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Association between Adiponectin, Serum Lipids and Obesity in a University Setting in Nigeria

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Summary: Obesity is an energy imbalance condition, which is accompanied by metabolic and cardiovascular complications. Adiponectin, produced by adipocytes, is an important adipokine involved in carbohydrate and lipid metabolism. Adiponectin level is altered in obesity in various populations. In Nigeria, very few studies regarding adiponectin exist, and none, to the best of our knowledge, investigated the relationship between adiponectin and lipid profile and obesity. Therefore, this study aims to evaluate changes in adiponectin level and serum lipids with body mass index, and investigate the relationship between adiponectin, serum lipids and obesity in Nigerian adults. Anthropometric parameters and blood pressure were measured, and blood samples were collected for biochemical assessment after 12 hours fasting, in a total of 280 subjects, comprising of 186 males and 94 females. Serum adiponectin level was evaluated by ELISA, while serum lipid profile was determined by enzymatic endpoint method. Quantitative data were analyzed for significant difference using ANOVA, and Pearson's correlation was used to evaluate relationships. Serum adiponectin level was significantly ($P < 0.05$) highest within overweight male subjects (1.6 ± 0.06 µg/ml), and lowest within normal male subjects (1.4 ± 0.03 µg/ml). The values for adiponectin concentrations were not significantly different in the female subjects. There was no association in serum lipids and adiponectin in both male ($r = -0.035$, $P > 0.05$; $r = -0.011$, $P > 0.05$; $r = -0.053$, $P > 0.05$; $r = -0.084$, $P > 0.05$) and female ($r = 0.061$, $P > 0.05$; $r = 0.018$, $P > 0.05$; $r = 0.057$, $P > 0.05$; $r = -0.021$, $P > 0.05$) for LDL, HDL, TC and TRIG respectively. Lipid profile was not different across BMI classes. There was no relationship between adiponectin and serum lipids in individuals in the study population of adult Nigerians.

Keywords*:* Adiponectin; Lipid profile; Obesity; Males; Females

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INTRODUCTION

Obesity is a condition of energy imbalance (Medeiros Nda *et al.*, 2015), which results in excess deposition of fat in the body (Altabas and Zjacic-Rotkvic, 2015). It is of multi-factorial origin that involves biological, environmental (Ogunbode *et al.*, 2011), nutritional, social and genetic factors (Fall and Ingelsson, 2014). Obesity predisposes to various diseases and complicates comorbid conditions such as insulin resistance, cardiovascular (CVS) diseases (Adamczak and Wiecek, 2013), and various forms of cancers (Kandala and Stranges, 2014). The prevalence of obesity all over the world is increasing at an alarming rate, and is seen in both developed and developing countries, including Nigeria (Iloh *et al.*, 2013). Although obesity has been studied by various researchers across the country (Amira *et al.*, 2012; Oladimeji *et al.*, 2014), there is a wide gap not only in reports from many parts of the country concerning the prevalence, but especially in studies on physiological and biochemical aspects relating to obesity. Data from studies on the prevalence of obesity in Nigeria have revealed variable but close rates. Southwest Nigeria reported the prevalence of overweight and obesity as 20.8 % and 8.4 % respectively, with class I obesity (body mass index, BMI = 30 – 34.9 kgm^2) (Aronne, 2002)as the most common pattern in that part of the country (Adebayo *et al.*, 2014). In northern Nigeria, a study conducted on civil servants has suggested that 35 % of civil servants were overweight, while 27 % were found to be obese (Oladimeji *et al.*, 2014). Similarly, Niger Delta region reported a prevalence of 39.8 % and 28.0 % for overweight and obesity, respectively in men (Idung *et al.*, 2014). In addition, the same study also reported on gender difference in obesity; showing

that more females were found to be overweight and obese than males in the population (Bakari*et al*., 2007).

Previous studies from other parts of the world suggest that overweight and obesity affects serum lipids (Nayak*et al*., 2012; Zhong*et al*., 2015). Many of such studies have reported an increase in triglyceride level, with an increase in BMI (Ozer*et al*., 2015). Elevated level of serum lipids, accompanied with a decrease in high-density lipoprotein cholesterol (HDL), is a condition called dyslipidaemia, which has been associated with adverse health consequences, including cardiovascular diseases, insulin-resistance, type 2 diabetes mellitus and metabolic syndrome, and these conditions are complicated by obesity (Tchernof and Despres, 2013).

