.6±1.0	2.0±1.2	6.8	<.001*
LDLC/HDLC	1.6±0.8	2.1±1.1	3.1±1.3	3.4±3.4	2.4±1.8	6.8	<.001*

*Values are in means ± S.D (standard deviation) and were adjusted for age, n = number of participants, F = F statistics, P = probability, * = significant, MS=metabolic syndrome, SBP = systolic blood pressure, DBP = diastolic blood pressure, FPG = fasting plasma glucose, B=Inhibin B, TG = Triglyceride, TC = total cholesterol, LDLC = low-density lipoprotein cholesterol, HDLC = high-density lipoprotein cholesterol, units for age, SBP, DBP, FPG and B= years, mmHg, mmHg, mg/dl and pg/ml respectively*

Table 3. Comparison of obesity measures in the males with different metabolic syndrome components

	Number of MS components groups				Total	F	*P*
Parameters	**0**	**1**	**2**	≥3			
n	30	30	30	16	106		
			General Obesity				
Height (m)	1.7±0.1	1.7±0.1	1.7±0.1	1.7±0.1	1.7±0.1	1.8	.154
Weight (Kg)	63.4±7.3	64.7±8.2	71.7±11.2	90.4±17.6	70.2±14.0	25.8	<.001*
BMI(Kg/m^2)	21.6±2.3	21.9±2.1	24.9±3.5	30.5±6.0	24.0±4.5	28.5	<.001*
			Subcutaneous Obesity				
HC (cm)	91.0±4.8	92.6±5.8	98.4 ±8.2	106.6±8.5	95.9 ±8.6	22.2	<.001*
			Central Obesity				
WC (cm)	80.5±6.4	81.4±7.9	91.0±10.4	108.6±13.6	88.0 ±13.5	38.0	<.001*
WHR	0.9±0.03	0.9±0.1	0.9±0.1	1.0±0.1	0.9±0.1	33.0	< .001*
WHtR	0.5±0.04	0.5±0.04	0.5±0.1	0.6±0.1	0.5±0.1	36.1	<.001*
PBF (%)	15.9±5.5	16.8±4.5	21.3±5.6	26.4±3.1	19.3±6. 2	19.8	<.001*
LAP	1081.3±853.2	1119.7±804.4	2010.2±1087.6	3511.4± 1381.7	1727.6±1310.9	25.2	<.001*
CI	5.4±0.7	5.5 ±0.8	6.5 ±1.2	8.6 ±1.9	6.2±1.6	35.1	<.001*
VAI	73.6±39.2	102.7±46.0	145.7±84.2	196.2±69.0	120. 7±73.7	16.5	<.001*

*Values are in means ± S.D (standard deviation), N = number of participants, F = F statistics, P = probability, * = significant, p< 0.05= Significant MS = metabolic syndrome, WC = waist circumference, PBF = Percentage body fat, WHtR = waist to height ratio, WHR = waist to hip ratio, BMI=body mass index, HC=hip circumference, LAP=lipid accumulation product, CI=Conicity index, VAI=visceral adiposity index. 0, 1, 2 and ≥3 represents number of MS components respectively*

Fig. 1 is a graph showing the pattern of MS components with increasing NMSC in males (0 - ≥3). SBP, DBP, FPG levels and WC increased while HDLC levels decreased consistently in males with increasing NMSC (0 - ≥3) (***P***<0.05). TG levels were similar among the males with 0≥3NMSC (***P***>0.05) while Inhibin B levels decreased from 0- 1 and 2 NMSC only (***P***<.05).

Fig. 2 is a graph showing the pattern of age, inhibin B levels and BMI among underweight, normal weight, overweight and obesity classes of the study participants. The mean (S.D) of BMI of underweight, normal weight, overweight and obesity groups were 17.5±1.0, 21.9±1.7, 26.9±1.4, 35.1±5.2, 24.0±4.5 respectively. There were significant differences among the groups (***P***<.001). The mean (S.D) of ages of underweight, normal weight, overweight and obesity groups were 38.2±14.8, 37.6±10.8, 40.4±7.7, 45.4±9.3, 39.0±10.3 years respectively. The differences among these groups were not significant (***P***=.189). The mean (S.D) of Inhibin B of underweight, normal weight, overweight and obesity groups were 334.1±233.3, 346.0±285.4, 363.0±242.9, 421.0±285.9, 354.6±270.0 pg/mL respectively. No significant differences were observed in Inhibin B levels among the various groups (***P***=.912).

3.1 Relationship of Inhibin B with Components of Metabolic Syndrome, Age and Measures of Obesity

Tables 4 and 5 show multiple regression of inhibin B with components of MS, age, obesity measures and lipids. Inhibin B had direct relationship with HDLC and TC but inverse relationship with VAI, LDLC and TC/HDLC.

