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The Metabolic Syndrome and Sexual Dysfunction in a State of Inflammation

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Abstract

Background: Diabetes is amongst the most researched diseases worldwide due to its debilitating effects on patients. Diabetics have a higher risk of developing erectile dysfunction. Evidence has linked erectile dysfunction severity to increased age, duration of diabetes, the metabolic syndrome and hypogonadism. However, the role of inflammatory markers in the pathogenesis of SD is still unclear. The contributions of hormonal parameters and adipokines to both macro and micro vascular complications are still poorly understood. This study was conducted to provide some evidence of an association between SD, the metabolic syndrome and inflammatory hormones. **Method:** A total of 130 diabetic males participated in this study. All participants were at least 18 years and were actively engaged in a stable heterosexual relationship for a minimum of two years before they were recruited for this study. The Diabetic men were evaluated using the Golombok Rust Inventory of Sexual Satisfaction for males (GRISS-M). The NCEP-ATP III, IDF and WHO criteria were used to assess the metabolic syndrome. Blood samples were taken for biochemical and hormonal assays. **Results:** Participants with raised Triglyceride levels showed significantly higher leptin levels for NCEP-ATP III and IDF criteria. Participants with impotence showed significantly lower leptin/adiponectin ratio (p = 0.0184) whilst participant with non-sensuality showed significantly higher values of leptin/adiponectin ratio (p = 0.0103). A significantly higher levels of insulin (p = 0.0265) was recorded in participants with Dissatisfaction problems. Participants with Non communication problems showed significantly higher levels of insulin (p = 0.0419) and lower levels of adiponectin (p = 0.0438) whilst participants with infrequency showed significantly lower levels of adiponectin (p = 0.0042). **Conclusion:** The relative balance between

pro inflammatory and anti-inflammatory mediators of endothelial dysfunction could possibly be essential for the progression of diabetes to SD and the MetS thus a longitudinal study which measures a range of both pro and anti-inflammatory hormones and adipokines as risk factors for SD and the MetS could potentially aid in improvements in assessing the risk of developing these conditions among diabetics.

Keywords

1. Introduction

Diabetes is one of the most researched diseases in the world due to its debilitating effects on patients and the many complications that could result from this disease. The number of people with diabetes is known to be increasing due to population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity [1]. Diabetics are reported to have a higher risk of developing erectile dysfunction (ED) [2] [3] [4], sexual dysfunction (SD) [5] [6] and other cardiovascular pathologies [6] [7]. Evidence has linked erectile dysfunction severity to increased age [8] and duration of diabetes [8], poor glycaemic control and cardiovascular disease [8] as well as the metabolic syndrome [9]. Chronic hyperglycaemias as well as dyslipidaemia underpinned by endothelial dysfunction are the major underlying biochemical factors in diabetes [10]. The contribution of these abnormalities to both macro and micro vascular complications is well known, however their contribution to SD or specific domains of SD and which specific pathophysiological mechanism are implicated is still open to debate. Furthermore, the pathophysiological role of inflammatory hormones and their roles in the development or worsening of SD and the MetS is still not clearly understood.

The metabolic syndrome (MetS) is also characterized by a cluster of factors such as hyperglycemia, dyslipidaemia, high blood pressure, obesity and insulin resistance and these have long been implicated in the causation or worsening of diabetes [11]. Similarities in aetiology of the MetS with diabetes as well as SD can be traced to endothelial dysfunction and it is therefore not surprising that an increased prevalence of SD and MetS is largely reported to be among diabetics [9]. Although the pathophysiology is incompletely understood, insulin resistance and abdominal obesity are central to subsequent abnormalities in circulating glucose and lipoproteins and vascular function that lead to type 2 diabetes, atherosclerosis and CVD [12]. Various researches have attempted to elucidate the relationship between SD, MetS, inflammatory markers and some hormonal parameters which are likely to influence this relationship with some evidence showing a positive association between fasting insulin levels and inverse relationship between free testosterone levels, SHBG and the development of diabetes [13].

Some research has shown that age related decrease in testosterone levels is significantly exacerbated in obese men with the metabolic syndrome [14] but the role of inflammatory hormones is yet to be fully elucidated. It is in this light that this research seeks to provide some evidence of an association between MetS, SD and some hormonal parameters which are potential markers of inflammation. This research therefore seeks to determine if there are differences in the measured hormonal parameters between subjects with and without SD and/or the MetS.

Adipocytes play an important role in regulating triglycerides and free fatty acids levels [15]. High levels of androgens drive differentiation towards myogenesis and thus inhibit adipogenesis [16]. Thus androgen levels as well as levels of hormones produced by these adipocytes are likely to influence the development of the MetS in both sexes. A plausible biological mechanism for obesity induced hypogonadism may result in part from increased feedback inhibition of the hypothalamic-pituitary axis due to high levels of estrogen in obese men [17].

