ROS

RESEARCH ARTICLE

Cardiovascular Risk Factors and Oxidative Stress Indices in Obese Women in Southern Nigeria

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ABSTRACT | Oxidative stress has been implicated in obesity-associated dyslipidemia and microvascular complications. In this study, the lipid profile and oxidative stress indices were evaluated in obese women. Ninety women (22–55 years) comprising 40 obese, 20 overweight and 30 controls were studied. Total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), malondialdehyde (MDA), lipid hydroperoxides, total antioxidant capacity (TAC), reduced form of glutathione (GSH), and nitric oxide (NO) were estimated colorimetrically, and low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), oxidative stress index (OSI), and atherogenic index of plasma (AIP) were determined by calculation. Anthropometric indices and blood pressure (BP) were also obtained. Our results showed that obese women had lower antioxidants and higher BP, lipid peroxidation, and OSI with unfavorable lipid profile (higher TC, TG, LDL, VLDL, and AIP; lower HDL) compared to overweight and controls ($p < 0.05$). Overweight women had higher BP, lipid peroxidation, and decreased antioxidants compared to controls ($p < 0.05$). Positive correlations were observed between MDA and TC ($r = 0.336$, $p = 0.034$) and LDL ($r = 0.322$, $p = 0.043$), and negative correlation between HDL and AIP ($r = –0.636$, $p < 0.001$) in obese women. In conclusion, obesity is associated with increased LDL-C, lipid peroxidation, and reduced antioxidants which may lead to oxidative stress and increased risk for atherosclerosis in obese women studied.

KEYWORDS | Dyslipidemia; Lipid peroxidation; Obesity; Oxidative stress; Total antioxidant capacity

ABBREVIATIONS | AIP, atherogenic index of plasma; BMI, body mass index; BP, blood pressure; DBP, diastolic blood pressure; GSH, reduced form of glutathione; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; LPH, lipid hydroperoxide; MDA, malondialdehyde; NO, nitric oxide; OSI, oxidative stress index; oxLDL, oxidized LDL; ROS, reactive oxygen species; SBP, systolic blood pressure; SNS, sympathetic nervous system; TAC, total antioxidant capacity; TBARS, thiobarbituric acid-reactive substances; TC, total cholesterol; TG, triglycerides; TNF-α, tumor necrosis factor-alpha; TPP, triphenylphosphine; VLDL-C, very low-density lipoprotein-cholesterol; WC, waist circumference

CONTENTS

1. INTRODUCTION

Obesity has become an epidemic and represents the major risk factor for several chronic diseases including diabetes, cardiovascular disease (CVD), and cancer. Although the exact biochemical mechanisms underlying the association between obesity and these chronic illnesses have not been completely elucidated [1], systemic oxidative stress and inflammation have been described as key factors in the pathology of these obesity-related complications [2]. Epidemiological, clinical, and animal studies have shown that obesity is associated with increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which are produced continuously in the body via oxidative metabolism, mitochondrial bioenergetics, and immune function [3], leading to disturbances in cellular redox homeostasis, oxidation of cell membranes and proteins, oxidative stress, and cellular damage [4]. Oxidative stress could play a causative role in the development of obesity through stimulation of white adipose tissue deposition, control of body weight via effects on hypothalamic neurons that control satiety and hunger behavior, and altering food intake [5]. Dyslipidemia, characterized by hypertriglyceridemia, hypercholesterolemia, and low concentrations of high-density lipoprotein (HDL)-cholesterol has been described in both overweight and obese subjects [6]. Chronic hypernutrition, high-fat and high-carbohydrate (HFHC) meals, as well as high dietary saturated fatty acids (SFA) and trans-fatty acids, have been implicated in obesity-associated lipoprotein abnormalities [7]. Their transformation into energy is accompanied by an increased generation of free radicals [8]. Elevated levels of markers of lipid peroxidation and oxidative DNA damage [9] with lower levels of vitamins C and E, and superoxide dismutase and catalase enzyme activities have been reported in overweight and obese subjects [10].

Studies have shown that genetic, environmental, cultural, and socio-economic factors contribute to obesity [7]. Ethnic and individual dietary peculiarities (increased intake of energy-dense foods and decreased intake of food rich in micronutrients and bioactive compounds) may directly or indirectly modulate redox balance, lipid profile, inflammatory biomarkers, and endothelial function, and contribute to oxidative stress [11]. Levels of some biomarkers of oxidative stress in conjunction with cardiovascular risk factors of women resident in Calabar, Southern Nigeria, whose dietary intake is predominated by consumption of palm oil containing high concentrations of saturated fatty acids (palmitic acid) were determined in this study. Knowledge of the levels of biomarkers of oxidative stress in obese individuals

may be useful for prevention and management of obesity-related complications.

