Transatlantic Journal of Multidisciplinary Research
(p-ISSN: 2672-5371)(e-ISSN:2735-9808)
Journal Homepage: https://tjmr.org/

TJMR
Vol. 6(1) 2024

| RESEARCH ARTICLE

Comparison Of Adiponectin and Atherogenic Risk Indices in Metabolically Healthy Obese and Normal Weight Individuals In Owerri, Nigeria

https://doi.org/10.5281/zenodo.14006761

Daniel Onyedikachi Dike[1], *, Jude Anaelechi Onuegbu[1], Chudi Emmanuel Dioka[1], Japhet Madu Olisekodiaka[1], Onyinyechi Ogechi Bede-Ojimadu [2], Chidiadi MaryAnn Njoku[1], Mabel A. Charles-Davis[3] and Emmanuel O Akhaumere[4]

[1]Department of Chemical Pathology, Faculty of Basic Clinical Sciences, Nnamdi Azikiwe University, Awka, Nigeria.
[2]Department of Medical Laboratory Science, School of Allied Health Sciences, Kampala International University, Uganda.
[3]Department of Chemical Pathology, College of Medicine, University of Ibadan, Nigeria.
[4]Department of Chemical Pathology, National Hospital, Abuja, Nigeria

Corresponding Author: Daniel Onyedikachi Dike E-mail: danybrowse@gmail.com

| ABSTRACT

A subphenotype of obesity defined as "metabolically healthy" due to the presence of favourable risk factors, seems to be a misnomer and may be misleading, especially in an obesogenic environment like Owerri, with a traditional perception of metabolically healthy obesity as a sign of wellness and prosperity. This research seeks to compare some metabolic profiles of metabolically healthy obese (MHO) and metabolically healthy normal weight (MHNW) individuals to underscore the metabolic healthiness of the MHO.

Aim: The assess the extent of the healthiness of MHO by comparing some metabolic profiles of MHO and MHNW.

Methods: A total of 130 enrollees (60 MHO and 70 MHNW) aged between 25 and 60 years participated in this study. Fasting lipid profile and adiponectin were analyzed using standard laboratory techniques while atherogenic risk indices (CRI-1, CRI-2 and AIP) were mathematically determined.

Results: Significant lower adiponectin and HDL were observed in MHO compared to MHNW ($p<0.05$). Conversely, other lipid fractions and artherogenic indices were statistically higher in MHO than MHNW ($p<0.05$). In MHO, no significant correlation was observed between adiponectin and (BMI, lipid fractions, lipid indices), however, moderate positive correlations were observed between systolic blood pressure and BMI ($r = .282$, $p=0.029$), TC ($r = .298$, $p=0.024$), LDL ($r = .298$, $p=0.021$), CRI-1 ($r = .257$, $p=0.047$), CRI-2 (.268, $p=0.038$). Additionally, strong positive and negative correlations were found between some lipid fractions and lipid indices.

Conclusion: The findings of this study shows that the MHO is not as safe as defined but ticks towards unfavourable profile.

| KEYWORDS

Adiponectin, Atherogenic Indices, Metabolically Healthy Obese, Nigeria.

Introduction

Obesity has been described as a time bomb ticking to explode in myriads of metabolic diseases (Alshaikh *et al.,* 2017). It has become a worrisome global public health challenge especially in low- and middle-income countries of the world including Nigeria, because of its contributions to impaired quality of life and reduced life expectancy (Blüher, 2020) up to approximately 20 years from increased mortality caused by non-communicable diseases (Fontaine, Redden, Wang, Westfall & Allison, 2003). Obesity defined as body mass index, BMI ≥30 kg/m^2 has drawn a robust attention in the research and scientific community as a result of its connectivity to several non-communicable diseases (Schulze & Stefan, 2024) as every 5 units increase in body mass index (BMI) above 25 kg/m^2 has been noted to be associated with about 31% higher risk of premature death (NCDRF, 2016). Report from WHO (2023) showed that 17 million people die from a non-communicable disease (NCD) annually before age 70 and 86% of these premature deaths occur in low- and middle-income countries including Nigeria. However, it has been noted that individual risks to development of obesity-related diseases varies (Blüher, 2020), implying that not everyone who meets obesity criteria comes down with metabolic complications (April-Sander & Rodriguez, 2021). This is the basis of the concept of metabolically healthy obese (MHO).