The Third National Health and Nutrition Examination Survey [17] reported that low free and bioavailable testosterone concentrations in the normal range were associated with diabetes, independent of adiposity. They suggested that low androgen levels may be a risk factor for diabetes in men. In a multivariable model adjusted for age, ethnicity and adiposity they observed that men in the first tertile (lowest) of free testosterone level were four times more likely to have prevalent diabetes compared with men in the third tertile. Similarly, men in the first tertile of bioavailable testosterone also were approximately four times as likely to have prevalent diabetes compared with men in the third tertile, these associations persisted even after excluding men with clinically abnormal testosterone concentrations. Others researchers [18] have demonstrated that the relationship between testosterone levels and adiposity is even dose dependent, with the effect of a 5 mg testosterone patch on body fat reduction being less in comparison to a 100 mg testosterone patch administered over the course of three months. They also showed that treatment with testosterone gel improved sexual function and mood, lean and fat mass as well as bone mineral density in hypogonadal men. Whether these established effects of testosterone on sexual function and body adiposity markers is mediated or influenced by inflammatory markers is still open to debate.

2. Methods

A total of 130 diabetic males who were attending the diabetic clinic and managed on oral diabetic medications at the Maamobi General Hospital in Accra between October, 2013 to September, 2014 were recruited for this study. Participants were consecutively sampled and those who were at least 18 years and were actively engaged in a stable heterosexual relationship were enrolled in the study. A stable heterosexual relationship was defined as having engaged in a continuous heterosexual relationship for a minimum of two years. An informed and signed consent was obtained from the participants before enrollment into the

study. Ethical approval was obtained from the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Science and the Komfo Anokye Teaching Hospital (KATH), Kumasi. The Diabetic men were evaluated blindly using the Golombok Rust Inventory of Sexual Satisfaction for males (GRISS-M) and they were further categorized into the various subscales of SD. The NCEP-ATP III, IDF and WHO criteria of the MetS were used to assess the metabolic syndrome and the participants were categorized into the various MetS components as well as MetS scores. Eight (8) mls of blood was obtained for biochemical and hormonal analysis. Fasting blood samples were collected from each participant in the morning between 06.00 to 09.00 GMT into fluoride oxalate tube and evacuated gel tubes for serum preparation (Becton Dickinson, Rutherford, NJ). Samples in the fluoride oxalate tubes were used for fasting blood glucose measurement after centrifugation at 18˚C whilst samples in the evacuated gel tubes were centrifuged at 3000 g for 5 minutes at 18˚C and the serum aliquoted and stored in cryovials at a temperature of −80˚C until time for biochemical and hormonal assay. Lipid profile and fasting blood glucose levels were determined using the BT 5000® Random Access Chemistry Analyzer (Biotecnica, Italy), the JAS Diagnostics® reagent kits were used in all of these assays. The hormonal assays were done using the Elabscience® reagent kits on the AxSYManalyser. The Sandwich-ELISA method was used in measuring the levels of leptin and adiponectin whilst the competitive ELISA method was used to assay Insulin levels. The methods adopted by the automated instruments for the determination of biochemical and hormonal parameters were done according to the reagent manufacturers' instructions (JAS Diagnostics, Inc. Miami Florida, USA and Elabscience Biotechnology Co. Ltd, Hubei Province, China). The Metabolic syndrome was defined by the NCEP-ATP III to include individuals with any three or more of the following five components: 1) abdominal obesity (waist circumference > 102 cm); 2) high TG ≥ 1.7 mmol/L; 3) low HDL-C: < 0.9 mmol/L; and 4) High BP (systolic BP ≥ 130 mm Hg or diastolic BP ≥ 85 mm Hg or treatment of hypertension); and 5) high fasting glucose ≥ 6.1 mmol/l (NCEP, 2001). The IDF criteria of the MetS was diagnosed if central obesity (waist measurement >90 cm) was accompanied by any 2 of the following 4 factors: 1) TG levels of 1.7 mmol/L or greater, 2) an HDL cholesterol lower than 1.03 mmol/L, 3) a blood pressure (BP) of 130/85 mm Hg or greater or treatment of previously diagnosed hypertension, and 4) a fasting blood glucose (FBG) of 5.6 mmol/L or greater or previously diagnosed type 2 diabetes. The WHO criteria was definedby the presence of diabetes mellitus, impaired glucose tolerance and any two of the following: 1) Body mass index (BMI) ≥30 kg/m² and/or waist-to-hip ratio >0.90, 2) blood pressure ≥140/≥90 mmHg or on medication, 3) diabetes ≥6.1 mmol/L or on medication for diabetes, impaired glucose tolerance, 4) triglyceride ≥1.7 mmol/L and/or HDL-C <0.91 mmol/L.

3. Statistical Analysis

All data analysis were performed using the SPSS software, version 11.0 systat,

Inc. Germany and GraphPad Prism, version 5.0, San Diego California, USA. Data presentation was done as the mean ±SD or percentages. In all the statistical analysis, a value of p < 0.05 was considered to be significant.

4. Results

The age range for those who responded was between 29 to 89 years, with a mean age of 63.04 ± 10.85 years and a mean duration of diabetes of 8.38 ± 6.53 years. The mean weight and BMI of the respondents was 82.20 ± 30.48 kg and 28.88 ± 11.32 kg/m^2 respectively. The mean SBP and DBP recorded was 157.50 ± 25.27 mmHg and 101.60 ± 14.96 mmHg respectively. The mean WC, HC and WHR were 95.25 ± 10.12 cm, 101.40 ± 8.70 cm and 0.94 ± 0.04 respectively. When the participants were stratified by sexual function, participants with SD were significantly older (66.67 ± 11.8 against 61.05 ± 9.79), and had a longer duration of diabetes (10.00 ± 7.79 against 7.53 ± 5.62) but there were no significant differences in the SBP, DBP, weight, BMI, waist circumference, hip circumference and waist to hip ratio amongst participants with or without SD (Table 1).