There is recent evidence that adipokines particularly adiponectin, which is secreted by adipocytes (Kojima *et al*., 1999; Wang and Scherer, 2016), promotes cardiovascular and metabolic health (Nayak*et al*., 2012). These physiological functions have been correlated with elevated levels of adiponectin, which fosters rise in HDL cholesterol, known to be beneficial to the cardiovascular system (Izadi*et al*., 2013). A recent study has discovered significantly higher prevalence of some cardio-metabolic co-morbidities in research participants, who had low adiponectin levels (Chiara *et al*., 2015). This finding was manifested as a high BMI, along with an equally-high TG level in subjects who were found to have low adiponectin concentration. In addition, respondents with low adiponectin in circulation also had a significantly lower HDL level than their counterparts, whose adiponectin level was higher (Chiara *et al*., 2015). It has been documented that adiponectin concentration decreases with an increasing in BMI; low adiponectin levels have been found in obese individuals (Yamauchi and Kadowaki, 2013).

Adiponectin increases sensitivity to insulin and performs cardioprotective role by preventing plaque formation in arteries (Bredella *et al*., 2011). Lowered adiponectin levels are associated with increased metabolic and cardiovascular risks, and low adiponectin exist in obesity (Yamauchi and Kadowaki, 2013). Consequently, a rise in the prevalence of obesity may be of great concern because it may possibly result in increased morbidity, disability and mortality from associated cardiovascular and metabolic complications. Therefore, the aim of this study was to determine the association between adiponectin and lipid profile in a segment of a Nigerian population, where such studies are lacking.

MATERIALS AND METHODS

Study setting

Kaduna State University is located in Kaduna State, Nigeria. It was established in 2004, and comprises two campuses; one in Kafanchan, and the other in Kaduna metropolis. It has a total of seven faculties, with over thirty-nine Departments. The students come across from all parts of Nigeria; however, residents in the Northern part of the country predominate. Staffs of the institution, likewise, are indigenes of various parts of Nigeria. It has a population of about 7,000 at the time of this study.

Study population

Apparently healthy males (n = 186) and females (n = 94), within the age-group of 18 - 72 years took part in the study. Participants with a normal BMI (18.5 - 24.9) served as the control group, while the other groups were either overweight (BMI of 25 – 29.9) or obese (BMI of ≥ 30). Individuals who smoke or took alcohol were excluded from this study; heavy smoking and/or drinking alcohol are known to modify the adiponectin levels (Nayak *et al.*, 2010). People with known cases of hypertension, diabetes, pregnant women and nursing mothers were also excluded from the study. Ethical approval for the study was obtained from the Health Research Ethical committee, Kaduna State Ministry of Health, Kaduna, with reference number MOH/ADM/744/Vol.1/61. Informed consent was signed by all participants.

Sample size was determined using a prevalence of 22.3 % for obesity in a Nigerian population (Adediran *et al.*, 2012). This calculation gave a sample size of 266.6. Using a finite correction for a population less than 10,000, a final sample size of 256 was obtained.

Data collection

Antecubital venipuncture was used to collect 5 ml of blood sample from each participant into sterile plain tubes after about 12 hours of fasting. Serum was separated and stored into serum storage tubes, then kept in the freezer at about - 80ºC, until needed for biochemical assays. Height and weight were measured, with participants lightly clothed, to the nearest 0.5 kg and 0.1 cm respectively, using a stadiometer. Body mass index (BMI) was calculated as weight-in-kilograms divided by the square of height (in metres). Other demographic parameters such as age, sex, and marital status, were collected. Participants were classified as underweight, if their BMI was < 18.5 kg/m^{-2}, normal weight if their BMI was 18.5- 24.9 kg/m^{-2}, overweight if their BMI was 25.0- 29.9 kg/m^{-2}, and obese if their BMI was ≥ 30 kg/m^{-2}.

Blood pressure (BP) was measured using of a mercury-in-glass sphygmomanometer (model WW-AG-10060, China) and stethoscope (Littman, model 70 – 2006 – 8166 -9, Germany). Participants were classified as hypertensive if their systolic BP was ≥ 140 mmHg; or if their diastolic BP was ≥ 90 mmHg; and if they were on anti-hypertensive drugs.

Biochemical Analyses:
Adiponectin concentration was determined by using ELISA kit, (WKEA) as described by Yamauchi *et al.*, (2001). Total cholesterol was determined using enzymatic method, described by Allain *et al.*, (1974). The cholesterol was determined after enzymatic hydrolysis and oxidation. Serum triglyceride was measured using GPO/PAP method as described by (Khan *et al.*, 1997). Serum high-density lipoprotein cholesterol (HDL) was measured by method of Burstein *et al*. (1970). Serum low-density lipoprotein cholesterol (LDL) was derived from Friedewald equation (Friedewald *et al*., 1972).

Statistical Analysis
Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21. Data are presented as mean ± standard error of mean (SEM) and percentages. One-way analysis of variance (ANOVA) was performed to determine differences between means, while Pearson's correlation analysis was used to test for the association between the means of the parameters. The values of $P < 0.05$ were considered significant.