An observation that a subphenotype of obese individuals has a lower risk of predisposition to metabolic complication gave rise to an obesity condition described as metabolically healthy obesity (MHO) (Vague, 1956) and since 2010, MHO has attracted increasing research attentions (Blüher, 2020). Metabolically healthy obese is an obesity phenotype with normal metabolic profile and reduced risks of cardiometabolic complications compared to metabolic unhealthy obese individuals (Blüher, 2020). Though the body mass index, BMI ≥30 kg/m^2 has been accepted as a prerequisite for definition of MHO, no universal standard definition has been

adopted, rather numerous definitions have been used in several clinical studies (Rey-López, de Rezende, Pastor-Valero & Tess, 2014). However, the absence of dyslipidemia, hyperglycaemia, hypertension and atherosclerotic cardiovascular disease in obese individuals has frequently been used to define MHO (Blüher, 2020; Magkos, 2019; Eckel, Meidtner, Kalle-Uhlmann, Stefan & Schulze 2016; Rey-López *etal.,* 2014). Metabolically, certain metabolic profile cut-off has been used to define MHO thus: serum triglycerides ≤1.7 mmol/l (≤150 mg/dl); HDL cholesterol serum concentrations >1.0 (>40 mg/dl) (in men) or >1.3 mmol/l (>50 mg/dl) (in women); systolic blood pressure (SBP) ≤130 mmHg; diastolic blood pressure ≤85 mmHg; fasting blood glucose ≤ 5.6 mmol/l (≤100 mg/dl); in absence of diabetes, hypertension, cardiovascular disease manifestation and without therapeutic treatment for dyslipidemia (Blüher, 2020). Summarily, most studies define MHO as less than or equal to one or two metabolic syndrome factor (NCEP, 2022) and as a result many people labelled as MHO are not actually metabolically healthy, but simply have fewer metabolic abnormalities than those with metabolically unhealthy obesity (MUO) (Smith, Mittendorfer & Klein, 2019).

Obesity has been reported to cause disturbances in lipid metabolism (Bay, 2024; Vekic, Stefanovic & Zeljkovic, 2023) and dyslipidemia increases with BMI (Bay 2024; Feingold, 2023; Skinner 2015) with approximately 60-70% of patients who are obese being dyslipidemic (skinner 2015). Higher concentrations of total cholesterol, triglycerides, low density lipoproteins and lower levels of high density lipoprotein are the pattern of dyslipidemia characteristic of obesity (Vekic *et al.,* 2023; She, Mangat, Tsai, Proctor & Richard, 2022). Unlike the metabolically unhealthy obesity (MUO), the MHO phenotype has a favorable lipid profile, even with similar adiposity as metabolically unhealthy obese (MUO) (April-Sanders & Rodriguez, 2021; Karelis, Brochu & Rabasa-Lhoret, 2004). The presence of normal metabolic parameters in MHO may be responsible to decreased risks of obesity-associated complications observed in MHO when compared with metabolically unhealthy obese. However,

MHO seems to have a significant higher risks to metabolic complications than metabolically healthy normal weight individuals (April-Sanders & Rodriguez, 2021, Blüher, 2020; Caleyachetty *et al.,* 2017). Several studies have demonstrated a higher concentrations of lipid fractions in MUO and a lower concentrations of the same fractions in normal weight individuals compared to MHO (Telle-Hansen, Christensen, Formo, Holven & Ulven, 2020; Wurtz *et al.,* 2015) placing MHO in an intermediate health risk level compared to MUO and normal weight individuals (Telle-Hansen, Christensen, Formo, Holven & Ulven, 2020; Wurtz *et al.,* 2015). Notwithstanding, similar risks to metabolic complication has been demonstrated between MHO and metabolically healthy normal weight individuals in review articles (April-Sanders & Rodriguez, 2021; Smith *et al.,* 2019).

Currently, great attention should be given to metabolically healthy obesity because of the limitations of the variant definitions used for MHO. Following the definitions, many obese individuals often labelled as metabolically healthy are not truly healthy but possess few cardiometabolic aberrations as metabolically unhealthy (Smith *et al.,* 2019). Additionally, MHO has been noted to not just been a clinical condition but a transitional metabolic phase as many MHO transit to MUO as age increases (Behnaz, Fatemeh Amir, Majid & Farhad, 2022; Lee, Kim & Shin, 2024).

Adiponectin is a 30 kDa (244 amino acids) adipocyte-secreted polypeptide that modulates a number of metabolic processes, including glucose and lipid metabolism (Ramakrishnan, Auger, Rahimi & Jialal, 2024). It suppresses a plethora of metabolic processes that may result in insulin resistance, T_2DM, metabolic syndrome, and cardiovascular disease (Hong *et al.,* 2023; Ramakrishnan *et al.,* 2024). Lower adiponectin has been reported in individuals with MHO (Ding et al., 2018) and adiponectin level are much more lower in MUO than MHO and differentiates between MHO and MUO (Ahl *et al.,* 2015). Hypoadiponectinemia poses a health threat on MHO individuals (Boyarinova *et al.*, 2016) and the confluence of hypoadiponectinemia and dyslipidemia in obesity (Tomono, Hiraishi &Yoshida, 2018; Wang, Wang & Luo, 2022; Yanai & Yoshida, 2019) increases risks of metabolic complications.