2. MATERIALS AND METHODS

2.1. Study Design

This case-control study was carried out in Calabar Municipal Local Government Area of Cross River state, Nigeria. The study population comprised obese, overweight, and normal weight women aged eighteen to fifty-five years. Informed consent was sought and obtained from subjects before recruitment into the study and the Cross River State Ministry of Health Research ethics committee approved the study protocol. This study was carried out in accordance with the ethical principles for medical research involving human subjects as outlined in the Helsenki declaration in 1975 and subsequent revisions. Obesity was defined according to the World Health Organization (WHO) criteria of body mass index (BMI) ≥ 30 kg/m^2. All women of the study population were classified based on the BMI: (1) normal weight, BMI (18.5– < 25 kg/m^2); (2) overweight, BMI (25.0–29.9 kg/m^2); and (3) obese, BMI (≥ 30.0 kg/m^2) [12]. The inclusion criteria were: female gender, age range 18–55 years, not pregnant, and with consent. The exclusion criteria were: pregnant and lactating mothers, presence of chronic organ or systemic illness or long-term medication and those without consent.

2.2. Selection of Subjects

A total of 90 consenting female subjects, comprising 40 obese women with BMI of ≥ 30 kg/m^2, 20 overweight women with BMI of 25.0–29.9 kg/m^2, and 30 normal weight women (controls) with BMI of 18.5– < 25 kg/m^2 living within Calabar Municipality, were recruited into the study. Anthropometric indices such as weight and height were obtained and used to calculate BMI; waist circumference and hip circumference were obtained and used to calculate waist to hip ratio. Systolic and diastolic blood pressure was also measured. Socio-demographic information was obtained by way of interview-administered study questionnaire to determine education, marital and socioeconomic status, and medical and drug history. Subjects were advised to come in fasting state on the day of sample collection.

2.3. Sample Collection

Five milliliters of whole blood sample were aseptically collected via venipuncture into a clean dry plain sample container and kept away from direct sunlight. The blood samples were taken to a laboratory and allowed to clot and retract, and then were spun at 500 *g* for 5 min to obtain the serum. The serum was extracted and dispensed into a 5 ml dry and chemically clean serum container, after which the samples were stored at 20^{o}C and analyzed within one week.

2.4. Laboratory Methods

2.4.1. Determination of Total Antioxidant Capacity

A standard solution of ferric ion-ethylenediaminetetraacetic acid (Fe-EDTA) complex was used to react with H_2O_2 by a Fenton-type reaction, leading to the formation of hydroxyl radicals. The formed hydroxyl radicals then degrade benzoate resulting in the release of TBARS (thiobarbituric acid-reactive substances). The antioxidant molecules from the added sample cause suppression of the production of TBARS. This reaction is measured spectrophotometrically at 532 nm, and the inhibition of color development is defined as the total antioxidant capacity (TAC) of the sample [13].

2.4.2. Estimation of Lipid Hydroperoxides

The level of lipid hydroperoxides (LHP) was estimated by FOX-2 assay in conjunction with triphenylphosphine (TPP). The reaction of ferrous-butylated hydroxytoluene-xylenol orange complex (FOX-2 reagent) with serum peroxides yields a colored complex that was measured spectrophotometrically at 560 nm. TPP, a selective LHP-reducing agent is included to ensure assay specificity. The absorbance difference between the samples without and with TPP indicates the presence of LHP and is expressed as μM H_2O_2 equivalent [14].

2.4.3. Calculation of Oxidative Stress Index

The ratio of TPP-sensitive LHP to TAC was calculated as the oxidative stress index (OSI), an indicator of the degree of oxidative stress: OSI (%) = [LHP (μM H_2O_2) × 100] ÷ [TAC (μM)] [14].

2.4.4. Estimation of Nitric Oxide

The Griess test was used for detecting total levels of nitrite or nitrous acid in the samples. The nitric oxide (NO)-containing compounds in the serum combine with alpha-naphthylamine to produce a pink azo dye whose absorbance was measured spectrophotometrically at 540 nm. Total nitrite and nitrate levels were represented as total nitric oxide metabolites (NOx) and measurement of NOx is considered a marker of in vivo NO production [15].