Table 1. General characteristics of the study population.

Variable	Total (n = 130)	NO SD (n = 46)	SD (n = 84)	P Value
Age (years)	63.04 ± 10.85	60.98 ± 9.80	66.67 ± 11.84	0.0043
Duration of diabetes (years)	8.38 ± 6.53	7.53 ± 5.62	10.00 ± 7.79	0.0418
Anthropometric Data				
SBP (mmHg)	157.50 ± 25.27	157.60 ± 27.86	157.50 ± 24.09	0.9841
DBP (mmHg)	101.60 ± 14.96	98.74 ± 14.13	103.20 ± 15.34	0.2572
Weight (kg)	82.20 ± 30.48	85.79 ± 32.38	80.24 ± 29.60	0.4869
Height (m)	1.69 ± 0.07	1.69 ± 0.07	1.69 ± 0.07	0.9317
BMI (kg/m^2)	28.88 ± 11.32	28.27 ± 11.32	29.99 ± 11.37	0.4116
HC (cm)	101.40 ± 8.70	101.10 ± 8.02	101.50 ± 9.14	0.8523
WC (cm)	95.25 ± 10.12	96.20 ± 9.60	94.73 ±10.47	0.5796
WHR	0.94 ± 0.04	0.95 ± 0.04	0.93 ± 0.04	0.0970
Biochemical parameters				
FBG (mmol/L)	8.73 ± 2.82	7.97 ± 2.65	9.15 ± 2.85	0.1076
Total cholesterol (mmol/L)	4.52 ± 1.31	4.78 ± 1.42	4.37 ± 1.24	0.2264
Triglyceride (mmol/L)	0.92 ± 0.49	0.89 ± 0.42	0.94 ±0.52	0.6917
HDL-cholesterol (mmol/L)	1.39 ± 0.51	1.53 ±0.60	1.31 ±0.45	0.0992
LDL-cholesterol (mmol/L)	2.67 ± 0.97	2.78 ±1.11	2.60 ±0.89	0.4709
Sexual Dysfunction				
Impotence	11.95 ± 1.54	11.09 ± 0.78	12.43 ± 1.65	< 0.0001
Premature Ejaculation	8.69 ± 1.86	7.78 ± 1.49	9.19 ± 1.85	< 0.0001
Non Sensuality	11.31 ± 1.31	10.65 ± 0.92	11.67 ± 1.35	< 0.0001
Avoidance	10.66 ± 2.22	11.26 ± 2.13	10.33 ± 2.20	0.0219
Dissatisfaction	10.89 ± 1.04	10.22 ± 1.03	11.26 ± 0.85	< 0.0001
Non Communication	5.15 ± 0.79	4.78 ± 0.79	5.36 ± 0.72	< 0.0001
Infrequency	5.86 ± 0.79	5.65 ± 0.48	5.98 ± 0.89	0.0239

The mean FBG, total cholesterol, triglyceride, HDL-cholesterol and LDL-cholesterol levels for the participants were 8.73 ± 2.82 mmol/L, 4.52 ± 1.31 mmol/L, 0.92 ± 0.49 mmol/L, 1.39 ± 0.51 mmol/L and 2.67 ± 0.97 mmol/L respectively. When the participants were stratified by sexual function, participants with SD recorded no significant difference in their biochemical parameters in comparism with those without SD (Table 1).

The SD scores recorded for impotence, PE, nonsensuality, avoidance, dissatisfaction, non communication and infrequency were 4.99 ± 2.05, 4.66 ± 1.77, 5.15 ± 2.05, 4.86 ± 1.94, 4.82 ± 2.02, 5.12 ± 1.88 and 4.72 ± 1.51. Participants with SD recorded significantly higher scores for impotence (5.60 ± 2.19 against 3.87 ± 1.14), PE (5.14 ± 1.73 against 3.78 ± 1.51), nonsensuality (5.70 ± 2.07 against 4.17 ± 1.64), dissatisfaction (5.52 ± 1.71 against 3.52 ± 1.93) as well as non communication (5.60 ± 1.70 against 4.26 ± 1.94) (Table 1).

The mean insulin, adiponectin, leptin and the leptin/adiponectin ratio recorded among the participants was 83.10 ± 22.79 pg/ml, 1.51± 0.35 ng/ml, 24.23 ± 12.00 ng/ml and 0.02 ± 0.00 respectively (Table 2). When the study participants were stratified by the MetS using the various criteria, the NCEP-ATP III recorded no significant differences in the insulin, leptin and the leptin/adiponectin ratio between subjects with or without the MetS. However participants with the MetS recorded increased adiponectin levels. The IDF and WHO criteria however did not show any significant difference in any of these parameters amongst subjects with or without the MetS (Table 2).When the mean values of

Table 2. Hormonal assays stratified by Presence or Absence of MetS.