Obesity is a condition of energy imbalance and diet has been implicated as one of the major drivers of obesity (Jiao, 2023) regulator of adiponectin (Janiszewska, Ostrowska, Szostak-Węgierek, 2021) and influencer of lipid metabolism (Fogacci, Borghi & Cicero, 2021). Owerri, Southeastern Nigeria is an obesogenic environment. In a recent systematic review and meta-analysis, the zone was found to be the most overweight and the second most obese geopolitical zone in Nigeria (Chukwuonye *et al.,* 2022). Secondly, the superimposition of westernized diet on the existing starchy traditional diets, coupled with the ancient traditional perception of metabolically healthy obesity as a sign of wellness and prosperity is the concern of this research. MHO prevalence represents 10-45% of the obese population (Carolina, Gonçalves, Glade & Meguid, 2013), but some studies in Nigeria have noted varying but related prevalence in metabolically healthy obesity (Ejike, Ugwu & Ezeanyika, 2009; Ijeh, Okorie, Ejike, 2010) in the range of 30 to 33.3%. Metabolically healthy obesity is a misnomer and may be misleading in a population where metabolically healthy obesity is traditionally perceived as sign of wellness and prosperity. Furthermore, because of the possibility of transition of MHO with adjudged favourable metabolic profile to MUO, there is a need to compare some metabolic profiles of metabolically healthy obese (MHO) and metabolically healthy normal weight (MHNW) individuals in order to expose the extent of the healthiness of the MHO and underscore the future translation of the now favourable profile to high risk unfavourable state.

Study Area

Owerri is the capital of Imo State in Nigeria, set in the heart of Igboland. It is also the state's largest city and consists of three Local Government Areas including Owerri Municipal, Owerri North and Owerri West. It has an estimated population of about 1,022, 922 as of 2024 and is approximately 100 square kilometres (40 sq m) in area. Owerri houses Federal University Teaching Hospital, Federal University of Technology, National Open University, Federal University of Education, Federal and state

secretariat, Imo State University, Federal Polytechnic etc. It is predominantly a civil servant dominant area. It is currently referred to as the entertainment capital of Nigeria because of its high density of spacious hotels, high street casinos, production studios and high quality centres of relaxation that attract people from other states and countries.

Study Design

This was a cross sectional study in which the study population made up of 130 enrollees (60 metabolically healthy obese and 70 metabolically healthy normal weight adults, aged 25-60years were selected by convenient sampling. The obese had a BMI ≥30 kg/m^2 while the normal weight had a BMI of 18 kg/m^2-24.9 kg/m^2 with waist circumference of less than 94cm and 80cm for men and women respectively. Metabolic syndrome screening was done using the criteria of Joint Interim Statement by Alberti *et al*, (2009) and the metabolically healthy obese participants were selected on the basis of having less or equal to one metabolic syndrome factors (NCEP, 2022). Participants with tumor or malignancy, physical or mental inability and with history of liver or kidney disease, smokers, alcoholics, hypertensive, diabetic, arthritis patients and pregnant or intending to be pregnant within the research duration, on treatment with hypolipidemic drugs were excluded.

Ethical Considerations

The study was conducted in accordance with the Declaration of Helsinki and ethical approval of the study protocol was obtained from Ethics and Research Committee of Imo State University Teaching Hospital, Orlu (IMSUTH/CS/121). The study design and protocol were explained to each participant and informed consent obtained from all subjects prior to participation.

Data Collection

Anthropometric Measurements

Standard questionnaires were used to collect participants socio-demographic data obtained through a face-to-face personal interview. The anthropometric parameters such as (weight [kg], height [m^2] and waist circumference) of the participants were

measured using weighing scale, stadiometer and measuring tape respectively while the blood pressure was measured using an aneroid sphygmomanometer.

The weight was then recorded in kilograms to the nearest 0.1 kg. Body mass index (BMI) was calculated by dividing weight (in kilograms) by the square of height (in meters) and expressed in kg/m^2. Based on the values of BMI, the participants with BMI ≥ 30 kg/m^2 and 18 —24.9 $kg/m^{2.}$ were classified as obese and non-obese and were enrolled. Waist circumference (WC) was measured to the nearest 0.1 cm using a measuring tape that is 1 cm in width and made of a material that does not stretch and cut-off values of >94 cm (male subjects) and >80 cm (female subjects) were used to define abdominal obesity.

