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OXIDATIVE STRESS DEMOGRAPHY IN METABOLICALLY HEALTHY OBESITY

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Abstract

Obesity is often linked to oxidative stress due to an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses. This oxidative stress plays a significant role in obesity-related complications, including insulin resistance and cardiovascular diseases. This study examines the pattern of some antioxidants in metabolically healthy overweight and obese Nigerians to understand their role in maintaining metabolic health despite excess adiposity. A prospective cross-sectional observational study was conducted with metabolically healthy participants categorized as normal weight, overweight, or obese. Participants were recruited from Lagos University Teaching Hospital (LUTH) and the general populace. Metabolically healthy status was defined by the absence of hypertension, diabetes, thyroid disorders, cancer, or obesity-related disorders, and not taking medications for these conditions. Anthropometric measurements, blood pressure, and blood samples were collected and analyzed for various biochemical markers, including glucose, lipid profiles, and antioxidant

levels. The study adhered to ethical standards, with approval granted by LUTH's Medical Ethical Committee. The age distribution of participants showed an increased prevalence of obesity in middle-aged Nigerians. Obesity prevalence significantly rose from early adulthood (21-30 years) to middle age (41-50 years) before slightly declining in older age groups. Antioxidant analysis revealed that glutathione (GSH) levels were highest in normal individuals, slightly lower in overweight, and lowest in obese individuals, indicating reduced antioxidant defenses in obesity. Superoxide dismutase (SOD) levels were similar across groups, with a slight decrease in obese individuals. Catalase (CAT) levels were consistently low across all groups, suggesting compromised hydrogen peroxide neutralization. Glutathione S-Transferase (GST) and glutathione peroxidase (GPX) levels were lower in obese individuals, indicating diminished detoxification and enzymatic antioxidant defenses. Malondialdehyde (MDA) levels, a marker of lipid peroxidation, were highest in obese individuals, confirming increased oxidative stress. The findings highlight the need for targeted interventions to manage obesity and oxidative stress among Nigerians, particularly in middle-aged and older adults. Despite being classified as metabolically healthy, obese Nigerians are at risk of oxidative stress due to higher levels of dyslipidemia, insulin resistance, and chronic inflammation. Enhancing antioxidant defenses through dietary and lifestyle interventions may mitigate health risks associated with obesity.

Key Words: Antioxidants, Metabolically Healthy Obesity, Oxidative Stress, Nigerians, Obesity.

Introduction

Obesity, characterized by an excessive accumulation of fatty tissue, is a medical condition associated with various health risks and reduced life expectancy. This condition can arise from a sedentary lifestyle, genetic predisposition, or a combination of these factors (Anderson et al., 2020). In Lagos, Nigeria, the prevalence of obesity is 13.6% (Adegoke et al., 2021), contributing significantly to the local disease burden. Globally, the epidemic of obesity and its associated diseases poses a serious public health challenge. Obese individuals are more likely to develop cardiovascular diseases, dyslipidemia, type 2 diabetes mellitus (T2DM), certain cancers, osteoarthritis, sleep apnea, and social and psychological issues such as stigmatization and compromised self-esteem. Additionally, obese adolescents have a higher likelihood of becoming obese adults, further increasing their risk for related health complications.

The economic impact of obesity is substantial, encompassing both direct and indirect costs. Direct medical expenses include costs for prevention, diagnosis, and treatment of obesity-related comorbidities. Indirect costs include those associated with morbidity (reduced productivity, absenteeism, hospital stays) and mortality (economic value of lost life years due to premature death). Understanding the mechanisms underlying metabolic health in obese individuals can lead to more effective healthcare practices, economic savings through preventive measures, and growth in the healthcare sector.

Research on metabolically healthy obese (MHO) individuals who exhibit favorable metabolic profiles, although excess weight, is limited but crucial. Generating data on antioxidants as markers of adiposity-based chronic diseases in MHO individuals can contribute to the body of knowledge on obesity and metabolic health. Recent research has challenged the traditional view

of obesity as a uniform state leading to negative metabolic consequences by identifying MHO individuals who, despite their excess weight, exhibit a favorable metabolic profile. This unexpected heterogeneity within obesity has sparked interest in exploring the biological factors that influence susceptibility to obesity-related complications. Notably, the presence of metabolic syndrome—a cluster of conditions including increased blood pressure, high blood sugar, excess body fat around the waist, and abnormal cholesterol or triglyceride levels—is prevalent in many obese individuals, further complicating the assessment of their metabolic health. Understanding the involvement of oxidative stress in MHO individuals could provide valuable insights into the mechanisms that protect these individuals from the adverse health effects typically associated with obesity. This knowledge could inform more personalized approaches to obesity management and prevention, ultimately improving health outcomes for a broader population.