2.4.5. Estimation of GSH

Estimation of the GSH content was carried out following the modified Ellman's method. The reagent, 5,5'-dithiobis(2-nitrobenzoic acid) (DTNB, Ellman's reagent) reacts with GSH to form a chromophore, which is measured spectrophotometrically at 412 nm [16].

2.4.6. Estimation of Malondialdehyde

Malondialdehyde (MDA) formed from the breakdown of polyunsaturated fatty acids serves as a convenient index for determining the extent of the peroxidation products that react with thiobarbituric acid to give a red species. This chromophore was measured spectrophotometrically at 532 nm [17].

2.4.7. Estimation of Total Cholesterol

Total cholesterol (TC) was measured enzymatically in the serum or plasma in a series of coupled reactions that hydrolyze cholesteryl esters and oxidize the 3-OH group of cholesterol, as described before [18]. One of the reaction byproducts, H_2O_2, was determined in a peroxidase-catalyzed reaction that produces a colored product, which was measured spectrophotometrically at 500 nm.

2.4.8. Estimation of Triglycerides

Triglycerides (TG) were measured enzymatically in the serum or plasma using a series of coupled reactions in which triglycerides are hydrolyzed to produce glycerol [19]. Glycerol was then oxidized using glycerol oxidase, and H_2O_2, one of the reaction products, was measured as described above for total cholesterol.

2.4.9. Estimation of HDL-Cholesterol

When the serum was combined with the polyethylene glycol reagent, all beta-lipoproteins (LDL and VLDL) were precipitated. The HDL fraction (alpha fraction) remained in the supernatant. The supernatant was then treated as a sample and assayed for HDL-cholesterol by an enzymatic method [20].

2.4.10. Estimation of LDL-Cholesterol

The LDL-cholesterol (LDL-C) concentration was calculated from the total cholesterol concentration, HDL-cholesterol concentration, and the triglyceride concentration using the formula of Friedewal et al. [21]: LDL-C (mmol/l) = total cholesterol – HDL-C – [triglyceride concentration ÷ 2.2].

2.4.11. Estimation of VLDL-Cholesterol

VLDL-cholesterol (VLDL-C) concentration was calculated from the triglyceride concentration using the formula of Friedewal et al. [21]: VLDL-C (mmol/l) = triglyceride concentration ÷ 2.2.

2.4.12. Estimation of Atherogenic Index of Plasma

Atherogenic index of plasma (AIP) was calculated from the concentrations of triglycerides and high HDL-C using the following formula [22]: AIP = log[triglycerides (mmol/l) ÷ HDL-C (mmol/l)].

2.5. Statistical Analysis

Data analysis was done using the statistical package for social sciences (SPSS version 20.0, IBM, USA). Analysis of variance was used to test significance of variations within and among group means and Fisher's least significant difference (LSD) post-hoc test was used for comparison of multiple group means. Pearson's correlation was used to determine associations between variables. A probability value $p < 0.05$ was considered statistically significant.

3. RESULTS

Table 1 shows age, cardiovascular risk factors, and oxidative stress indices in normal weight, overweight, and obese women. Significant variations were ob-

TABLE 1. Age, cardiovascular risk factors, and oxidative stress indices in normal weight, overweight, and obese women