Sample Collection and Preparation

Eight (8ml) of venous blood was collected aseptically after 10-12 hours overnight fast and dispensed into plain tubes. The sample was allowed to clot, retract and centrifuged at 3000rpm for 10 minutes. The serum was separated, kept away from sunlight and stored at -20^0C until analysed. Sample analysis was batched trice within the three months of collection to avoid loss of bioactivity.

Sample Analysis

Adiponectin was analysed with ELISA technique using reagents acquired from Melsin Medical Company Ltd, China (LOT NO: P20210430, CAT NO: EKHU-0843 and LOT NO: P20210430, CAT NO: EKHU-1751 respectively). Lipid parameters (total cholesterol, triglycerides, high density lipoproteins were analysed using Cholesterol oxidase and Glycerol-3-phosphate- peroxidase (GPO-POD) method while low density lipoprotein, and atherogeic indices (CRI-1, CRI-2 and AIP) were mathematically determined {Atherogenic index of plasma (AIP) = log (TG/HDL-C), CRI-1= TC/HDL; CRI-2= LDL/HDL}.

Statistical Analysis

Statistical analysis was carried out with SPSS version 21. Frequencies and percentages were used to present categorical data. Continuous data were reported as means ± standard deviations (SD) for variables with a parametric distribution and student t-test was used to compare means of parametric quantitative variables between two groups. Pearson's correlation coefficient was employed to study the association of the variables. A significance level of $p < 0.05$ was considered statistically significant.

Results

Table 1: Mean ± SD of Anthropometric, Adiponectin and Atherogenic Profile of Metabolically Healthy Obese and Metabolically Healthy Normal Weight Subjects.

Parameter	MHO (n = 60)	MHNW (n = 70)	p-value[a]
Height (m)	1.63 ± 0.06	1.69 ± 0.07	0.041
Weight (kg)	90.67 ± 6.88	65.01 ± 6.22	0.001
BMI (kg/m^2)	34.37 ± 2.90	22.81 ± 1.28	0.001
Systolic (mmHg)	121.75 ± 9.20	113.71 ± 7.55	0.001
Diastolic (mmHg)	82.67 ± 6.07	76.14 ± 5.53	0.001
Total cholesterol (mmol/L)	4.84 ± 0.94	3.99 ± 0.67	0.026
Triglyceride (mmol/L)	1.55 ± 0.20	1.11 ± 0.15	0.030
HDL (mmol/L)	0.96 ± 0.11	1.09 ± 0.17	0.002
LDL (mmol/L)	3.18 ± 0.96	2.38 ± 0.66	0.009
CRI-1	5.12 ± 1.11	3.72 ± 0.77	0.001
CRI-2	3.37 ± 1.11	2.24 ± 0.74	0.001
AIP	0.21 ± 0.06	0.01 ± 0.08	0.001
Adiponectin (ug/ml)	15.80 ± 3.15	18.11 ± 4.48	0.021
Age (yrs)	40.10 ± 11.31	38.99 ± 10.85	0.625

[a] = *p* values are based on Student t-test; Arithmetic mean ± standard deviation is presented; HDL= High density lipoprotein, LDL= Low density lipoprotein, CRI= Castelli risk index, AIP= Atherogenic index of plasma, BMI= Body mass index, MHO= metabolically healthy obese, MHNW= metabolically healthy normal weight, P<0.05.

Table 2: Pearson Correlation of Adiponectin, Anthropometric and Atherogenic Indices in Metabolically Healthy Obese individuals.

Parameters	r	p value	Parameters	r	p value
Weight vs AIP	.281*	0.030	TC vs CRI-2	.877**	0.000
BMI vs Weight	.576**	0.000	TG vs CRI-2	-.507**	0.000
BMI vs Systolic	.282*	0.029	HDL vs CRI-2	-.358**	0.005
BMI vs HDL	-.290*	0.024	LDL vs CRI-2	.938**	0.000
Systolic vs TC	.298*	0.025	Adiponectin vs BMI	-.026	0.841
Systolic vs LDL	.298*	0.021	Adiponectin vs TG	-.056	0.672
Systolic vs CRI-1	.257*	0.047	Adiponectin vs TC	-.009	0.945
Systolic vs CRI-2	.268*	0.038	Adiponectin vs HDL	.078	0.552
TC vs AIP	-.371**	0.004	Adiponectin vs LDL	-.026	0.845
LDL vs AIP	-.360**	0.005	Adiponectin vs AIP	-.019	0.887
HDL vs AIP	-.517**	0.000	Adiponectin vs CRI-1	-.065	0.621
TG vs AIP	.639**	0.000	Adiponectin vs CRI-2	-.062	0.636
TC vs CRI-1	.849**	0.000	BMI vs AIP	.229	0.078
TG vs CRI-1	-.450**	0.000	BMI vs CRI-1	.078	0.552
HDL vs CRI-1	-.416**	0.001	BMI vs CRI-2	.053	0.689
LDL vs CRI-1	.913**	0.000			