Free radicals are extremely reactive molecules with unpaired electrons in their outer orbitals. In aerobic biological systems, these radicals and other reactive oxygen species (ROS) exhibit a wide range of reactivity levels. Highly reactive free radicals with half-lives of about 1 second coexist with less reactive molecules like melanin, which has a half-life related to solar exposure, and other molecules such as nitric oxide and ubisemiquinone, which have intermediate reactivity levels (Riana et al., 2024). A healthy person experiences approximately 10,000-20,000 free radical attacks on their body's cells daily (Riana et al., 2024). Although hydrogen peroxide (H2O2) is not a radical, it can react to form the hydroxyl ion (OH^-) and the hydroxyl radical (OH·), both of which are highly reactive and can initiate chain reactions.

ROS are typically considered harmful and are controlled by natural antioxidant enzymes. Excessive ROS formation, caused by either the failure of the body's defense mechanisms or exposure to exogenous oxidants, leads to oxidative damage to proteins, lipids, DNA, and other macromolecules, increasing the risk of various diseases (Wong et al., 2000). Oxidative stress occurs when there is an imbalance favoring oxidants over antioxidants, often due to increased oxidative metabolism. This imbalance can lead to conditions such as diabetes, cancer, cardiovascular diseases (CVDs), aging, neurological conditions, and other chronic illnesses. Antioxidants are defensive compounds that neutralize free radicals, thus preventing cellular damage (Aziz et al., 2019). These antioxidants help maintain the balance by naturally regulating free radical production.

A well-balanced diet is rich in natural antioxidants and offers numerous health benefits, including kidney support, dental health maintenance, improved nervous system and reproductive health, anti-aging effects, liver protection, immune system bolstering, and enhanced overall body defenses. Antioxidants can also reduce fat, prevent digestive issues, preserve good vision, and improve sleep quality. Effective defense mechanisms are essential because highly reactive oxidants like hydroxyl radicals constantly threaten mammalian cells.

The human body utilizes both enzymatic and non-enzymatic antioxidant systems to combat free radical damage. Non-enzymatic antioxidants include carotenoids, ubiquinone (coenzyme Q), and vitamins E and C. α-tocopherol, for example, can halt the spread of free radicals and reduce

glutathione functions as an antioxidant in cells (Paravicini et al., 2008). The enzymatic defense system comprises superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and glutathione reductase (GR). SOD scavenges superoxide radicals and accelerates their conversion to H2O2 and O2, serving as the first line of defense against ROS. Human SOD exists in three forms: extracellular SOD3, cytosolic SOD1, and mitochondrial SOD2. Catalase, composed of four polypeptide chains and heme groups, converts millions of H2O2 molecules into water and oxygen per second. Glutathione peroxidase, found in the cytoplasm, reduces H2O2 in collaboration with glutathione (GSH), preventing oxidative damage and the formation of hydroxyl radicals. Glutathione reductase, using NADPH as an electron donor, converts oxidized glutathione (GSSG) back to its reduced form (GSH). A high GSH/GSSG ratio indicates effective oxidative stress management, as GSSG can oxidize and damage many enzymes.

Adipose tissue is a significant contributor to systemic oxidative stress due to its secretion of adipokines and production of ROS (Colak et al., 2021). Oxidative stress and obesity are linked through several mechanisms, including fatty acid oxidation by peroxisomal and mitochondrial enzymes and increased oxygen consumption during mitochondrial oxidative phosphorylation. High-fat diets can exacerbate oxidative stress by altering oxygen metabolism. Accumulated adipose tissue can reduce the activity of antioxidant enzymes, leading to oxidative stress and associated abnormalities such as endothelial dysfunction. This dysfunction, characterized by reduced nitric oxide bioavailability and increased endothelium-derived contractile factors, is associated with a higher risk of atherosclerotic diseases.