VariableTotal	No MetS	MetS	P Value
ATP			
Insulin (pg/ml) 83.10 ± 22.79	104.22 ± 64.46	37.65 ± 21.30	0.1354
Adiponectin (ng/ml) 1.51 ± 0.35	1.31 ± 0.43	1.81 ± 0.32	0.0450
Leptin (ng/ml) 24.23 ± 12.00	22.40 ± 10.12	27.43 ± 13.35	0.2556
Leptin/Adiponectin Ratio 0.02 ± 0.00	0.02 ± 0.00	0.01 ± 0.00	0.4764
IDF			
Insulin (pg/ml)	69.54 ± 37.36	97.76 ± 48.33	0.2689
Adiponectin (ng/ml)	1.58 ± 0.40	1.42 ± 0.50	0.4710
Leptin (ng/ml)	23.43 ± 13.31	24.47 ± 10.43	0.2590
Leptin/Adiponectin Ratio	0.01 ± 0.0	0.02 ± 0.00	0.0725
WHO			
Insulin (pg/ml)	42.97 ± 32.65	102.43 ± 75.82	0.0922
Adiponectin (ng/ml)	1.74 ± 0.30	1.39 ± 0.80	0.1033
Leptin (ng/ml)	23.36 ± 13.46	45.15 ± 22.53	0.3256
Leptin/Adiponectin Ratio	0.01 ± 0.00	0.03 ± 0.01	0.2753

the biochemical parameters for the diabetics who recorded 0, 1, 2, 3 and 4 component scores of the MetS were compared for intergroup variations using the ATP III and IDF classifications, there were no significant differences recorded for insulin, adiponectin, leptin and leptin/adiponectin ratio but the WHO criteria recorded significant differences in the component score range with a generally increasing trend of adiponectin from 1 to 4 component scores (Table 3).

As shown in Table 4 and Table 5, when the diabetic participants were stratified based on the presence or absence of the MetS components with regards to the various hormonal parameters, participants with the presence of Abdominal Obesity, represented by WC, showed no significant difference in the levels of insulin, adiponectin, leptin and Leptin/Adiponectin ratios for the NCEP-ATP III and IDF MetS criteria. This observation was also recorded for diabetic participants who recorded the presence of Central obesity as represented by WHR using the WHO MetS criteria.

Diabetic male participants with raised FBG showed significantly higher levels of insulin for NCEP-ATP III (104.63 ± 76.39 against 29.44 ± 13.80), IDF (106.45 ± 79.74 against 42.63 ± 12.80) and the WHO criteria (97.48 ± 48.74 against 42.33 ± 28.76) in comparison with participants without raised FBG. Participants with raised Triglyceride levels showed significantly higher leptin levels for NCEP-ATP III (46.44 ± 22.24 against 21.32 ± 10.65) and IDF criteria (44.27 ± 24.92 against 20.26 ± 11.27). There was however no observed differences between subjects with or without the presence of raised BP in their levels of insulin, adiponectin, leptin and Leptin/Adiponectin ratios irrespective of the MetS criteria used.

Table 3. Hormonal parameters stratified by MetS component scores.

Variable	MetS Score					F Value	P Value
	0	1	2	3	4		
ATP							
Insulin (pg/ml)	45.04 ± 23.55	13.97 ± 5.62	127.40 ± 58.10	50.91 ± 25.30	39.54 ± 13.46	$F_{4, 120} = 1.4600$	0.2258
Adiponectin (ng/ml)	1.73 ± 0.13	1.73 ± 0.19	1.28 ± 0.12	1.93 ± 0.09	1.63 ± 0.13	$F_{4, 120} = 1.0550$	0.3869
Leptin (ng/ml)	15.72 ± 7.44	13.90 ± 5.70	24.46 ± 11.09	25.02 ± 13.46	35.11 ± 16.35	$F_{4, 120} = 0.6965$	0.5973
Leptin/Adiponectin Ratio	0.01 ± 0.00	0.01 ± 0.00	0.02 ± 0.01	0.02 ± 0.00	0.02 ± 0.00	$F_{4, 120} = 0.3536$	0.8405
IDF							
Insulin (pg/ml)		33.54 ± 12.93	97.74 ± 68.60	117.00 ± 58.30	55.43 ± 24.67	$F_{3, 122} = 1.499$	0.2238
Adiponectin (ng/ml)		1.29 ± 0.12	1.49 ± 0.11	1.38 ± 0.11	2.10 ± 0.10	$F_{3, 122} = 1.0350$	0.3835
Leptin (ng/ml)		12.77 ± 6.43	23.64 ± 12.21	25.45 ± 13.22	25.65 ± 10.29	$F_{3, 122} = 0.5073$	0.6787
Leptin/Adiponectin Ratio		0.01 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.01 ± 0.00	$F_{3, 122} = 1.8060$	0.1558
WHO							
Insulin (pg/ml)		33.44 ± 19.77	79.10 ± 38.00	121.50 ± 52.65	52.54 ± 24.45	$F_{3, 122} = 1.8010$	0.1564
Adiponectin (ng/ml)		1.28 ± 0.12	1.66 ± 0.11	1.30 ± 0.15	2.26 ± 0.12	$F_{3, 122} = 2.2360$	0.0433
Leptin (ng/ml)		12.22 ± 9.21	24.30 ± 15.55	23.49 ± 12.38	30.45 ± 13.36	$F_{3, 122} = 0.6795$	0.5680
Leptin/Adiponectin Ratio		0.01 ± 0.00	0.01 ± 0.00	0.02 ± 0.01	0.01 ± 0.00	$F_{3, 122} = 0.9963$	0.4007

Table 4. Insulin, Adiponectin levels stratified by Presence or Absence of MetS components.