** p<0.01, *p<0.05. HDL= High density lipoprotein, LDL= Low density lipoprotein, CRI= Castelli risk index, AIP= Atherogenic index of plasma, BMI= Body mass index, P<0.05.

Anthropometric Parameters

One hundred and thirty participants {60 metabolically healthy obese (MHO) and 70 normal weight metabolically healthy individuals(MHNW) were enrolled for this study with a mean age of 40.10 $\pm$ 11.31 and 38.99 $\pm$ 10.85 respectively. The anthropometric parameters (BMI, Weight, Systolic, Diastolic) were significantly ($p<0.05$) higher in MHO than MHNW individuals (Table 1)

Lipid Fractions and Adiponectin

The mean $\pm$ SD of lipid fraction of the MHO (TC: 4.84 $\pm$ 0.94; TG: 1.55 $\pm$ 0.20; LDL: 3.18 $\pm$ 0.96) were statistically higher ($p<0.05$) than the MHNW (TC: 3.99 $\pm$ 0.67; TG: 1.11 $\pm$ 0.15; LDL: 2.38 $\pm$ 0.66) individuals respectively. Conversely, statistically significant

lower HDL and adiponectin levels were observed in MHO compared to MHNW subjects (Table 1)

Lipid Indices

All indices of atherogenicity evaluated in this study were significantly higher ($p<0.05$) in MHO (CRI-1: 5.12 $\pm$ 1.11; CRI-2: 3.37 $\pm$ 1.11; AIP: 0.21 $\pm$ 0.06) than MHNW (CRI-: 3.72 $\pm$ 0.77; CRI-2: 2.24 $\pm$ 0.74; AIP: 0.01 $\pm$ 0.08) respectively.

Associations of Adiponectin, Anthropometrics and Atherogenic Indices of Metabolically Healthy Obese Individuals

No significant correlation was observed between adiponectin and (BMI, lipid fractions, and lipid indices) as well as between BMI and the lipid indices (CRI-1, CRI-2 and AIP). However, there was a moderately positive correlation between systolic blood pressure and BMI ($r = .282$, $p=0.029$), TC ($r = .298$, $p=0.024$), LDL ($r = .298$, $p=0.021$), CRI-1 ($r = .257$, $p=0.047$), CRI-2 (.268, $p=0.038$). Additionally, a very strong positive correlations were found between TC and CRI-1($r = 0.849$ p=000) CRI-2 ($r = 0.877$, $p=0.000$) and also between LDL and CRI-1 ($r = 0.913$, p=000), CRI-2 ($r = 0.938$, $p=0.000$). In contrast, a strong negative correlation was observed between HDL and AIP ($r = -.517$, $p=0.000$), CRI-1 ($r = -.416$, $p=0.001$), CRI-2 ($r = -.358$, $p=0.005$).

Discussion

The pandemic of obesity has become a very serious global public health concern especially in low-and middle-income countries (Blüher, 2020). Identification of variant obesity phenotypes has led to the categorization of obesity into metabolically healthy and metabolically unhealthy (Blüher, 2020). Comparison of metabolic biomarkers of metabolically heathy obese with metabolically unhealthy obese puts metabolically healthy obese in a safe mode, however, the terminology-metabolically obese seem to be a misnomer when same metabolic biomarkers are brought in view with metabolically healthy normal weight individuals (Marcus *et al.,* 2023).

The participation of adipose tissue as an endocrine organ contributes significantly to the plethora of obesity associated metabolic complications (Aisike *et al.,* 2023). Obesity has been described as a chronic low grade inflammation of adipose tissues

and dysfunctional tissues secrete multiple pro-inflammatory and anti-inflammatory factors including adiponectin (Khanna, Khanna, Khanna, Kahar & Patel, 2022).