Understanding the interplay between free radicals, oxidative stress, and antioxidants is crucial for our knowledge of health, aging, and age-related illnesses. Antioxidants, whether enzymatic or non-enzymatic, play vital roles in protecting the body from oxidative damage. In the context of MHO, maintaining a balance between oxidants and antioxidants is essential to mitigate the effects of oxidative stress and its associated health risks. Recent studies have indicated that oxidative stress plays a significant role in the pathophysiology of obesity and metabolic syndrome (de Mello et al., 2018; Keaney et al., 2020). Oxidative stress, resulting from an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, can lead to cellular damage and inflammation, contributing to insulin resistance, endothelial dysfunction, and other metabolic disturbances. Despite the excess weight, MHO individuals may possess a more robust antioxidant defense system or lower levels of systemic inflammation, protecting them from the metabolic derangements typically seen in obesity (Phillips et al., 2013; Wildman et al., 2016).

Materials and methods

Study Design and Participants: This prospective, cross-sectional observational study was conducted among metabolically healthy individuals who were categorized as normal weight, overweight, or obese. Participants were recruited from the Obesity Clinic at Lagos University Teaching Hospital (LUTH), the hospital community, and the general populace.

Inclusion and Exclusion Criteria: Metabolically healthy status was defined by the absence of a history of hypertension, diabetes, thyroid disorders, cancer, or any obesity-related disorders. Participants were not taking any medications for these conditions. The inclusion criteria required participants to meet the classification of metabolically healthy, which included normal blood pressure and blood glucose levels, and no history or presentation of metabolic syndrome. Subjects were between 21 to 75 years of age with a BMI ≥ 30.0 kg/m² and a waist circumference above 80 cm for women and 100 cm for men. For comparison, age- and gender-matched metabolically healthy individuals with a BMI of 20.0 kg/m² were also included in the study.

Ethical Considerations: The study was conducted following ethical standards and was approved by the Medical Ethical Committee of Lagos University Teaching Hospital (LUTH). Written informed consent was obtained from all participants. The identities of participants were kept anonymous, and all collected data were treated confidentially and used solely for this study.

Data Collection: A structured questionnaire was used to collect socio-demographic information, including age, smoking status, menstrual history, eating and drinking habits, and other relevant details.

Anthropometric Measurements: Height was measured using a portable collapsible stadiometer, and weight was measured using a BF511 body composition monitor. Body Mass Index (BMI) was calculated using the formula: weight (kg)/height (m²). Waist circumference (WC) was measured using a tape measure, with gender-specific classifications based on the National Cholesterol Education Program (NCEP) and International Diabetes Federation (IDF) guidelines for sub-Saharan Africa (IDF, 2014). For males, WC ≥ 102 cm was classified as obese, and for females, WC ≥ 94 cm was classified as obese.

Blood Pressure Measurement: Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured and classified as elevated if the readings were ≥ 140 mmHg and ≥ 90 mmHg, respectively. Hypertension was defined according to the JNC 7 classification, where either the SBP or DBP, or both, met these criteria.

Biochemical Analysis: Blood samples (20.0 mL) were collected between 08:00 and 10:00 AM after an overnight fast. Plasma Glucose: Plasma glucose was assayed using the glucose oxidase (GOD/PAP) method (Kadish et al., 1969).

Plasma Lipid Profile: Quantitative determination of plasma total cholesterol was performed using the enzymatic colorimetric assay method (Allain et al., 1974). Plasma triglycerides were

measured using the enzymatic colorimetric method (Nagele et al., 1984). High-density lipoprotein cholesterol (HDL-C) was determined by precipitating low-density lipoproteins using phosphotungstic acid in the presence of magnesium ions. The remaining HDL cholesterol fraction in the supernatant was then measured using the method for total cholesterol. Low-density lipoprotein cholesterol (LDL-C) concentration was calculated using the formula by Sniderman et al. (2003): LDL-C = Total cholesterol – HDL-C - 0.2(Triglycerides).

Insulin: Plasma insulin levels were quantified using an enzyme immunoassay kit based on the method described by Frier et al. (1981).