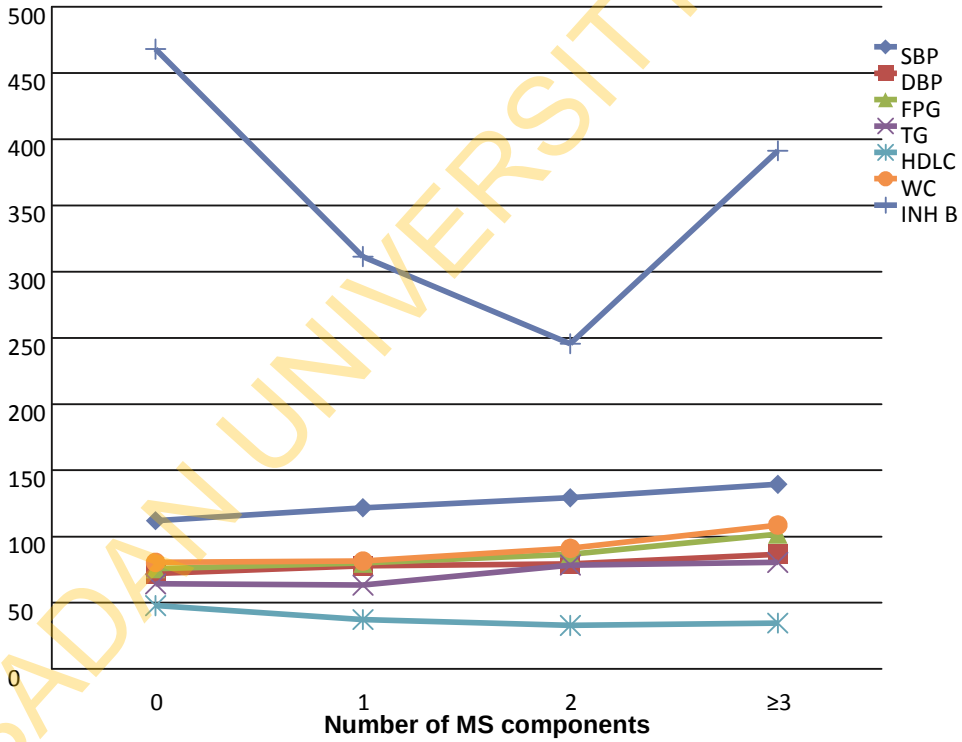

Fig. 1. Graph showing the pattern of metabolic syndrome components and Inhibin B in males with increasing number of metabolic syndrome components (0-≥3)

WC = waist circumference (cm), SBP = systolic blood pressure (mmHg), DBP=diastolic blood pressure (mmHg), TG = triglycerides (mg/dL), HDLC = high-density lipoprotein cholesterol (mg/dL), FPG = fasting plasma glucose (mg/dL), INH B= Inhibin B (pg/mL)