RESULTS

Characteristics of study participants
Among the study participants, 152 (54.3 %) were within the normal BMI class, 55 (19.6 %) were overweight, and 73 (26.1 %) were obese (Table 1). The mean age for participants with normal BMI was 28.1±0.63 years; the overweight participants were aged 37.0±1.90 years, while the obese subjects had a mean age of 38.4±2.08 years (Table 1). The difference in age across the BMI classification was significant ($P < 0.001$) (Table 1). Age was significantly ($P < 0.05$) lowest within subjects with normal BMI, both in males (28.1±0.63 years) and in females (24.8±1.07 years). There were more male respondents (n = 186) in this study than females (n = 94). More male participants in this study also had normal BMI (67 %), while only 21.7 % of females had normal BMI (Table 1). In addition, obesity was higher in the female subjects (54.8%) than within male subjects (45.2%). Mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) were not significantly different between the groups in males and in females in the study.

Changes in Adiponectin Concentrations in study participants by Body mass index
In the overall study population, mean adiponectin concentration was not significantly different between normal (1.4 ± 0.03 µg/L), overweight (1.5 ± 0.05 µg/L) and obese (1.5 ± 0.03 µg/L) subjects (Table 2). However, when separated according to sex, mean values of serum adiponectin level varied significantly ($P < 0.05$) among male study participants, where adiponectin level was lowest in the normal group of male participants (1.4 ± 0.03 µg/ml), and highest (1.6 ± 0.06 µg/ml) in the overweight group (Table 2). In the female respondents, mean adiponectin concentration was not significantly different between the groups (Table 2).

Changes in Lipid profile of study participants
There were no significant differences in the lipid profile in any of the sexes (Table 3). All the serum lipids, except for HDL, showed an insignificantly high value in the overweight groups, in both males and females. HDL did not vary between the groups in male and in female subjects.

Correlations
There were no significant association(s) between adiponectin and any of fractions of serum lipids which were assayed; LDL, HDL, TC and TG were not significant in males and females (Table 4).

Table 1. Age and Sex Variations in blood pressure of participants according to BMI

	Variable	Normal (n = 152)	Overweight (n = 55)	Obese (n = 73)	P-value
BMI	BMI (kg/m^2)	18.5 – 24.9	25 – 29.9	>30	
	Percentages	54.3	19.6	26.1	
Age (years)	Mean age	27.6 ± 6.79	36.8 ± 12.00	36.5 ± 11.57	0.000**
	< 25	69 (76.6%)	8 (8.9%)	13 (14.4 %)	
	25- 39	71 (54.2 %)	28 (21.4 %)	32 (24.4 %)	
	≥ 40	12(20.3%)	19 (32.2 %)	28 (47.5 %)	
Sex	Males	113 (60.8%)	40 (21.5%)	33 (17.7%)	
	Females	39 (41.5%)	15 (16.0%)	40 (42.6%)	
Blood pressure (mm Hg)	SBP	116.5 ± 1.15	119.1 ± 2.64	115.1 ± 1.54	NS
	DBP	80.5 ± 1.90	78.9 ± 1.24	79.0 ± 0.7157	NS

SBP = systolic blood pressure, DBP = diastolic blood pressure, SEM = standard error of mean, BMI = body mass index, NS = non-significant difference

Table 2: Adiponectin level in Male and Female subjects based on Body mass index

	Variables	Normal	Overweight	Obese	P-value
	n	152	55	73	
	Adiponectin (µg/L)	1.4 ± 0.03	1.5 ± 0.05	1.5 ± 0.03	> 0.05
Males	n	113	40	33	
	Adiponectin (µg/L)	1.4 ± 0.03	1.6 ± 0.06	1.5 ± 0.05	< 0.05
Females	n	39	15	40	
	Adiponectin (µg/L)	1.5 ± 0.06	1.4 ± 0.07	1.5 ± 0.05	NS

Table 3: Changes in Serum lipids in Males and Females according to BMI

	Variables	Normal	Overweight	Obese	p-value
Males	N	113	40	33	
	LDL-c (mmol/L)	1.8 ± 0.10	2.2 ± 0.30	2.0 ± 0.19	NS
	HDL-c (mmol/L)	0.8 ± 0.05	0.8 ± 0.05	0.8 ± 0.08	NS
	Total Cholesterol (mmol/L)	3.3 ±0.10	3.6 ± 0.30	3.5 ± 0.21	NS
	Triglycerides (mmol/L)	1.4 ± 0.08	1.7 ± 0.23	1.5 ± 0.15	NS
Females	N	39	15	40	
	LDL-c (mmol/L)	2.3 ± 0.22	2.6 ± 0.36	2.0 ± 0.19	NS
	HDL-c (mmol/L)	0.8 ± 0.04	0.8 ± 0.08	0.8 ± 0.05	NS
	Total Cholesterol (mmol/L)	3.6 ± 0.21	4.0 ± 0.33	3.4 ± 0.17	NS
	Triglycerides (mmol/L)	1.4 ± 0.12	1.9 ± 0.25	1.4 ± 0.09	NS