Glycosylated Hemoglobin (HbA1c): HbA1c was measured using the method described by Wålinder et al. (1982).

Oxidative Stress Markers: Superoxide Dismutase (SOD) Activity: SOD activity was assessed based on its ability to inhibit the autoxidation of epinephrine (Sun and Zigma, 1978).

Catalase Activity: Catalase activity was determined as described by Sinha et al. (1972).

Reduced Glutathione (GSH): Plasma GSH levels were estimated using the method described by Sedlak and Lindsay (1968).

Malondialdehyde (MDA): MDA, an indicator of lipid peroxidation, was measured according to the method described by Buege et al. (1978).

Glutathione-S-Transferase (GST) Activity: GST activity was measured using the method described by Habig et al. (1974).

Statistical Analysis: Statistical analysis was performed using SPSS software, version 25. Descriptive statistics and bar charts were used to summarize the data. The frequency and prevalence of various parameters were calculated where relevant. Differences in means between study groups and controls were assessed using one-way ANOVA, with statistical significance set at $p < 0.05$. Pearson's correlation coefficient was used to evaluate correlations between variables.

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RESULT

Table 1: Age distribution of participants

Age (years)	Normal	Overweight	Obese	Total
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
21-30	35 (10%)	29 (8.3%)	36 (10.3%)	100 (28.6%)
31-40	9 (2.5%)	11 (3.1%)	36 (10.3%)	56 (16.1%)
41-50	16 (4.6%)	37 (10.6%)	49 (14%)	102 (19.3%)
51-60	17 (4.9%)	22 (6.3%)	12 (3.4%)	51 (14.6%)
61-70	10 (2.9%)	6 (1.7%)	9 (2.6%)	25 (7.1%)
71-75	8 (2.3%)	4 (1.1%)	4 (1.1%)	16 (4.6%)
Total	95 (27.2%)	109 (31.1%)	146 (41.7%)	350 (100.0%)

Table 2: Age distribution of participants using body mass index

Age (Years)	Normal	Overweight	Obese	Total
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
21-30	49 (14.0)	31 (9.0)	23 (6.6)	103 (29.6)
31-40	11 (3.1)	19 (5.4)	28 (8.0)	58 (16.5)
41-50	20 (5.7)	34 (9.7)	38 (10.9)	92 (26.3)
51-60	18 (5.1)	19 (5.4)	16 (4.6)	53 (15.1)
61-70	12 (3.4)	7 (2.0)	6 (1.7)	25 (5.3)
71-75	7 (2.0)	6 (1.7)	6 (1.7)	19 (5.4)
Total	117 (33.4)	116 (33.1)	117 (33.4)	350 (100.0)

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Table 3: Age distribution of participants using waist circumference

Age (Years)	Normal	Overweight	Obese	Total
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
21-30	35 (10)	29 (8.3)	36 (10.3)	100 (28.6)
31-40	9 (2.6)	11 (3.1)	36 (10.3)	56 (16.1)
41-50	16 (4.6)	37 (10.6)	49 (14.0)	102 (29.2)
51-60	17 (4.9)	22 (6.3)	12 (3.4)	51 (14.6)
61-70	10 (2.9)	4 (1.1)	9 (2.6)	23 (6.6)
71-75	8 (2.3)	6 (1.7)	4 (1.1)	18 (5.1)
Total	95 (27.2)	109 (31.1)	146 (41.7)	350 (100)

Table 4: Anthropometry of participants

Parameters	Normal	Overweight	Obese	F	P
Age (yrs)	48.2±2.6	42.3±1.5	46.2±2.10	0.76	0.840
Height (m)	1.71±0.06	1.62±0.07	1.61±0.06	75.654	0.000
Weight (kg)	63.0±4.90	73.89±6.50*	84.28±6.99*	327.872	0.000
BMI (kg/m^2)	21.57±1.53	27.97±1.14*	32.55± 4.12*	1989.228	0.000
WC (cm)	79.8±4.11	93.2±4.24*	114.2±11.83*	5.84	0.010
SBP (mmHg)	110± 4.70	116± 6.30	108±2.60	63.33	0.010
DBP (mmHg)	80±5.10	87±4.40	83±2.50	0.31	0.74

Values were reported as Mean ± Standard Deviation (Mean ± SD). Statistical significance for differences in means was set at $p < 0.05$.