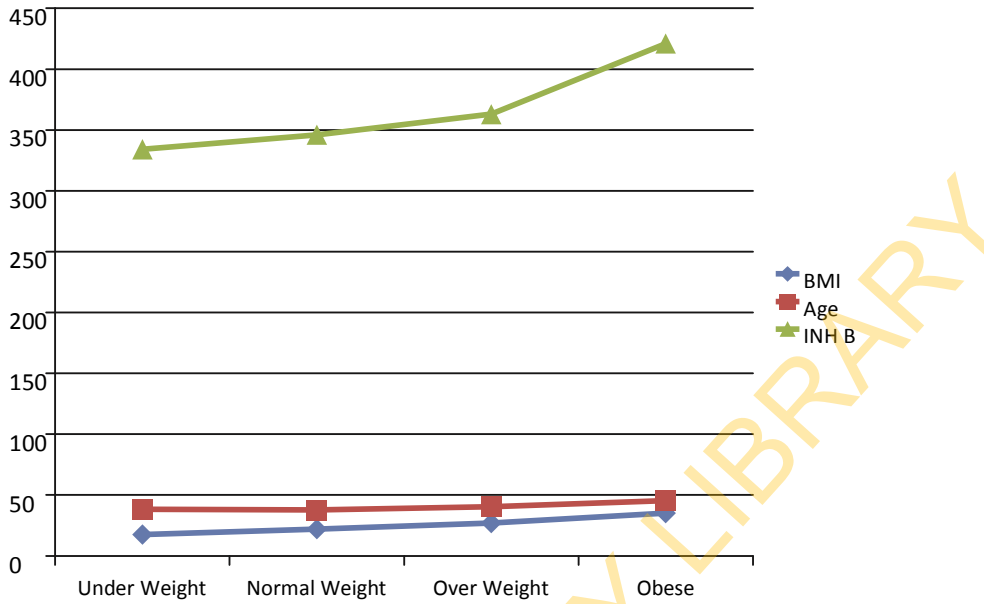

Fig. 2. Graph showing pattern of body mass index (BMI), age and inhibin B (INH B) levels in the various BMI classes: underweight = <18.5 Kg/m^2, normal weight = 18.5 – 24.9 Kg/m^2, overweight = 25.0 – 29.9Kg/m^2, obese= ≥ 30.0 Kg/m^2

Table 4. Multiple regression of inhibin B with metabolic syndrome components and obesity measures

Dependent variable		Predictors	Beta	t	*P*
Inhibin B	R^2adj.10.2%, F = 2.8, ***P***= .015*	**MS components**			
		TG	-.0	-.1	.960
		HDLC	.4	3.6	<.001*
		FPG	-.1	-1.3	.187
		SBP	.0	.1	.960
		DBP	-.0	-.1	.900
		WC	.1	.8	.438
	R^2adj. 4.5%, F = .2, ***P*** = .969	**Age and obesity measures**			
		Age	-.1	-.4	.678
		Height	.0	.2	.824
		Weight	.1	.2	.870
		HC	-.2	-.6	.578
		PBF	.2	.8	.418

P=significant, WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, FPG = fasting plasma glucose, TG = triglycerides, HDLC = high density lipoprotein cholesterol, HC = hip circumference, PBF = percentage body fat

4. DISCUSSION

The increasing incidence of MS in African communities has been attributed to increasing ageing of the population and lifestyle changes caused by rapid urbanization and westernization [27]. Differences in genetic background, diet, levels of physical activity and sex structure also influence the prevalence of both MS and its components [28]. Inhibin B is the physiological feedback signal for FSH and a serum marker of Sertoli cell function, predicting semen quality and male factor infertility [25,29,30]. Testosterone on the other hand is a serum marker of Leydig cell function and the physiological feedback signal for LH. Reduction in testosterone (male hormone) levels was recently demonstrated in males with MS but was attributed to increased conversion of testosterone to oestradiol by aromatase in increased adipose tissue. Hormones of the pituitary (luteinizing hormone (LH), FSH, prolactin) and adipose tissue (leptin) and parity were similar between MS and control groups [14].

These findings suggest that Sertoli and Leydig cells functions may be different or in synergy in male reproduction. Inhibin B has previously been shown to be unrelated to testosterone [25]. In this present study, a decline in spermatogenesis (decreasing inhibin B levels) was observed in males with 0 to 1 and 2 NMSC only while age increased from males with 0 to ≥3 NMSC (***P***<0.05). Mahmoud et al. [31] had long demonstrated an age related decline of inhibin B levels in younger men, which stabilized at an older age, contrasting the more progressive increase of low serum free testosterone. It thus appears that at the mean age of 48.0±8.7 years of males with MS (≥3 NMSC) in this present study, inhibin B levels appear stable.

Obesity is related to altered reproductive hormone status and is now considered a growing disease in developed and underdeveloped countries [13]. BMI, a measure of general obesity cannot distinguish between lean and fat body mass [32]. Changes in BMI can be attributed to skeletal muscle rather than body fat [33]. Comparison of age and Inhibin B levels did not show significant differences among BMI classes in our present study. Neither did Inhibin B relate with age nor BMI (***P***>.05). These observations, which are consistent with previous studies suggest that general obesity may be unrelated to age or spermatogenesis in the younger males (19-64 years) investigated [34,35,36].

In Africa, the predominance of MS among the elderly has been reported [37]. Individuals within the ages of 55 and 64 had the highest prevalence of MS (66%) in the general population [5]. Age correlated positively with all metabolic factors except HDLC in the general population [5]. In this present study, only HDLC in the lipid profile (TG, HDLC, TC, LDLC) differed significantly, reducing with increasing NMSC (***P***<0.05).

Our observations in males in this study appear to contradict the postulate that visceral obesity, key component of MS, measured by waist circumference delivers free fatty acids to the liver, leading to a reduced hepatic insulin clearance with subsequent increase in TG, LDLC, reduced HDLC and other components of MS observed [38]. Moreover in the younger men studied, reduced HDLC, high BP, and elevated WC were the more frequent MS components, represents 55.7%, 33.0% and 31.1% respectively. Elevated FPG and raised TG were less frequent, representing 14.2% and 0.9% of individuals respectively. Reduced HDLC was the commonest MS component, while TG was the least frequent component. This is similar to our previous study in the general population of male traders (younger and elderly males) [5]. High-density lipoprotein cholesterol (HDLC), which has antithrombotic, anti-inflammatory and antioxidant properties, has a key role in reverse cholesterol transport and has been shown to be cardioprotective [39].