Index	Controls (n = 30)	Overweight (n = 20)	Obese (n = 40)	F ratio	p Value
Age (age)	30.87 ± 7.70	30.75 ± 6.18	30.15 ± 7.05	0.101	0.904
WC (cm)	77.18 ± 8.31	75.97 ± 7.41	113.25 ± 13.88	122.350	< 0.001
BMI (kg/m^2)	22.47 ± 1.76	27.34 ± 1.54	35.51 ± 5.52	99.329	< 0.001
SBP (mmHg)	111.30 ± 9.03	122.50 ± 4.58	124.77 ± 8.23	26.559	< 0.001
DBP (mmHg)	62.13 ± 2.46	68.00 ± 4.21	72.85 ± 9.21	22.452	< 0.001
TC (mmol/l)	4.08 ± 0.82	4.52 ± 0.89	5.13 ± 1.15	9.724	< 0.001
TG (mmol/l)	0.74 ± 0.24	0.93 ± 0.40	1.05 ± 0.53	4.829	0.010
LDL-C (mmol/l)	2.27 ± 0.71	2.50 ± 0.88	3.47 ± 1.09	15.997	< 0.001
VLDL-C (mmol/l)	0.33 ± 0.11	0.42 ± 0.18	0.48 ± 0.24	4.810	0.010
HDL-C (mmol/l)	1.47 ± 0.37	1.54 ± 0.25	1.15 ± 0.28	15.301	< 0.001
AIP	–0.39 ± 0.19	–0.25 ± 0.21	–0.06 ± 0.23	13.000	< 0.001
MDA (nmol/ml)	0.92 ± 0.55	1.67 ± 0.66	1.95 ± 1.15	11.695	< 0.001
GSH (µmol/l)	66.55 ± 12.26	50.83 ± 5.13	50.72 ± 5.52	35.877	< 0.001
NO (µmol/l)	8.06 ± 5.91	1.304 ± 1.75	0.95 ± 0.65	39.023	< 0.001
LHP (µmol/l)	336.51 ± 68.94	385.36 ± 83.63	494.22 ± 122.69	22.966	< 0.001
TAC (µmol/l)	1966.24 ± 666.63	1184.26 ± 191.43	704.53 ± 133.72	83.300	< 0.001
OSI (%)	24.08 ± 22.82	33.21 ± 7.99	70.74 ± 12.84	80.512	< 0.001

served in all the biochemical indices among the 3 groups studied ($p < 0.05$).

The comparison of cardiovascular risk factors and oxidative stress indices in normal weight, overweight, and obese women using LSD post hoc analysis was depicted in **Table 2**. The waist circumference **(**WC), BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), TC, TG, LDL-C, VLDL-C, AIP, MDA, LHP, and OSI were significantly higher and HDL-C, GSH, NO, and TAC lower in obese compared to controls; higher BMI, SBP, DBP, and MDA and lower GSH, NO, and TAC were observed in overweight individuals compared to control subjects ($p < 0.05$). Obese subjects had higher WC, BMI, DBP, TC, LDL-C, AIP, LHP, and OSI and lower HDL-C and TAC compared to overweight subjects ($p < 0.05$).

Figure 1 shows the correlation plot of TC against MDA in obese women. A significant positive correlation was observed between TC and MDA ($r = 0.336$, $p = 0.034$) in the obese women studied. The correlation plot of LDL-C against MDA in obese women is shown in **Figure 2**. A significant positive correlation was observed between LDL-C and MDA ($r = 0.322$, $p = 0.043$) in the obese women studied.

Figure 3 shows the correlation plot of AIP against HDL-C in obese women. As shown, a significant negative correlation was observed between AIP and HDL-C ($r = –0.636$, $p < 0.001$) in the obese women studied.

4. DISCUSSION

Obesity-related complications, including hypertension, dyslipidemia, insulin resistance, type 2 diabetes, and cardiovascular events, have been associated with increasing rate of morbidity, reduced life expectancy, and mortality among young people. ROS and the associated oxidative stress have been implicated in the development of obesity and its related complications. Some cardiovascular risk factors and biomarkers of oxidative stress were evaluated in obese women in this study.

In our study, obese and overweight women had higher WC, BMI, DBP, and SBP (though within normal) than controls. Obesity has been described as a state of hemodynamic overload associated with increase in cardiac output and blood pressure. Obesity-related hypertension have been described as a multifactorial and polygenic trait, and multiple potential pathologic mechanisms including hyperinsulinemia, activation of the renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system (SNS) stimulation, abnormal levels of certain adipokines such as leptin, or cytokines acting at the vascular en-

TABLE 2. Comparison of cardiovascular risk factors and oxidative stress indices in normal weight, overweight, and obese women using LSD post hoc analysis

