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Cortisol and Metabolic Syndrome Components in Obese and Overweight Young Adults of a Nigerian Private University

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Authors' contributions

This work was carried out in collaboration between all authors. Author AIO designed the study, wrote the protocol, and wrote the first draft of the manuscript. Authors APO and AWA managed the literature searches. Authors TTD and AJO managed the analyses of the study. Author AAA performed the statistical analysis. All authors read and approved the final manuscript.

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ABSTRACT

Background: Metabolic syndrome is a cluster of metabolic abnormalities which confers upon an individual a substantial increase in cardiovascular disease risk – approximately twice as high as those without the syndrome.
Aim: The study assessed the relationship between serum cortisol and the components of metabolic syndrome among overweight and obese students.

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Materials and Methods: A total of ninety (n=90) subjects were recruited for this study which consisted of thirty (30) obese participants, thirty (30) overweight individuals and thirty (30) normal weight individuals who served as controls. About 7 ml of venous blood sample was collected from each participant within the age range of 17-25 years and serum was extracted. Anthropometric measurements were determined using standard methods. Fasting blood glucose, HDL-cholesterol, triglycerides and total cholesterol were determined using enzymatic methods while serum cortisol was determined using enzyme-linked immunosorbent assay (ELISA) technique. Data obtained were statistically analyzed using ANOVA, Post-hoc, Pearson's correlation and $P<0.05$ was considered significant. In this study, metabolic syndrome was defined according to the National Cholesterol Education Program (NCEP) criteria.

Results: There was a significant increase in the level of serum cortisol in overweight and obese subjects in comparison to the control participants. There was also positive significant correlation between cortisol and glucose, cortisol and triglyceride. In contrast, there was a negative correlation between cortisol and HDL cholesterol in both overweight (r=-0.917, $P=0.02$) and obese (r=-0.365, $P=0.04$) subjects.

Conclusion: This study revealed that increased serum cortisol level in obese and overweight subjects correlates with more than two components of the metabolic syndrome. Taken together, data from this study revealed a noteworthy relationship between cortisol and metabolic syndrome among Nigerian young adults which suggests that metabolic stress is an underlying factor for elevated cortisol.

Keywords: Metabolic syndrome; cortisol; obese; overweight; young adults.

1. INTRODUCTION

The trend of obesity among young adults worldwide especially university undergraduate students is gradually escalating [1,2]. Young adults between the ages of 18-25 undergo significant life style changes during this period which make them vulnerable to energy imbalance leading to excessive weight gain [3,4].

The World Health Organization (WHO) defined overweight and obesity as body mass index ≥25 kg/m^2 and ≥30 kg/m^2 respectively and they are associated with diabetes mellitus, cardiovascular disease and several types of cancer [5-7]. Obesity dysregulates glucose and lipid metabolic processes and thus it is believed to be the driving force for metabolic syndrome, a complex web of metabolic risk factors consisting of dysglycaemia, atherogenic dyslipidemia, hypertension, procoagulant state [8-10].

Contrary to the impression of many people in Africa that overweight and obesity are common among young adults in the western countries, due to their lifestyles and heavy consumption of calorie-rich diet, some studies have reported increase in the rate of obesity among people aged 15 years and above in Sub-Saharan Africa [11,12]. The prevalence of obesity among old and young adults in Nigeria, is of epidemic proportion [13-15]. Cross-sectional studies by Onyenekwu et al. [16] and Adejumo et al. [17] reported prevalence of metabolic syndrome among overweight and obese young adults at a private university in Nigeria. It then means that, as obesity is escalating among young adults, there is a parallel increase in the incidence of metabolic syndrome.

Systemic stress induced by obesity causes dysregulation in the production of adipokines which contributes to the development of metabolic syndrome [18]. Such dysfunction could enhance the conversion of inactive cortisone to active cortisol through the expression of 11-betahydroxysteroid dehydrogenase type-1 [19, 20].