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Table 6: Metabolic demography of participants

Clinical Variables	Normal	Overweight	Obese	F	P
FPI (µU/mL)	2.5±0.2	3.1±0.51	3.8±0.6	0.44	0.060
FBG (mmol/L)	4.6± 1.7	5.1± 1.40	4.9± 1.30	0.36	0.760
HbA1c (%)	3.6± 0.71	3.6± 2.90	4.0± 1.10	0.51	0.630
HOMA-IR	0.5± 0.1	0.6± 0.13	0.7± 0.1	0.44	0.230
T. CHOL (mmol/L)	3.66 ± 0.21^{ab}	4.06 ± 1.01^{a}	4.33 ± 0.18^{b}	49.01	0.010
TG (mmol/L)	1.11 ± 0.08^{ab}	1.04 ± 0.21^{a}	1.38 ± 0.39^{b}	90.44	0.010
HDLc (mmol/L)	1.44 ± 0.31^{ab}	1.71 ± 0.41^{a}	1.30 ± 0.36^{b}	68.48	0.010
LDLc (mmol/L)	2.00 ± 0.22^{ab}	2.14 ± 0.61^{a}	2.16 ± 0.31^{b}	3.51	0.010*
AI	1.39±0.04	1.25±0.07	1.66±0.06	0.51	0.590
CRI	2.54±0.12	2.37±0.13	3.33±0.10	0.93	0.350

Values are expressed as mean ± standard deviation (Mean ± SD), and mean differences were considered significant at $p < 0.05$. where FPI = Fasting plasma insulin, FBG = Fasting blood glucose, HbA1c = Glycated hemoglobin, TG = Triglycerides, LDL-C = Low

density lipoprotein cholesterol, HDLC = High-density lipoprotein cholesterol, T. CHOL = Total cholesterol, and HOMA-IR = Homeostatic model of assessment of insulin resistance.

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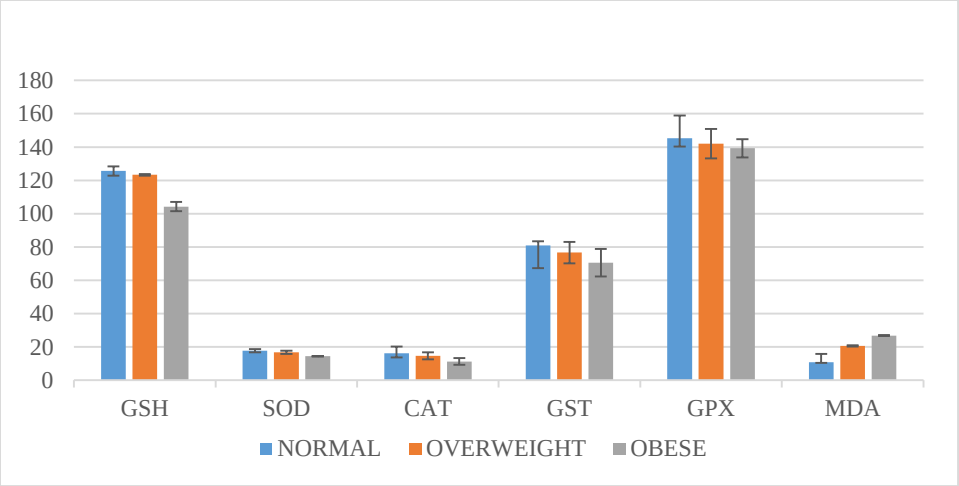

Figure 1: Pattern of some antioxidants in normal, overweight, and obesity using bmi as index of obesity

Values are statistically significant at $p < 0.05$; where GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST; = Glutathione –s-transferase, GPX; = Glutathione peroxidase