Index	Group		Mean difference	p Value
	Controls (n = 30)	*Obese (n = 40)*		
WC (cm)	77.18 ± 8.31	113.25 ± 13.88	–36.07 ± 2.66	< 0.001
BMI (kg/m^2)	22.47 ± 1.76	35.51 ± 5.52	–13.04 ± 0.94	< 0.001
SBP (mmHg)	111.30 ± 9.03	124.77 ± 8.23	–11.20 ± 2.27	< 0.001
DBP (mmHg)	62.13 ± 2.46	72.85 ± 9.21	–10.72 ± 1.59	< 0.001
TC (mmol/l)	4.08 ± 0.82	5.13 ± 1.15	–1.05 ± 0.24	< 0.001
TG (mmol/l)	0.74 ± 0.24	1.05 ± 0.53	–0.32 ± 0.10	0.003
LDL-C (mmol/l)	2.27 ± 0.71	3.47 ± 1.09	–1.20 ± 0.23	< 0.001
VLDL-C (mmol/l)	0.33 ± 0.11	0.48 ± 0.24	–0.14 ± 0.05	0.003
HDL-C (mmol/l)	1.47 ± 0.37	1.15 ± 0.28	0.32 ± 0.07	< 0.001
AIP	–0.39 ± 0.19	–0.06 ± 0.23	–0.25 ± 0.05	< 0.001
MDA (nmol/ml)	0.92 ± 0.55	1.95 ± 1.15	–1.03 ± 0.21	< 0.001
GSH (µmol/l)	66.55 ± 12.26	50.72 ± 5.52	15.83 ± 2.01	< 0.001
NO (µmol/l)	8.06 ± 5.91	0.95 ± 0.65	7.09 ± 0.85	< 0.001
LHP (µmol/l)	336.51 ± 68.94	494.22 ± 122.69	–157.71 ± 23.98	< 0.001
TAC (µmol/l)	1966.24 ± 666.63	704.53 ± 133.72	1261.70 ± 97.85	< 0.001
OSI (%)	24.08 ± 22.82	70.74 ± 12.84	–46.66 ± 3.91	< 0.001
	Controls (n=30)	*Overweight (n = 20)*		
BMI (kg/m^2)	22.47 ± 1.76	27.34 ± 1.54	–4.87 ± 1.12	< 0.001
SBP (mmHg)	111.30 ± 9.03	122.50 ± 4.58	–11.20 ± 2.27	< 0.001
DBP (mmHg)	62.13 ± 2.46	68.00 ± 4.21	–5.86 ± 1.91	0.003
MDA (nmol/ml)	0.92 ± 0.55	1.67 ± 0.66	–0.75 ± 0.26	0.004
GSH (µmol/l)	66.55 ± 12.26	50.83 ± 5.13	15.72 ± 2.41	< 0.001
NO (µmol/l)	8.06 ± 5.91	1.304 ± 1.75	6.75 ± 1.02	< 0.001
TAC (µmol/l)	1966.24 ± 666.63	1184.26 ± 191.43	781.98 ± 116.96	< 0.001
	Obese (n=40)	*Overweight (n = 20)*		
WC (cm)	113.25 ± 13.88	75.97 ± 7.41	37.27 ± 3.02	< 0.001
BMI (kg/m^2)	35.51 ± 5.52	27.34 ± 1.54	8.17 ± 1.07	< 0.001
DBP (mmHg)	72.85 ± 9.21	68.00 ± 4.21	4.85 ± 1.82	0.009
TC (mmol/l)	5.13 ± 1.15	4.52 ± 0.89	0.61 ± 0.27	0.029
LDL-C (mmol/l)	3.47 ± 1.09	2.50 ± 0.88	0.96 ± 0.26	< 0.001
HDL-C (mmol/l)	1.15 ± 0.28	1.54 ± 0.25	–0.40 ± 0.08	< 0.001
AIP	–0.06 ± 0.23	–0.25 ± 0.21	0.18 ± 0.06	0.002
LHP (µmol/l)	494.22 ± 122.69	385.36 ± 83.63	108.85 ± 27.19	< 0.001
TAC (µmol/l)	704.53 ± 133.72	1184.26 ± 191.43	–479.73 ± 110.95	< 0.001
OSI (%)	70.74 ± 12.84	33.21 ± 7.99	37.53 ± 4.43	< 0.001

dothelial level probably contribute to the development of higher BP in obese humans [23]. Obesity activates the RAAS leading to increased aldosterone levels, sodium retention, expansion of extracellular fluid volume, augmented cardiac output, and increased BP [24]. Hyperinsulinemia associated with obesity results in increased SNS activity and high BP. This is supported by studies which demonstrated concomitant decreases in BP and SNS activity when insulin is lowered by low energy diets in obese patients. Insulin also directly act on the kidney to stimulate sodium retention [25]. A higher prevalence of hypertension has been reported in obese individuals when compared to those with normal body weight, confirming previously documented associations between increased body size and hypertension [26].