Adiponectin, an adipokine of adipocyte origin, exhibits multiple modulatory effects on several metabolic processes including lipid and glucose metabolism, energy regulation, immune response and inflammation, and insulin sensitivity (Khoramipour *et al.,* 2021). Lower levels of adiponectin in obese individuals have been reported in literatures in Nigeria (Agu, Ogbuabor, Okwuosa, & Achukwu, 2022; Ciroma, *et al.,* 2017; Dike *et al.,* 2024; Nri-Ezeadi *et al.,* 2022) and foreign countries (Fiorotti *et al.,* 2024; Jonas *et al.,* 2017; Nezhadali *et al.,* 2022). However, paucity of data on adiponectin concentrations in MHO exists in Nigeria especially in Owerri. In the present study a significant higher level of adiponectin was observed in metabolically healthy normal weight individuals compared to metabolically healthy obese. Several research findings have demonstrated higher adiponectin levels in MHO compared to MUO (Ahl *et al.,* 2015; Doumatey *et al.,* 2012; AP, Morrison *et al.,* 2010) and such comparison places the metabolically healthy obese in a safe mode. However, comparison with metabolically healthy normal weight individuals raises concern on acclaimed normality of the metabolic profiles.

Dyslipidemia characterized by higher concentrations of total cholesterols, triglycerides low density lipoproteins and lower levels of low density lipoproteins are common in obese individuals. However, a body of literature has demonstrated a normal metabolic profile in MHO (Blüher, 2020) Kruger *et al.,* 2022). The findings of the present study showed a normal levels of total cholesterol, triglyceride and low density lipoprotein. However, in comparison with MHNW individuals, significant variations in lipid fractions were observed indicating that metabolic healthy obese subphenotype are not as safe as postulated. Extensive epidemiological studies and meta-analyses have challenged the benign nature of MHO subphenotype by demonstrating that individuals with MHO are at a higher risk for cerebrovascular disease, heart failure (Zheng, Zhuo & Zhu, 2016), cardiovascular events (Eckel *et al.,*

2016), type 2 diabetes (Moussa *et al.,* 2019), and all-cause mortality (Krammer, Zinman & Retnakaran, 2013) in comparison to metabolically healthy lean individuals (Blüher, 2020). A lower high density lipoprotein typical of MHO was observed in the MHO and was lower than the MHNW individuals. The reason for the observation is unclear.

CRI-I and CRI-II (estimated as TC/HDL-c and LDLc/HDL-c ratios) have been shown to be a more accurate predictors of cardiovascular risk than traditional lipid fractions including total cholesterol (TC), triglyceride(TG), high density lipoprotein ratio of cholesterol fraction (HDL-c) and low density lipoprotein cholesterol fraction (LDL-c) (Adedokun *et al.,* 2017). CRI-I and CRI-11 computated as (TC/HDLc) and (LDLc/HDLc) are both reported as independent risk factors and predictors of cardiovascular disorders is similar with CRI-II in risk evaluation (Adedokun *et al.,* 2017, Bhardwaj, Bhattacharjee, Bhatnagar & Tyagi, 2013)

It has been observed that when changes in these lipid indices are compared with changes in absolute levels of lipids or lipoproteins, they possess better utility and predictability for cardiovascular risk reduction (Millán *et al.,* 2009, Adedokun *et al.,* 2017) especially when the absolute lipid fractions are normal. The absolute values of the lipid fractions detectable in the MHO of this study were normal but the lipid indices (CRI-1 = 5.12, CRI-2 = 3.37) denoted intermediate risk levels (The low risks values: CRI-1<3.5; CRI-11<3.0) (Olamoyegun, Oluyombo & Asaolu, 2016). This shows that the MHO in this population may be at risk of cardiovascular challenges despite the normal lipid fraction values. This is in tandem with the prediction of MHO as not a benign but a transient condition with possible futuristic metabolically unfavourable outcome (Krammer *et al.,* 2013; Moussa *et al.,*2019). In a particular Nurses´ Health Study-(a 30 year follow up from a prospective cohort study), it was observed that participants who maintained MHO over a long time still had a 57% higher risk of CVD than those women with a stable normal body weight (Eckel, 2018).

Additionally, Dobiasova and Frohlich, (2001) proposed another marker of plasma atherogenicity and a lipid ratio of significant predictive value, defined as artherogenic

index of plasma (AIP) calculated as log (TG / HDLc). Studies revealed that in circumstances where other atherogenic risk factors such as TG and HDLc are not altered significantly or show no changes, AIP is a useful diagnostic tool for possible replacement (Nwagha *et al.*, 2010) implying that the AIP calculation estimates the values of "zone of atherogenic risk" (Adedokun *et al.,* 2017; Nwagha *et al.*, 2010). AIP value of 0.21 was observed in MHO of this study and significantly higher than the MHNW individuals, showing that the MHO maintained an intermediate risk levels.