Cortisol is a glucocorticoid hormone whose major function is adaptation to biological stress. Moderate levels of cortisol are important for many physiological functions. However, chronically elevated levels could result into obesity and insulin resistance [21]. It has been demonstrated in both human and animal models that dysregulation of hypothalamic-pituitary adrenal (HPA) axis which leads to the increased secretion of cortisol, promotes the accumulation of fat cells and weight gain [22]. Although there have been previous conflicting reports about the relationship between cortisol and obesity, there is paucity of data on the association between cortisol and metabolic syndrome. This study is therefore designed to assess the relationship between cortisol and components of metabolic

syndrome in young adults at a private university in Nigeria.

2. MATERIALS AND METHODS

A total of 90 apparently healthy undergraduate students of Babcock University, Ilishan Remo, Ogun state aged 17-25 years participated in this cross sectional study. They comprised of thirty (30) obese students and thirty (30) overweight students as test subjects. The control subjects were thirty (30) normal weight students. A semi-structured questionnaire was used to obtain demographic data and information about medical conditions, current medications, alcohol use and smoking habits. Body weight in kilogram (kg) was measured using a standard weighing scale and height (m) was measured using a stadiometer. Body mass index was calculated as the ratio of body weight (kg) to the square of height (m^2). Waist circumference was measured midpoint between the inferior margin of the last rib and the crest of the ileum using a measuring tape. Blood pressure was measured using a mercury sphygmomanometer with appropriate cuff size. Korotkoff phases 1 and 5 were used.

Participants whose BMI was above 30 kg/m^2 were classified as obese, those with body mass index between 25.0-29.9 kg/m2 were classified as overweight subjects while control subjects were normal weight individuals having a body mass index between 18.5-24.9 kg/m^2.

This study excluded individuals who take alcohol, those who smoke, individuals with HIV, individuals with hepatitis, those on medications and individuals who have other known chronic medical conditions such as hypertension. Underweight individuals and those unwilling to give their consent were also excluded from this study.

2.1 Defining Criteria for Metabolic Syndrome

Metabolic syndrome was diagnosed using National Cholesterol Education Program-Adult treatment Panel III (NCEP-ATPIII) criteria [23]. The defining criteria was the presence of any three or more of these features: waist circumference (male: ≥102 cm, female: ≥88 cm), elevated blood pressure (≥130/≥85 mmHg), elevated triglycerides: ≥150 mg/dL, reduced HDL-C (males: <40 mg/dL, females: <50 mg/dL) and elevated fasting plasma glucose (≥100 mg/dL).

2.2 Sample Collection and Assay Methodology

The blood sample was collected in the morning from the study participants, after overnight fast which lasted for 10-12 hours. About 7 ml of venous blood was obtained from the cubital vein of each study participant, using pyrogen-free disposable vacutainer tubes. About 3 ml of venous blood was collected into fluoride oxalate bottle for the assay of fasting plasma glucose (FPG) which was performed within 12 hours, while 4ml was collected into plain bottle and was centrifuged at 4000 rpm for 3 minutes to obtain serum which was aliquoted into small vial and stored at -20^{O}C for the determination of HDL-C, triglycerides (TG) and cortisol.

Plasma glucose was determined by the glucose oxidase method (Randox Laboratories Ltd., UK). Triglyceride (TG) was determined using standard enzymatic method (Randox Laboratories Ltd., UK) and high density lipoprotein-cholesterol (HDL-c) was determined by a two-step procedure using a precipitant to isolate non-HDL-c component in the plasma and this was followed by quantitative determination of HDL-c by standard enzymatic method for cholesterol determination (Randox Laboratories Ltd., UK). Serum cortisol was determined using ELISA (GenWay Biotech Inc., USA).