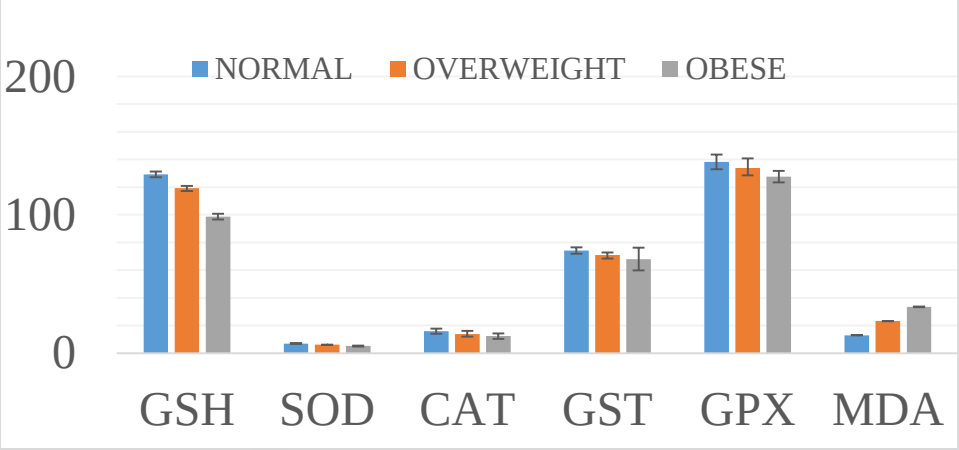

Figure 2: Pattern of some antioxidants in normal, overweight and obese individuals using waist circumference as index of obesity

Values are statistically significant at $p < 0.001$; where GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST = Glutathione –s-transferase, GPX; = Glutathione peroxidase

Table 7: Correlation of body mass index with biochemical parameters

PARAMETER	CORRELATION COEFFICIENT "R"	P – VALUE
AGE	0.452	0.261
WC	0.930*	0.000
GSH	0.121	0.740
SOD	-0.002	0.996
CAT	0.623*	0.050
MDA	0.323	0.363
GST	-0.184	0.611
GPX	0.161	0.656

Values are statistically significant at $p < 0.05$; where BMI = Body Mass Index, WC = Waist circumference, IL-6 = Interleukin-6, HS-CRP = High sensitivity C-reactive protein, GHR = Ghrelin, VCAM = Vascular Cell Adhesion Molecule, TSH = Thyroid stimulating hormone, Ft3 = Free triiodothyronine, Ft4 = Free thyroxine, GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST = Glutathione-s-transferase, GPX = Glutathione Peroxidase, VCAM = Vascular Cell Adhesion Molecule

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Table 8: Correlation of waist circumference with biochemical parameters

Parameter	Correlation coefficient "r"	P-value
AGE	-0.087	0.787
BMI	0.900*	0.000
GSH	-0.616*	0.043
SOD	-0.418	0.201
CAT	0.458	0.156
MDA	0.736*	0.004
GST	-0.131	0.700
GPX	0.091	0.790

Values are statistically significant at $p < 0.05$; where BMI = Body Mass Index, WC = Waist circumference, , GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST = Glutathione-s-transferase, GPX = Glutathione Peroxidase, VCAM = Vascular Cell Adhesion Molecule

Table 9: Regression of body mass index against biochemical parameters

Parameter	ODDS	P-value
CAT	0.400	0.050*
WC	0.603	0.001*

Values are statistically significant at $p < 0.05$; where BMI = Body Mass Index, WC = Waist circumference, GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST = Glutathione-s-transferase, GPX = Glutathione Peroxidase, VCAM = Vascular Cell Adhesion Molecul

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Table 10: Regression of waist circumference against biochemical parameters

Parameter	ODDS	P-value
BMI	0. 603	0.001*
GSH	0.380	-0.043*
MDA	0.017	0.699

Values are statistically significant at $p < 0.05$; where BMI = Body Mass Index, WC = Waist circumference, GSH = Glutathione, SOD = Superoxide dismutase, CAT = Catalase, MDA = Malonaldehyde, GST = Glutathione-s-transferase, GPX = Glutathione Peroxidase, VCAM = Vascular Cell Adhesion Molecule

DISCUSSION

Obesity is commonly associated with an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, leading to oxidative stress. This oxidative stress is pivotal in the development of obesity-related complications, such as insulin resistance, cardiovascular diseases, and type 2 diabetes mellitus (Vincent et al., 2018; Hill et al., 2021). This study investigated the mechanisms of antioxidant function in metabolically healthy overweight and obese Nigerians to elucidate their role in preserving metabolic health despite the presence of excess adiposity.