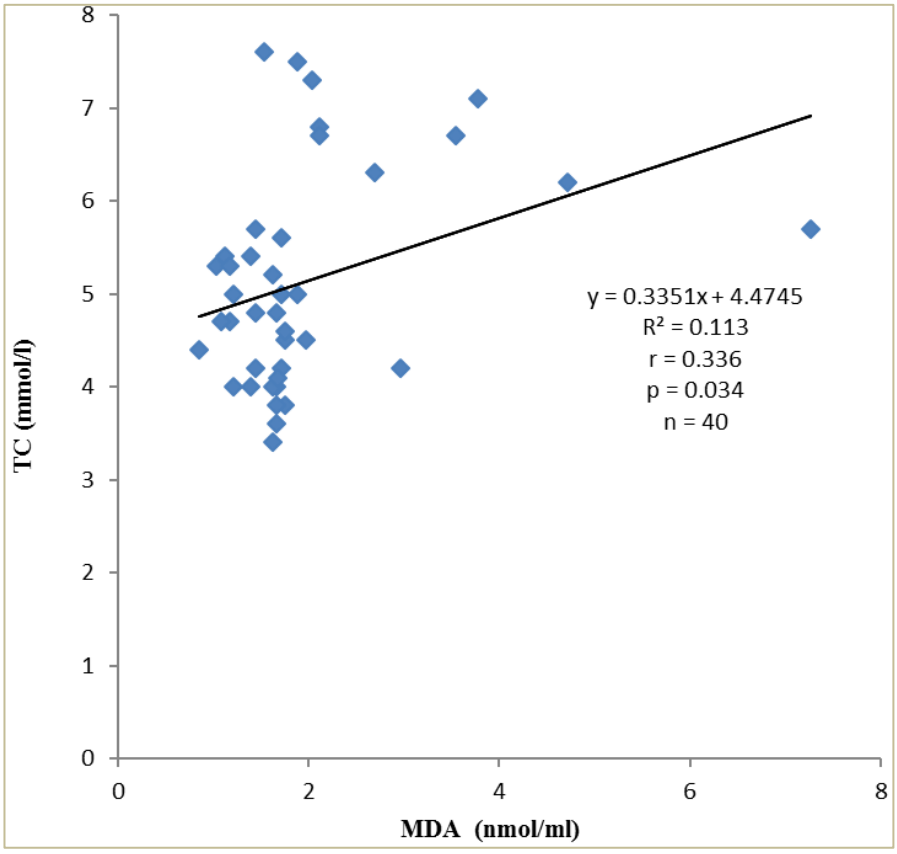

FIGURE 1. Correlation of TC against MDA in obese subjects. As shown, a significant positive association was observed between TC and MDA in the obese subjects.

The MDA, lipid hydroperoxides, and OSI were significantly higher and GSH, NO, and TAC lower in obese and overweight women compared to control subjects studied. Previous studies have shown that low-grade chronic inflammation found in obesity increases the expression and activity of pro-oxidant enzymes including myeloperoxidase and NADPH oxidases and promotes the production of reactive free radicals [27]. Although the mechanisms for obesity-induced oxidative stress remain unclear, leptin, an adipocyte-derived hormone, has been considered as an important contributor. Leptin is responsible for regulating energy intake and expenditure and is also known to play a key role in mediating pro-inflammatory state in obese individuals [28]. Stimulation of mitochondrial oxidation of fatty acids and the elevation of pro-inflammatory cytokines have been described as possible mechanisms for the leptin-induced oxidative stress [29]. Obesity can independently cause increased lipid peroxidation by progressive and cumulative cell injury resulting from pressure from the large body mass. Cell injury causes the release of cytokines, especially tumor necrosis factor-alpha (TNF-α) which generates ROS from the tissues which in turn cause lipid peroxidation and hence higher levels of MDA seen in overweight and obese subjects studied [30]. Our previous study has reported higher levels of TNF-α in obese subjects compared to non-obese controls [31]. Overnutrition and decreased physical activity seen in obesity lead to increased glucose and free fatty acid loads in cells. Their transformation into energy is accompanied by an increased generation of free radicals and peroxidation of biomolecules [32]. Elevated levels of markers of lipid peroxidation and oxidative DNA damage have been demonstrated in overweight and