2.3 Statistical Analysis

Data analysis was done using the statistical package for social sciences (SPSS 17th edition) computer software. Comparison of variables between groups was done using one-way analysis of variance (ANOVA) followed by a *post-hoc* test, while Pearson's correlation was used to determine the relationship between variables. All tests were two-tailed, and $P < 0.05$ was considered to be statistically significant.

3. RESULTS

Table 1 shows the frequency of metabolic syndrome components among obese and overweight subjects. Among the obese subjects, the proportion of those who had elevated blood pressure was 50% (15 participants), reduced HDL-C was 43.3% (13 participants), elevated TG was 16.7% (5 participants) and elevated FBG was 30% (9 participants). Among overweight subjects, the proportion of those who had

elevated blood pressure was 33.3% (10 participants), reduced HDL-C was 33.3% (10 participants), elevated TG was 6.7% (2 participants) and elevated FBG was 20% (6 participants).

Table 2 shows the proportion of obese and overweight subjects who had metabolic syndrome. Among obese and overweight subjects, 33.3% and 20% respectively had metabolic syndrome.

The anthropometric and biochemical parameters of the study participants are presented in Table 3. The test and control groups were compared using ANOVA and *post hoc*. There were remarkable significant increases in the mean waist circumference, systolic BP, diastolic BP, triglyceride, glucose, HDL cholesterol and cortisol ($P<$ 0.001) in the test group when compared with the control group.

Table 4 shows correlation between cortisol and metabolic syndrome components in overweight subjects. There was significant positive correlation between cortisol and triglyceride (r= 0.014, $P<0.05$) meanwhile, there was a negative correlation between cortisol and HDL cholesterol (r= -0.917, $P<0.05$). There was no significant correlation between cortisol and waist circumference, diastolic blood pressure and systolic blood pressure.

Table 5 shows correlation between cortisol and metabolic syndrome components in obese subjects. There was significant positive correlation between cortisol and glucose (r=0.383, $P<0.05$), cortisol and triglyceride (r= 0.393, $P<0.05$) meanwhile, there was a negative correlation between cortisol and HDL cholesterol (r= -0.365, $P<0.05$). Furthermore, there was no significant correlation between cortisol and waist circumference, diastolic blood pressure and systolic blood pressure.

Table 1. Frequency of components of metabolic syndrome in obese and overweight subjects

Metabolic syndrome components	Obese (n=30)	Overweight (n=30)
High blood pressure	15 (50%)	10 (33.3%)
Elevated FBG	9 (30%)	6 (20%)
Elevated TG	5 (16.7%)	2 (6.7%)
Reduced HDL	13 (43.3%)	10 (33.3%)

Table 2. Proportion of study participants with metabolic syndrome using NCEP-ATP III criteria

Subjects	Metabolic syndrome	No metabolic syndrome
Obese (n=30)	10 (33.3%)	20 (66.7%)
Overweight (n=30)	6 (20%)	24 (80%)
Control (n=30)	0 (0%)	30 (100%)

Table 3. Characteristics of study participants

Parameters	Obese subjects n=30	Overweight subjects n=30	Control subjects n=30	F	P-value
WC (cm)	108.42±9.41[a, b]	92.18±10.30[a, c]	78.36±7.60[b, c]	80.950	0.000*
SBP (mmHg)	131.03±16.30[a]	128.27±11.37[a]	114.47±12.60[b, c]	12.970	0.000*
DBP (mmHg)	85.07±13.24[a]	81.47±9.48[a]	73.40±6.60[b, c]	10.400	0.000*
FBG (mg/dl)	110.57±24.47[a, b]	98.83±22.842[a]	86.63±11.640[b]	4.163	0.001*
HDL-C (mg/dl)	46.3±13.39[a]	40.077±13.3[a]	53.183±13.76[b, c]	7.083	0.001*
TG (mg/dL)	114.582±55.84[a]	108.243±55.856[a]	72.447±35.54[b, c]	6.295	0.003*
Cortisol (ng/mL)	190.97±55.93[a, b]	156.37±54.92[a, c]	115.11±53.31[b, c]	13.920	0.000*