Variable	Insulin (pg/ml)			Adiponectin (ng/ml)		
	Absent	Present	P Value	Absent	Present	P Value
ATP III						
Abdominal Obesity-WC	98.51 ± 44.60	12.33 ± 4.98	0.0704	1.46 ± 0.12	1.71 ± 0.11	0.4868
Raised FBG	29.44 ± 13.80	104.63 ± 76.39	0.0389	1.93 ± 0.10	1.94 ± 0.12	0.1243
Raised TG	87.88 ± 26.53	40.37 ± 10.33	0.5982	1.51 ± 0.13	1.59 ± 0.11	0.8579
Raised BP	92.87 ± 34.76	82.62 ± 54.48	0.8859	1.74 ± 0.11	1.49 ± 0.11	0.6419
Reduced HDL-c	106.20 ± 87.49	43.66 ± 12.54	0.0372	1.27 ± 0.10	2.49 ± 0.13	0.0002
IDF						
Abdominal Obesity-WC	49.44 ± 2.32	98.46 ± 16.99	0.1583	1.47 ± 0.11	1.54 ± 0.11	0.8285
Raised FBG	42.63 ± 12.80	106.45 ± 79.74	0.0383	1.92 ± 0.10	1.39 ± 0.11	0.1243
Raised TG	87.59 ± 33.48	40.54 ± 27.80	0.4822	1.57 ± 0.11	1.59 ± 0.11	0.8579
Raised BP	70.41 ± 45.47	84.27 ± 48.44	0.3685	1.81 ± 0.11	1.44 ± 0.11	0.3272
Reduced HDL-c	97.88 ± 38.36	33.34 ± 14.32	0.0937	1.28 ± 0.11	2.22 ± 0.09	0.0025
WHO						
Central Obesity-WHR	50.47 ± 21.35	86.44 ± 53.71	0.3897	1.53 ± 0.12	1.52 ± 0.11	0.9908
Raised FBG	42.33 ± 28.76	97.48 ± 48.74	0.0083	1.91 ± 0.10	1.40 ± 0.11	0.1243
Dyslipidemia	106.36 ± 72.47	19.56 ± 11.28	0.0341	1.25 ± 0.11	2.22 ± 0.07	0.0011
Raised BP	43.54 ± 13.37	92.44 ± 37.26	0.1074	1.65 ± 0.11	1.47 ± 0.11	0.5364

Table 5. Leptin, Leptin/Adiponectin ratio stratified by presence or absence of MetS components.

Variable	Leptin (ng/ml)			Leptin/Adiponectin Ratio		
	Absent	Present	P value	Absent	Present	Pvalue
ATP						
Abdominal Obesity-WC	22.46 ± 12.32	29.24 ± 11.34	0.0946	0.02 ± 0.00	0.02 ± 0.00	0.6348
Raised FBG	22.12 ± 210.32	24.21 ± 11.33	0.5433	0.01 ± 0.00	0.01 ± 0.00	0.1845
Raised TG	21.32 ± 10.65	46.44 ± 22.24	0.0023	0.01 ± 0.00	0.03 ± 0.01	0.2593
Raised BP	17.38 ± 9.21	23.37 ± 12.43	0.4133	0.01 ± 0.00	0.02 ± 0.00	0.4962
Reduced HDL-c	22.39 ± 12.54	24.54 ± 10.48	0.2481	0.02 ± 0.00	0.01 ± 0.00	0.0017
IDF						
Abdominal Obesity-WC	23.58 ± 11.37	24.99 ± 12.71	0.6392	0.02 ± 0.00	0.02 ± 0.00	0.2845
Raised FBG	22.18 ± 12.33	24.26 ± 12.16	0.2481	0.01 ± 0.00	0.02 ± 0.01	0.1842
Raised TG	20.26 ± 11.27	44.27 ± 24.92	0.0019	0.01 ± 0.00	0.03 ± 0.01	0.4329
Raised BP	23.52 ± 11.39	24.37 ± 14.88	0.4819	0.01 ± 0.00	0.02 ± 0.00	0.6299
Reduced HDL-c	23.44 ± 12.63	23.98 ± 12.59	0.7372	0.02 ± 0.00	0.01 ± 0.00	0.1893
WHO						
Central Obesity-WHR	21.49 ± 10.61	25.37 ± 12.88	0.4922	0.01 ± 0.00	0.02 ± 0.00	0.6391
Raised FBG	22.68 ± 11.41	24.51 ± 12.49	0.2718	0.01 ± 0.00	0.02 ± 0.00	0.0928
Dyslipidemia	23.27 ± 15.66	25.61 ± 12.55	0.6449	0.02 ± 0.01	0.01 ± 0.00	0.0426
Raised BP	21.16 ± 11.54	26.43 ± 15.49	0.2844	0.01 ± 0.00	0.02 ± 0.00	0.6291