Furthermore, lack of significant association of adiponectin with anthropometric and atherogenic indices in the MHO in this study confirms the normality of metabolic profiling characteristic of MHO. However, the positive correlation of systolic blood pressure with BMI and lipid parameters and indices as well as the strong inverse association of HDL with lipid indices shows that the MHO are at risk of cardiovascular complication [Telle-Hansen]

Conclusion

Metabolically healthy obesity, a subphenotype with normal metabolic profiling is adjudged normal with the presence of favourable risk profile. However, comparative evaluation of the metabolic profiles of the MHO with MHNW alongside the atherogenic indices values of MHO supports the earlier propositions that MHO phenotype possesses intermediate metabolic and cardiovascular risks in comparison to MHNW and MUO. Therefore, special attention should be given to MHO as MUO to prevent future translation to MUO.

Reference

Adedokun, A.K., Olisekodiaka, M.J., Adeyeye, D.A., Muhihi, A. M., Ojukuku, O.H., Adepeju, A.A *et al*., (2017). Castelli Risk Index, Atherogenic Index of Plasma, and Atherogenic Coefficient: Emerging Risk Predictors of Cardiovascular Disease in HIV-Treated Patients. *Saudi Journal of Medical and Pharmaceutical Sciences*, 10.21276/sjmps.2017.3.10.15.

Agu, N.C., Ogbuabor, A.O., Okwuosa, C.N., & Achukwu, P.U. (2022). Some Serum Cytokines (Adiponectin, Apolipoprotein B, hsCRP, IL-6) in a Cohort of Type 2 Diabetes Mellitus Patients. *International Journal of Health Sciences and Research*, 12(12). doi.org/10.52403/ijhsr.20221216.

Aisike, G., Kuerbanjiang, M., Muheyati, D., Zaibibuli, K., Lv, M-X., & Han J. (2023). Correlation analysis of obesity phenotypes with leptin and adiponectin. *Scienific Reports* 13, 17718 (2023). https://doi.org/10.1038/s41598-023-43550-8.

Alberti, K.G., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A., Fruchar,t J.C., James, W.P., Loria, C.M., & Smith, S.C. Jr. (2009). International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; International Association for the Study of Obesity. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation*, 120(16):1640-1645.

Ahl, S., Guenther, M., Zhao, S., James, R., Marks, J., Szabo, A., & Kidambi, S. (2015) Adiponectin Levels Differentiate Metabolically Healthy vs Unhealthy Among Obese and Nonobese White Individuals. *Journal of Clinical Endocrinology Metabolism*, Nov;100(11):4172-80. doi: 10.1210/jc.2015-2765.

Alshaikh, M.K., Filippidis, F.T., Al-Omar, H.A., Rawaf S., Majeed, A., & Salmas,i A-M. (2017). The ticking time bomb in lifestyle-related diseases among women in the Gulf Cooperation Council countries; review of systematic reviews. *BMC Public Health*, 17, 536. https://doi.org/10.1186/s12889-017-4331-7.

April-Sanders, A.K., & Rodriguez, C.J. (2021). Metabolically Healthy Obesity Redefined. *JAMA Network Open,* 4(5):e218860. doi:10.1001/jamanetworkopen.2021.8860.

Bays, H.E., Kirkpatrick, C.F., Maki, K..C, Christensen, S.M., Dixon, D.L., Jacobson, T.A. *et al*. (2024). Obesity, dyslipidemia, and cardiovascular disease: A joint expert review from the Obesity Medicine Association and the National Lipid Association. *Journal of Clinical Lipidology*, 18 (3): e320 - e350.

Behnaz, A., Fatemeh, K., Amir E., Majid, V., & Farhad, H. (2022). Transition from metabolically healthy to unhealthy overweight/obesity and risk of cardiovascular disease incidence: A systematic review and meta-analysis. *Nutrition, Metabolism and Cardiovascular Diseases*, 32 (9), 2022, 2041-2051.

Bhardwaj, S., Bhattacharjee, J., Bhatnagar, M. K., & Tyagi, S. (2013). Atherogenic index of plasma, castelli risk index and atherogenic coefficient new parameters in assessing cardiovascular risk. *International Journal of Pharmacology and Biological Science, 3*, 359–364.

Blüher M. (2020). Metabolically Healthy Obesity. *Endocrine Reviews*, 41 (3) bnaa004, https://doi.org/10.1210/endrev/bnaa004.