*Results are expressed in mean±standard deviation. * Statistically significant at the levels indicated, a= significantly different from control subjects; b= significantly different from overweight subjects; c= significantly different from obese subjects. WC-waist circumference; SBP-systolic blood pressure; DBP-diastolic blood pressure; FBG-fasting blood glucose; HDL-C-high density lipoprotein-cholesterol; TG-triglyceride.*

Table 4. Correlation between cortisol and metabolic syndrome components in overweight subjects

Cortisol	r	P-value
HDL-C	-0.917	0.02*
WC	0.16	0.40
SBP	0.824	0.05*
DBP	0.232	0.218
FBG	0.493	0.04*
TG	0.104	0.03*

**Statistically significant at the levels indicated*

Table 5. Correlation between cortisol and metabolic syndrome components in obese subjects

Cortisol	r	P-value
HDL-C	-0.365	0.04*
WC	0.02	0.907
SBP	0.347	0.06
DBP	0.245	0.191
FBG	0.383	0.03*
TG	0.393	0.006*

**Statistically significant at the levels indicated*

4. DISCUSSION

In this study, we assessed obese and overweight young adults in a Nigerian University using NCEP-ATP III criteria for metabolic syndrome. It was observed that one-fourth of the test subjects had metabolic syndrome although there was no correlation between cortisol and waist circumference, an observation which had also been reported by [24-26]. Glucocorticoids play active roles in human adipocyte differentiation and redistribution from peripheral to central depots [27,28]. The current study revealed increase in serum cortisol levels among overweight and obese volunteers. An explanation for the significantly higher levels of cortisol observed in this study was provided by [29, 30] and they implicated increased expression of 11β-hydroxysteroid dehydrogenase type 1 (11- β HSD1) which catalyzes enhanced conversion of inactive cortisone to active cortisol in obesity. High cortisol levels exhibited by obese individuals, could also be in response to increased production of adipokines [18, 31].

The current study also revealed significant positive correlation between triglycerides and cortisol. This is in agreement with previous studies by [32-35].This observation affirmed the interrelationship among the process of lipoprotein metabolism and therefore, any fundamental metabolic defect such as increased fasting triglyceride, decreased HDL cholesterol, and increased small dense LDL particles could be for responsible dyslipidemic changes that are seen as part of the components of metabolic syndrome.

This study also established a strong correlation between cortisol and glucose. This is in agreement with the findings of [22, 36] and this observation suggests that glucocorticoid mediates hepatic gluconeogenesis, thereby leading to the elevation of fasting glucose levels in the test subjects. In addition to this mechanism, the inhibition of insulin action on skeletal muscles and the potentiation of insulin action on adipose tissues is exhibited by glucocorticoids. Furthermore Andrews et al. [37] and McMillen et al. [38] reported that cortisol potentiates the lipolytic action of the β adrenergic receptors which are exclusively predominant in visceral adipose tissue, thus increasing free fatty acid flux and promoting insulin resistance which will ultimately give rise to metabolic syndrome.

5. CONCLUSION

This study has been able to establish that elevated serum cortisol level in obese and overweight study subjects positively correlates with more than two components of metabolic syndrome. It has also revealed a striking relationship between cortisol and metabolic syndrome among the study participants which are Nigerian young adults.

While results from larger cross-sectional studies would be far-reaching and would play a significant role in understudying the observations reported in this study among participants from different population, race and ethnic groups, longitudinal studies would also facilitate even better understanding of the observed parameters and changes in the study participants over a given period of time.

CONSENT

All authors declare that 'written informed consent was obtained from the participants enlisted for this study'.

ETHICAL APPROVAL

Informed written consent was obtained from each participant who enrolled for this study and ethical clearance was granted by Babcock University Health Research Ethics Committee (BUHREC).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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