Diabetic participants with the presence of reduced HDL-Cholesterol levels showed significantly lower levels of insulin for NCEP-ATP III criteria (43.66 ± 12.54 against 106.20 ± 87.49), significantly higher adiponectin levels for the NCEP-ATP III (2.49 ± 0.13 against 1.27 ± 0.10) and IDF criteria (2.22 ± 0.09 against 1.28 ± 0.11) and significantly lower leptin/adiponectin ratio (ATP) (0.01 ± 0.00 against 0.02 ± 0.00 in comparison with diabetic participants without presence of reduced HDL-Cholesterol levels. Participants with the presence of Dyslipidaemia which includes reduced HDL levels in its definition (WHO criteria) showed significantly lower levels of insulin (19.56 ± 11.28 against 106.36 ± 72.47), significantly higher levels of adiponectin (2.22 ± 0.07 against 1.25 ± 0.11) and a significantly lower leptin/adiponectin ratio (0.01 ± 0.00 against 0.02 ± 0.01) in comparison to participants without the presence of Dyslipidaemia.

When the diabetic participants were stratified based on the presence or absence of SD domains (Table 6), participants who had impotence showed significantly lower leptin/adiponectin ratio (0.01 ± 0.00 against 0.02 ± 0.01) but no significant difference in the levels of insulin, adiponectin, leptin whilst participants with the presence of premature ejaculation showed no difference in insulin, adiponectin, leptin and leptin/adiponectin ratios in comparison with subjects without the presence of premature ejaculation. Participants with the presence of non-sensuality showed significantly higher values of leptin /adiponectin ratio (0.03 ± 0.00 against 0.02 ± 0.00) but did not show any significant difference in the levels of insulin, adiponectin and leptin when compared to participants

Table 6. Sexual Dysfunction (SD), SD subscales against hormonal assays.

Variable	Insulin (pg/ml)			Adiponectin (ng/ml)		
	Absent	Present	P Value	Absent	Present	P Value
Impotence	106.42 ± 79.32	51.37 ± 22.43	0.1103	1.31 ± 0.12	1.70 ± 0.10	0.1522
Premature ejaculation	50.32 ± 22.40	119.00 ± 55.10	0.0682	1.39 ± 0.11	1.64 ± 0.10	0.3828
Non sensuality	124.68 ± 89.76	66.44 ± 34.36	0.1135	1.36 ± 0.13	1.57 ± 0.26	0.5087
Avoidance	91.63 ± 51.82	73.72 ± 43.94	0.4201	1.66 ± 0.18	1.35 ± 0.13	0.2666
Dissatisfaction	46.30 ± 3.54	113.40 ± 98.40	0.0265	1.38 ± 0.15	1.60 ± 0.10	0.4384
Non communication	54.39 ± 17.40	101.48 ± 62.44	0.0419	2.06 ± 0.18	1.37 ± 0.10	0.0438
Infrequency	39.33 ± 18.55	100.98 ± 72.20	0.1310	2.15 ± 0.11	1.28 ± 0.10	0.0042

Variable	Leptin (ng/ml)			Leptin/Adiponectin ratio		
	Absent	Present	P Value	Absent	Present	P Value
Impotence	24.20 ± 12.24	22.29 ± 11.63	0.4879	0.02 ± 0.01	0.01 ± 0.00	0.0184
Premature ejaculation	22.83 ± 12.48	25.46 ± 12.22	0.2590	0.02 ± 0.00	0.02 ± 0.01	0.6293
Non sensuality	25.32 ± 11.46	24.64 ± 12.22	0.3174	0.02 ± 0.00	0.03 ± 0.00	0.0103
Avoidance	28.39 ± 18.43	20.75 ± 13.66	0.4573	0.02 ± 0.00	0.02 ± 0.00	0.5492
Dissatisfaction	25.37 ± 12.38	23127 ± 12.99	0.3753	0.02 ± 0.00	0.01 ± 0.00	0.1093
Non communication	22.28 ± 12.44	25.98 ± 12.72	0.9862	0.01 ± 0.00	0.02 ± 0.00	0.2603
Infrequency	23.24 ± 11.39	25.53 ± 12.77	0.3854	0.01 ± 0.00	0.02 ± 0.00	0.0431

without the presence of non-sensuality. There were no significant differences recorded in the levels of adiponectin, leptin and leptin/adiponectin ratio levels for diabetic male participants with or without the presence of Dissatisfaction problems. However a significantly higher levels of insulin was recorded for participants with the presence of Dissatisfaction problems (113.40 ± 98.40 against 46.30 ± 3.54) in comparison to those without dissatisfaction problems. Participants with the presence of Non communication problems showed significantly higher levels of insulin (101.48 ± 62.44 against 54.39 ± 17.40) and lower levels of adiponectin (1.37 ± 0.10 against 2.06 ± 0.18) whilst participants who experienced infrequency showed significantly lower levels of adiponectin and a higher leptin/adiponectin ratio in comparison with participants without the presence of infrequency problems (1.28 ± 0.10 against 2.15 ± 0.11 and 0.01 ± 00 against 0.02 ± 0.00).