WC (a measure of central obesity) has been shown as a better predictor of risk factors of MS

Table 5. Multiple regression of inhibin B with obesity measures and lipids

Dependent variable		Predictor	Beta	t	*P*
Inhibin B	R^2adj. 4.3%, F = 1.7, ***P***= .126	**Obesity measures**		-	
		BMI (Kg/m^2)	.1	.3	.771
		WHR	.2	.9	.391
		WHtR	.2	.4	.705
		LAP	.5	1.9	.058
		CI	-.7	-1.4	.167
		VAI	-.4	-2.9	.005*
		Lipids			
	R^2adj. 11.2%, F = 3.4, ***P***= .007*	TC	1.4	2.8	.007*
		LDLC	-1.5	-2.2	.034*
		TG/HDLC	.1	.6	.548
		TC/HDLC	-2.0	-2.2	.032*
		LDLC/HDLC	2.1	2.0	.050

**significant, BMI = body mass index, WHR = waist to hip ratio, WHtR = waist to height ratio, LAP = lipid accumulation product, CI = conicity index, VAI = visceral adiposity index, TC = total cholesterol, LDLC = low density lipoprotein cholesterol, TG/HDLC = triglyceride to high density lipoprotein cholesterol ratio, TC/HDLC = total cholesterol to high density lipoprotein cholesterol ratio, LDLC/HDLC = low-density lipoprotein cholesterol to high-density lipoprotein cholesterol ratio*

than BMI [33]. All anthropometric measures (general, visceral and subcutaneous obesity), BP, FPG and atherogenic indices (TG/HDLC, TC/HDLC and LDLC/HDLC) increased significantly with increasing NMSC (***P***<0.05). Elevated TC/HDLC ratio is a marker of CVD, with risk increasing substantially when the ratio is above five [40]. TG/HDLC is an indicator of LDLC particle size and small dense LDLC is the best predictor of future cardiovascular risks and dyslipidaemia in MS [41]. Similar to findings in this present study in males, atherogenic dyslipidaemia associated with obesity, hypertension, and glucose intolerance as observed in MS has been reported in the general population [5,26,40,42]. These findings may represent a substantial and evolving cardiovascular risk and should be of great public health concern. The increasing economic progress in Nigeria has resulted in lifestyle and dietary transition, which has caused increased inactivity and a shift towards high-fat, low-fibre diet [43]. Improvement of cardiometabolic, inflammatory and oxidative factors by short term dietary modification for six months has been reported [44].

Inhibin B had a positive relationship with HDLC and TC but was negatively related with VAI, LDLC and TC/HDLC (***P***<.05). VAI is strongly associated with MS. It is a valuable indicator of visceral adipose function, combining WC, BMI, TG and HDLC in its calculation. Interestingly, VAI was the only measure of central obesity that inversely and significantly predicted inhibin B levels (p<.005). Inhibin B appears related to specific CVD risk factors. Thus increased alteration of these risk factors may lead to reduced fertility potential. Several studies also found a positive association between HDLC and testosterone [45,46,47]. Wang et al. [48] reported the association of obesity with a higher incidence of male factor infertility through alterations in hormone profiles. However, Umoh et al. (2010) [10] showed an inverse relationship between HDLC and testosterone in males with MS and T2DM but not in apparently healthy parous males without MS and/or T2DM.

5. CONCLUSION

All measures of obesity, BP, FPG and lipid ratios increased with increasing NMSC. HDLC was the only lipid that was significantly different among the NMSC and decreased with increasing NMSC. Reduced HDLC was the most frequent component while elevated TG was the least component. Our observations are similar to previous reports in the general population. Spermatogenesis declined with increasing NMSC up to 2 components but normalized in males with ≥3 NMSC, contrary to the similar Inhibin B levels in all BMI classes. Inhibin B appeared to relate directly with HDLC and TC but indirectly with LDLC, TC/HDLC and VAI. VAI (a combination of WC, BMI, TG and HDLC) is a valuable indicator of visceral adipose function. It is the only obesity (adiposity) measure that related with Inhibin B. The involvement of visceral and not general or subcutaneous obesity in defective spermatogenesis is indicated in males in this study. These findings demonstrate the predisposition of younger males to CVD risk with increasing NMSC. However, mechanisms involved in normal reproductive potential in males with MS in this study are not clear.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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