The age distribution of participants highlights the increased prevalence of obesity in middle-aged Nigerians and its association with oxidative stress. The data indicate that obesity prevalence significantly increases from early adulthood (21-30 years) to middle age (41-50 years) before declining slightly in older age groups. This trend underscores the importance of considering oxidative stress in different age groups. In young adults, the balanced distribution among normal, overweight, and obese individuals suggests an early onset of weight gain. Young obese adults may experience increased oxidative stress due to higher adiposity and related metabolic demands. In middle-aged individuals, there is a noticeable increase in overweight and obese individuals, facing higher oxidative stress due to prolonged exposure to adiposity-related metabolic changes and inflammation. Older adults show a decline in obesity prevalence but persistent overweight status, experiencing compounded oxidative stress due to aging and prolonged exposure to metabolic dysfunction. Understanding these patterns is crucial for developing targeted interventions to mitigate oxidative stress and improve health outcomes.

Fasting Plasma Insulin and HOMA-IR increase from normal to obese categories, though not significantly ($P > 0.05$). Increased insulin resistance (higher FPI and HOMA-IR) in obesity is associated with elevated oxidative stress. Insulin resistance can lead to hyperglycemia, which

enhances the production of reactive oxygen species (ROS) (Colak et al., 2021). Fasting Blood Glucose (FBG) and HbA1c levels are relatively stable across BMI categories. Although glycemic control appears maintained in MHO individuals, chronic low-grade inflammation associated with obesity can still promote oxidative stress and contribute to insulin resistance and endothelial dysfunction (Phillips et al., 2013).

Significant differences in total cholesterol (T. CHOL), triglycerides (TG), HDL cholesterol (HDLc), and LDL cholesterol (LDLc) across BMI categories, with worse lipid profiles in obese individuals ($P < 0.05$) was observed, dyslipidemia in obesity exacerbates oxidative stress. Elevated LDLc and TG levels promote lipid peroxidation, a key source of ROS, while reduced HDLc diminishes antioxidant capacity (Paravicini et al., 2008). Atherogenic Index (AI) and Cardiovascular Risk Index (CRI), show no significant differences across obesity categories. Despite AI and CRI remaining stable, increased oxidative stress in obese individuals can still contribute to endothelial dysfunction and cardiovascular risk (Phillips et al., 2013). This implies that MHO individuals who appear metabolically healthy might experience heightened oxidative stress due to increased adiposity and associated metabolic activities. Adipose tissue secretes pro-inflammatory cytokines, which can elevate ROS levels and overwhelm antioxidant defenses (Colak et al., 2021)Increased adipose tissue leads to higher production of ROS. Adipocytes, particularly in visceral fat, are metabolically active and secrete inflammatory cytokines that contribute to oxidative stress (Colak et al., 2021). Obesity is associated with chronic low-grade inflammation, which exacerbates oxidative stress. Adipose tissue releases pro-inflammatory cytokines such as TNF-α and IL-6, increasing ROS production and depleting antioxidant defenses (Wong et al., 2000). Excessive adiposity contributes to endothelial dysfunction, characterized by reduced nitric oxide bioavailability and increased production of vasoconstrictors. This dysfunction is closely linked to oxidative stress and increases the risk of cardiovascular diseases (Phillips et al., 2013). Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) are crucial enzymes in neutralizing ROS and protecting against oxidative damage. In obesity, these systems are often overwhelmed due to excessive ROS production (Paravicini et al., 2008). Vitamins E and C, carotenoids, and ubiquinone (coenzyme Q) help neutralize free radicals. A diet rich in these antioxidants can support the body's defense against oxidative stress (Aziz et al., 2019).

The findings highlight the need for targeted interventions to manage obesity and oxidative stress among Nigerians, especially in middle-aged and older adults. Potential strategies include promoting healthy diets rich in natural antioxidants, encouraging regular physical activity to reduce adiposity and improve antioxidant defenses, and implementing public health campaigns to raise awareness about the risks of obesity and oxidative stress.