When the −SD/−MetS, +SD/−MetS, −SD/+MetS and +SD/+MetS groups were compared for insulin, adiponectin, leptin and leptin/adiponectin ratio, there was a significant difference in the insulin levels for NCEP-ATP III (p = 0.0186, $F_{3,122}$ = 3.5722), IDF (p = 0.0487, $F_{3,122}$ = 2.6982) and adiponectin levels for NCEP-ATP III criteria (p = 0.0256, $F_{3,122}$ = 1.0633), WHO criteria (p = 0.0396, $F_{3,122}$ = 2.5945). Insulin levels was generally highest among the +SD/−MetS group, followed by the +SD/+MetS group, with the −SD/+MetS group generally recording the lowest insulin levels. For adiponectin, the lowest levels were generally recorded in the −SD/−MetS with the +SD/+MetS group generally recorded the highest levels of adiponectin. When the assayed hormonal parameters were considered as risk factors for SD and the MetS after adjustment for age and BMI, none of the assayed hormonal parameters recorded as a determinant of either the MetS or SD.

5. Discussion

Subjects with reduced HDL-cholesterol levels recorded higher levels of adiponectin whilst Dyslipidaemia which has reduced HDL-cholesterol levels in its definition also recorded significantly higher levels of adiponectin. This could explain the potential role of adiponectin levels in the pathogenesis of the MetS and possibly diabetes. This is further supported by the observation of higher levels of leptin (ATP/IDF) amongst subjects with raised triglyceride levels which is a cardinal event in the early metabolic derangements involved in the pathogenesis of the MetS. Since raised triglycerides is a marker of increased fatty acid availability, it is possible that higher leptin levels could have triggered the suppression of testosterone levels via leptin receptors present on leydig cells or by the increased aromatization of androgens to oestrogens. This could potentially cause a reduction in the levels of free and bioavailable testosterone in circulation thus inducing a state of hypogonadism. Whether the increased leptin levels in a state of increased abdominal obesity (Table 4) directly results in the reduction in testosterone levels via suppression of production mediated by leptin receptors on leydig cells or by the increased aromatization to oestrogens, reduced testosterone levels could without doubt further promote adipocytosis as decreased testosterone le-

vels has been shown to promote adipocytosis in various research. The resultant increase in adipocytes coupled with the hypogonadism could be a major trigger in the events that leads to development of the MetS. Furthermore, as testosterone levels decrease further in the face of persistent increase in adipocytes, Nitric Oxide (NO) availability could be compromised by direct inactivation of eNOS. A reduction in the availability of NO in the endothelial wall could result in increased free radical damage and increased oxidative stress which will eventually compromise endothelial integrity. As NO availability is compromised in the presence of a progressive and persistently unresolved dyslipidaemic derangements and hyperglycaemia, neuronal glycation coupled with unavailability of NO could trigger the series of events which eventually promotes the progression from the MetS characterised by dyslipidaemia to a competition for the remaining NO. Thus a vicious cycle could be created between endothelial dysfunction, the MetS and SD. The importance of the fine balance between the levels of adiponectin and leptin is showed by the lower leptin/adiponectin ratio recorded for participants with reduced HDL levels, Dyslipidaemia (Table 4), Impotence and Non-sensuality (Table 5). It is therefore not surprising that the participants with the presence of Impotence (ED) which is the SD sub component likely to be directly affected by NO unavailability recorded significantly lower values for the leptin/adiponectin ratio.

The finding of lower levels of adiponectin in participants with problems of Non-communication and Infrequency in sexual activity could be due to the important role of adiponectin as an anti-inflammatory hormone. It is possible that as endothelial dysfunction progresses, with attendant increase in inflammatory mediators, the decreasing levels of adiponectin could have triggered a state of increased oxidative stress that could have resulted in tiredness and a general lack of energy and interest to engage in sexual activity thus reflecting as sexual infrequency problems. This is supported by the observation of a higher leptin/adiponectin ratio seen among participants with problems of infrequency in sexual activity. Thus the role of pro and anti-inflammatory mediators in endothelial dysfunction could be equally important in the mechanisms that results in sexual dysfunction. It is therefore not surprising that various researchers have identified endothelial dysfunction as a common denominator underlining both MetS and SD. This is also supported by the observation in this study that insulin and adiponectin levels showed significant differences when various shades of MetS/SD were compared (Table 7). But the fact that leptin did not show a difference when the various shades of MetS/SD were compared could mean that increased leptin levels could possibly have been an earlier event before the development of both MetS and SD. Thus leptin could have played a significant role in the development of diabetes and thus could not have been varied among a group of diabetics with various shades of MetS/SD but still remained an important mediator as evidenced by the significance in the ratio of leptin to adiponectin seen in this study. Even though none of the assayed hormonal parameters recorded as determinants of SD and the MetS (Table 8), a longitudinal study which meas-

ures a range of both pro and anti-inflammatory hormones and adipokines as risk factors for SD and the MetS could potentially aid in assessing the risk of developing these conditions among diabetics.

Table 7. Hormonal parameters stratified by the various shades of the SD/MetS groups.