NS= non-significant difference

Table 4: Correlation (r) between adiponectin and serum lipids

Correlated Parameters	Males (n = 186)	Females (n = 94)
	r (P value)	r (P value)
Adiponectin and Low-density lipoprotein	-0.035 NS	0.061 NS
Adiponectin and High-density lipoprotein	-0.011 NS	0.018 NS
Adiponectin and Total cholesterol	-0.053 NS	0.057 NS
Adiponectin and Triglycerides	-0.084 NS	-0.021 NS
Adiponectin and Glucose	0.087 NS	0.016 NS

NS = non-significant difference

DISCUSSION

In the present study, the result showed a significant difference in age between the normal and overweight subjects. As was expected, subjects who were within the normal BMI class of 18.5 – 24.9 kg/ m^2 had the lowest age (27.0 ± 6.79 years), while older (36.8 ± 12.00 and 36.5 ± 11.57 years) subjects were overweight and obese respectively. The observed gradient increase in BMI with age agrees with the finding of Chinedu *et al*. (2013), who observed increased BMI in older age group in both males and females. The female subjects had higher BMI than the male subjects in the study, and this observation conforms to the study of Bakari *et al*. (2006), who reported that females had a higher BMI than their male counterparts (26.6 ± 7.2 kg/m^2 versus 24.0 ± 5.4 kg/m^2) in a study conducted in Zaria (Bakari *et al*., 2006); and the result of Meilleur *et al*. (2010), conducted on West-Africans, which also found obesity to be higher in females than in males (Meilleur *et al*., 2010). Also, in the present study, increased BMI that was observed in older women agrees with the findings of (John *et al*., 2015). Reason for increased BMI in women could be due to changes in estrogens. Activities of estrogens before menopause, confers some cardiovascular protection in women, and the protection is lost during and after menopause, with a consequent physiologic outcome of decrease in basal metabolism and weight gain (Okafor *et al*., 2014). These, together, enhance fat deposition in the body. Besides, despite the fewer number of females in the study compared to male subjects (94 versus 186), 54.8 % of the obese participants were females and 45.2 % were males. The finding clearly demonstrates that females physiologically have the ability to store more subcutaneous fat than males, as established in previous literature (Palmer and Clegg, 2015).

Adiponectin, one of the proteins that are almost exclusively secreted from adipocytes, is a potent modulator of glucose and lipid metabolism and an indicator of metabolic disorders (Martin *et al*., 2005). In the present study, serum adiponectin level was significantly higher within overweight males, compared with normal-weight males. The value for adiponectin concentration was not significantly different across the groups in female subjects. Previous studies have reported increase in adiponectin level with lower BMI, have associated adiponectin with anthropometric indices and triglyceride concentration in obesity (Ayina *et al*., 2016). However,

other studies also failed to establish a relationship between adiponectin level and BMI in an Iranian population (Vayghan *et al*. (2013). Calorie-restriction has been found to increase adiponectin level (Weiss *et al*., 2006), but major diet in Nigeria consist of carbohydrates, which have high-calories. The amount of energy intake have been reported as a key factor in controlling adiponectin expression and circulating level, where high calories are found to decrease adiponectin concentration (Lee and Shao, 2014).

Ryan *et al.* (2003) reported that the duration of overweight/obese status could contribute to the disparity in results, while also considering that moderate weight loss may not significantly change the level of adiponectin.

None of the assayed serum lipids significantly changed with BMI in both male and female subjects in the study, and this agrees with the study of Shah *et al*. (2016), who failed to observe significant changes in serum lipids with BMI (Shah *et al.*, 2016). In contrast, overweight and obese individuals in various geographic locations have been reported to have higher total cholesterol in the body (Del Mar Bibiloni *et al.*, 2016).

Adiponectin was not significantly correlated with LDL, HDL, TC, and TG in males and females. The finding suggests that adiponectin concentration may not be determined by level of serum lipids in the present study. Other studies in various populations have observed positive correlations between adiponectin and HDL, and adiponectin and TG (Song *et al*., 2014). In addition, Maghosoudi *et al*. (2016) reported positive and significant association between adiponectin and HDL.The findings in the present study could be due to the relatively small sample size which may be too small to capture significant differences in the serum lipids.

In conclusion, there is no significant association between adiponectin and serum lipids in both adult males and females in a university setting in Nigeria. Adiponectin levels differed with BMI only in male subjects, in the current study.

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