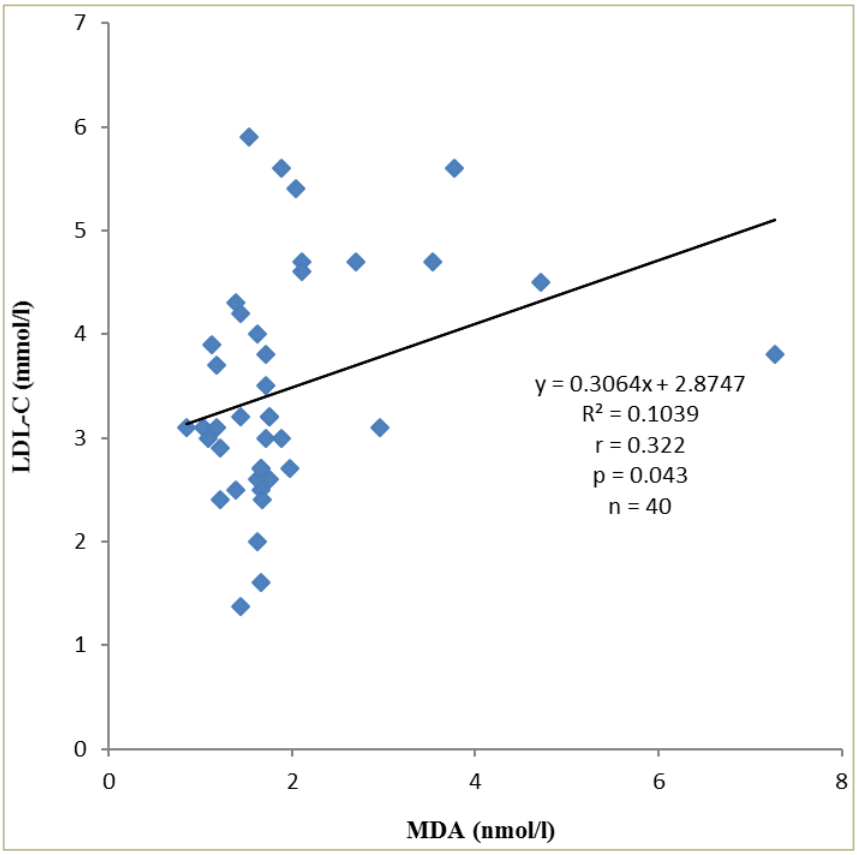

FIGURE 2. Correlation of LDL-C against MDA in obese subjects. As shown, a significant positive association was observed between LDL-C and MDA in the obese subjects.

obese subjects [9]. Lower NO levels were observed in obese and overweight subjects compared to controls studied. High levels of free fatty acids under conditions of overweight and obesity in the presence of hypercholesterolemia have been shown to inhibit nitric oxide synthase (NOS) and reduce NO production. An increase in the production of superoxide and peroxynitrite in persons with obesity has been linked to diminished availability of NO. NO is an important anti-atherogenic agent and physiological regulator of diverse functions in several tissues including cardiovascular, neuromuscular, neurological, genitourinary, gastrointestinal, and renal tissues [33]. Lower GSH and TAC levels were observed in overweight and obese subjects studied compared to controls. Lower GSH and TAC seen in overweight and obese women studied may be as a result of their consumption in the neutralization of excess ROS generated in overweight and obese conditions. Overweight and obese subjects have also been documented to have an inadequate antioxidant defense that contributes to oxidative stress while BMI and bodyweight have been inversely associated with serum concentrations of antioxidants [34, 35]. Oxidative stress has been implicated in all the stages of atherogenesis, from endothelial dysfunction to atheromatous plaque formation and rupture [36].

Unfavorable lipid profile characterized by higher levels of TC, TG, LDL-C, VLDL-C, and AIP and lower levels of HDL-C were observed in obese subjects compared to controls studied. Dyslipidemia characterized by elevated postprandial TG in combination with preponderance of small dense LDL-C and low HDL-C have been described in obesity [37]. The pathophysiology of the typical dyslipidemia observed in obesity is multifactorial and includes hepat-