Despite being classified as metabolically healthy, obese Nigerians are at risk of oxidative stress due to higher levels of dyslipidemia, insulin resistance, and chronic inflammation. Addressing oxidative stress through lifestyle modifications, dietary interventions, and possibly antioxidant supplementation could mitigate health risks associated with obesity in this population. The

analysis of antioxidant levels revealed that Glutathione (GSH) levels are highest in normal individuals, slightly lower in overweight, and lowest in obese individuals. GSH is a critical non-enzymatic antioxidant that protects cells from oxidative damage. Lower levels in obese individuals indicate reduced antioxidant defenses, leading to increased susceptibility to oxidative stress (Aziz et al., 2019). Superoxide Dismutase (SOD) levels are similar across all groups with a slight decrease in obese individuals. SOD catalyzes the dismutation of superoxide radicals into oxygen and hydrogen peroxide. Decreased SOD levels in obesity suggest impaired enzymatic antioxidant defense, contributing to higher oxidative stress (Paravicini et al., 2008). Catalase (CAT) levels are low across all groups with minor variations. CAT converts hydrogen peroxide into water and oxygen, preventing the harmful effects of hydrogen peroxide. Consistently low CAT levels indicate a compromised ability to neutralize hydrogen peroxide, exacerbating oxidative stress in obesity (Paravicini et al., 2008). Glutathione S-Transferase (GST) levels are slightly higher in normal and overweight individuals compared to obese individuals. GST detoxifies electrophilic compounds, including lipid peroxides. Reduced GST activity in obesity suggests decreased detoxification capacity, heightening oxidative stress (Colak et al., 2021). Glutathione Peroxidase (GPX) levels are highest in normal individuals, slightly lower in overweight, and further decreased in obese individuals. GPX reduces hydrogen peroxide and lipid peroxides, protecting cells from oxidative damage. Lower GPX levels in obesity indicate diminished enzymatic antioxidant defenses (Paravicini et al., 2008). Malondialdehyde (MDA) levels are lowest in normal individuals and highest in obese individuals. MDA is a marker of lipid peroxidation and oxidative stress. Elevated MDA levels in obese individuals signify increased oxidative damage to lipids, confirming higher oxidative stress in obesity (Wong et al., 2000).

A very strong positive correlation ($r = 0.930$, $p = 0.000$) between BMI and WC confirms their close relationship as indicators of adiposity (Wong et al., 2000). The moderate positive correlation ($r = 0.623$, $p = 0.050$) suggests that higher BMI is associated with increased CAT activity, reflecting an adaptive response to oxidative stress (Paravicini et al., 2008). The significant negative correlation ($r = -0.616$, $p = 0.043$) between WC and GSH indicates that increased WC is associated with reduced antioxidant defenses, suggesting that higher obesity levels may lead to decreased antioxidant capacity (Aziz et al., 2019). The strong positive correlation ($r = 0.736$, $p = 0.004$) with WC suggests that increased oxidative damage is associated with higher WC, highlighting the role of oxidative stress in obesity (Colak et al., 2021). The lack of significant correlations between Superoxide Dismutase (SOD) and Glutathione-S-Transferase (GST) with WC indicates that these oxidative stress markers may not be directly influenced by WC in this context.

Despite the increased oxidative stress markers, our study identified a subset of overweight and obese individuals who maintained normal metabolic profiles, characterized by normal insulin sensitivity, lipid levels, and blood pressure. These individuals, termed "metabolically healthy obese" (MHO), exhibited higher levels of certain antioxidants compared to their metabolically unhealthy counterparts in previous studies, specifically, MHO individuals demonstrated relatively higher SOD and GSH levels, indicating a better antioxidant defense mechanism that may protect against oxidative damage (Phillips et al., 2017). The mechanisms underlying the

maintenance of metabolic health in MHO individuals may involve several factors. Higher antioxidant levels could reduce oxidative stress and inflammation, key contributors to insulin resistance and cardiovascular disease. Additionally, lifestyle factors such as a diet rich in antioxidants, physical activity, and genetic predispositions may contribute to the antioxidant capacity and metabolic health of these individuals (Bluher, 2019).

CONCLUSIONS

This study highlights the critical role of antioxidants in modulating oxidative stress in obesity. While overweight and obese individuals generally exhibit reduced antioxidant defences and increased oxidative stress, those maintaining metabolic health (MHO) demonstrate relatively higher levels of key antioxidants. Enhancing antioxidant defenses through dietary and lifestyle interventions may be a valuable strategy in managing obesity and preventing its associated disorders.

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