Variables	−SD/-MetS	+SD/−MetS	−SD/+MetS	+SD/+MetS	F value	P value
ATP						
Insulin (pg/ml)	20.36 ± 12.53	157.34 ± 65.10	13.33 ± 8.31	59.27 ± 26.43	F3, 122 = 3.5722	0.0186
Adiponectin (ng/ml)	1.50 ± 0.11	1.26 ± 0.13	1.86 ± 0.09	1.85 ± 0.14	F3, 122 = 1.0633	0.0256
Leptin (ng/ml)	23.58 ± 12.48	29.54 ± 11.37	22.39. ± 10.26	30.83 ± 13.45	F3, 122 = 1.0946	0.0593
Leptin/Adiponectin Ratio	0.02 ± 0.00	0.02 ± 0.00	0.01 ± 0.00	0.02 ± 0.00	F3, 122 = 0.3997	0.4729
IDF						
Insulin (pg/ml)	25.88 ± 17.49	96.36 ± 54.56	39.50 ± 13.64	147.49 ± 83.34	F3, 122 = 2.6982	0.0487
Adiponectin (ng/ml)	1.86 ± 0.10	1.41 ± 0.11	1.23 ± 0.11	1.53 ± 0.12	F3, 122 = 0.5422	0.3865
Leptin (ng/ml)	21.45 ± 11.60	24.39 ± 12.35	19.33 ± 10.27	26.92 ± 15.42	F3, 122 = 0.0597	0.1938
Leptin/Adiponectin Ratio	0.01 ± 0.00	0.02 ± 0.01	0.02 ± 0.00	0.02 ± 0.00	F3, 122 = 0.8519	0.3920
WHO						
Insulin (pg/ml)	46.97 ± 17.82	163.44 ± 75.19	29.41 ± 12.38	124.49 ± 68.27	F3, 122 = 0.3250	0.6320
Adiponectin (ng/ml)	1.14 ± 0.11	1.37 ± 0.15	1.43 ± 0.09	1.58 ± 0.22	F3, 122 = 2.5945	0.0392
Leptin (ng/ml)	17.84 ± 11.28	26.39 ± 12.34	21.49 ± 12.38	23.44 ± 14.47	F3, 122 = 0.1385	0.2901
Leptin/Adiponectin Ratio	0.02 ± 0.00	0.02 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	F3, 122 = 0.2474	0.4255

Table 8. Hormonal Determinants of Sexual Dysfunction and MetS.

Variable	OR (CI)	P Value	aOR (CI)	P Value
SEXUAL DYSFUNCTION				
Insulin				
Normal				
High	0.00 (0.00 - 0.00)	1.0000	0.00 (0.00 - 0.00)	1.0000
Leptin				
Normal				
High	0.91 (0.08 - 10.60)	0.9390	0.62 (0.04 - 8.87)	0.7260
Adiponectin				
Normal				
High	0.86 (0.06 - 9.46)	0.8549	0.54 (0.02 - 7.65)	0.7044
METABOLIC SYNDROME				
Insulin				
Normal				
Low	8.43 (2.06 - 10.43)	0.9880	5.83 (1.04 - 8.76)	0.9800
Leptin				
Normal				
High	0.22 (0.02 - 2.59)	0.2290	0.26 (0.02 - 3.75)	0.3250
Adiponectin				
Normal				
High	0.75 (0.08 - 7.66)	0.6949	0.43 (0.01 - 6.35)	0.5430

6. Conclusion

The relative balance between pro inflammatory and anti-inflammatory mediators of endothelial dysfunction could possibly be essential for the progression of diabetes to SD and the MetS thus a longitudinal study which measures a range of both pro and anti-inflammatory hormones and adipokines as risk factors for SD and the MetS could potentially aid in improvements in assessing the risk of developing these conditions among diabetics.

Competing Interests

The authors declare that they have no competing interests.

Authors' Contributions

WKBAO, NA, HA, CO and CKGS developed the concept and designed the study. NA, WKBAO, HA, PPMD, CO and ATB administered the questionnaire, analysed and interpreted the data. NA, WKBAO, HA, PPMD, CO and ATB performed all the assay procedures. WKBAO, HA, NA, CO, PPMD and ATB drafted the manuscript. NA, HA, WKBAO, PPMD, CKGS and ATB revised the manuscript for intellectual content. All authors read and approved the final manuscript.

Ethics, Consent and Permissions

Ethical approval was obtained from the Committee on Human Research Publication and Ethics (CHRPE) of the School of Medical Science and the KomfoAnokye Teaching Hospital (KATH), Kumasi. All participants gave an informed and signed consent to partake in this study.

Consent for Publication

All participants gave an informed and signed consent for research to be used for publication.

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List of Abbreviations

ADT	Androgen Deprivation Therapy
AV	Avoidance
BP	Blood Pressure
DIS	Dissatisfaction
NO	Nitric Oxide
ED	Erectile Dysfunction
GRISS-M	Golombuk-Rust Inventory for Sexual Satisfaction-Male
IMP	Impotence
INF	Infrequency
IDF	International Diabetes Federation
MetS	Metabolic syndrome
NCEP-ATP III	National Cholesterol Education Programme-Adult Treatment Panel III
NO	Nitric Oxide
NS	Non-sensuality
PE	Premature Ejaculation
SHBG	Sex Hormone Binding Globulin
SD	Sexual Dysfunction