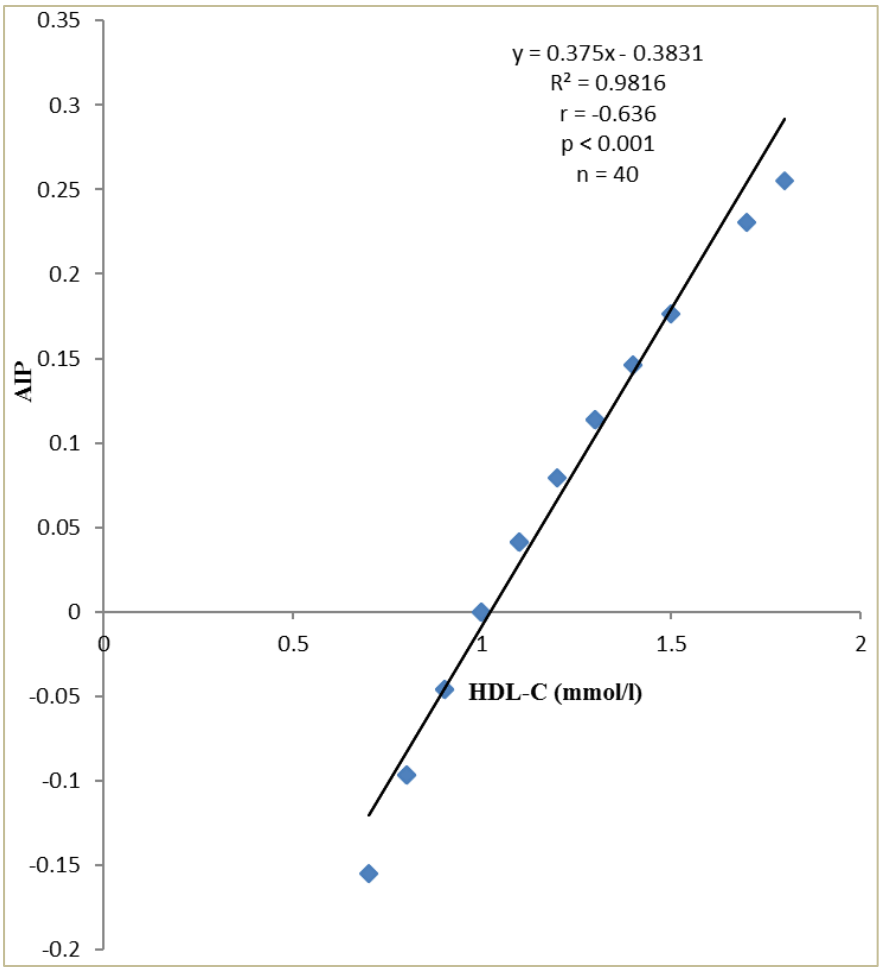

FIGURE 3. Correlation of AIP against HDL-C in obese subjects. As shown, a remarkably significant negative association was observed between AIP and HDL-C in the obese subjects.

ic overproduction of VLDL-C, decreased circulating TG lipolysis, impaired peripheral free fatty acid (FFA) trapping, increased FFA fluxes from adipocytes to the liver and other tissues, and increased formation of small dense LDL [37]. Hypertriglyceridemia in part is due to increased FFA fluxes to the liver, which leads to hepatic accumulation of TG. This causes an increased hepatic synthesis of VLDL-C, which hampers the lipolysis of chylomicrons with increased remnant TG being transported to the liver [38]. Hypertriglyceridemia has also been associated with other lipid abnormalities because of its role in delayed clearance of the TG-rich lipoproteins and formation of small dense LDL [38]. Lower HDL-C levels observed in obese subjects have been attributed to increased fractional clearance of HDL-C secondary to depletion of its cholesterol. Many key enzymes involved in HDL metabolism have been shown to be altered in obese individuals with insulin resistance [39]. On the other hand, effect of hypertriglyceridemia on the functioning of the mitochondrial respiratory chain promotes the generation of superoxide leading to oxidative stress. Oxidative stress has been associated with hypertriglyceridemia and decreased HDL-C [40].

Positive correlations were observed between MDA and TC, and MDA and LDL-C in obese subjects studied. Nutritional obesity which is the predominant

form in our study population implies the consumption of hyperlipidemic diets which may be involved in oxygen metabolism. Oxidation of the double bonds in the fatty acid molecules consequently results in lipid peroxidation and higher MDA levels [4]. Thus, the higher the TC and LDL-C levels as seen in obese subjects studied, the higher the peroxidation product MDA and vice versa. A positive relationship between lipid peroxidation level and plasma cholesterol concentration has also been described [41]. The oxidative conversion of LDL to oxidized LDL (oxLDL) is considered to be a key factor in the pathophysiological process that initiates and accelerates the development of early atherosclerotic lesion [42].

5. CONCLUSION

The findings of this study have shown that obesity is associated with depletion of antioxidants, increased lipid peroxidation, and moderately elevated LDL-C which may result in oxidative stress, oxidative conversion of LDL to oxLDL with increased risk for development of atherosclerosis in obese women studied.

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