Boyarinova, M.A.B., Orlov, A.V.O., Rotar, O.P.R., Alieva, A.S.A., Moguchaya, E.V.M., Vasileva, E.U.V., et al. (2016). Adipokines Level in Metabolically Healthy Obese Saint-Petersburg Inhabitants (ESSE-RF). *Kardiologiia*, 8, 40–45. doi:10.18565/cardio.2016.8.40-45.

Caleyachetty, R., Thomas, G.N., Toulis, K.A., Mohammed, N., Gokhale, K.M., Balachandran, K., & Nirantharakumar, K. (2017). Metabolically healthy obese and incident cardiovascular disease events among 3.5 million men and women. *Journal of American College of Cardiology*, 70(12):1429-1437. doi:10.1016/j.jacc.2017.07.763.

Carolina, G., Gonçalves, M.J., Glade, M.M. & Meguid. (2013). Metabolically healthy obese individuals: Key protective factors, Nutrition. 2013; 32(1): 14-20.

Ciroma, F.L., Ayo, J.O., Mohammed, A., Akor-Dewu, M.B., Ana, M.A., Kase, S.N. (2017). Association between Adiponectin, Serum Lipids and Obesity in a University Setting in Nigeria. *Nigerian Journal of Physiological Science*, 30,32(1):69-74.

Collaboration NCDRF. (2016). Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19.2 million participants. *Lancet*, 387(10026):1377–96.

Dike, D.O., Onuegbu, J.A., Dioka, C.E., Oliseodiaka, J.A., Bede-Ojimadu, O.O., Njoku, C.M., Charles-Davis, M.A., & Okhaumere, E.O. (2024). Comparative assessment of

adiponectin and insulin resistance markers in obese and non-obese individuals in Owerri, Southeastern, Nigeria. GSC Biological and Pharmaceutical Sciences, 29(01), 166–174. Doi : https://doi.org/10.30574/gscbps.2024.29.1.0379.

Dobiasova, M., & Frohlich, J. (2001). The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate inapob-lipoprotein-depleted plasma (FERHDL), *Clinical Biochemistry*, 34,7, 583–588, https://doi.org/10.1016/S0009-9120(01)00263-6, 2-s2.0-0035668546.

Doumatey, A.P., Bentley, A.R., Zhou, J., Huang, H., Adeyemo, A., & Rotimi, C.N. (2012). Paradoxical hyperadiponectinemia is associated with the metabolically healthy obese (MHO) phenotype in African Americans. Journal of Endocrinology Metabolism, 2(2):51–65.

Eckel, N., Meidtner, K., Kalle-Uhlmann, T., Stefan, N., & Schule, M.B. (2016). Metabolically healthy obesity and cardiovascular events: a systematic review and meta-analysis. *European Journal of Preventive Cardiology*, w3(9):956-966.

Eckel, N., Li, Y., Kuxhaus, O., Stefan, N., Hu, F.B., & Schulze, M.B. (2018). Transition from metabolic healthy to unhealthy phenotypes and association with cardiovascular disease risk across BMI categories in 90 257 women (the Nurses' Health Study): 30-year follow-up from a prospective cohort study. *Lancet of Diabetes and Endocrinology*, 6(9):714-724. doi: 10.1016/S2213-8587(18)30137-2.

Eckel, N., Meidtner, K., Kalle-Uhlmann, T., Stefan, N., & Schulze, M.B. (2016). Metabolically healthy obesity and cardiovascular events: a systematic review and meta-analysis. *European Journal of Preventive Cardiology*, 23(9):956–966.

Ejike, C.E.C.C., Ugwu, C.E., & Ezeanyika, L.U.S. (2009). Nutritional status, prevalence of some metabolic risk factors for cardiovascular disease and BMI-metabolic-risk sub-phenotypes in an adult Nigerian population. *Biokemistri*, 21:17-24.

Feingold, K.R (2023). Obesity and Dyslipidemia. [Updated 2023 Jun 19]. In: Feingold KR, Anawalt B, Blackman MR, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK305895/

Fiorotti, AM., Gomes, A.C.A., Bortoli, A.M., Brito, B.B., Nunes, K.Z., Haraguchi, F.K., & Bolsoni-Lopes, A. (2024). Dynamic Changes in Adiponectin and Resistin Drive Remission of Cardiometabolic Risk Biomarkers in Individuals with Obesity Following Bariatric Surgery. *Pharmaceuticals*, 17, 215. https://doi.org/10.3390/ph17020215.

Fogacci, F., Borghi, C., & Cicero, A.F.G.(2021). Diets, Foods and Food Components' Effect on Dyslipidemia. *Nutrients,* Feb 26, 13(3):741. doi: 10.3390/nu13030741.

Fontaine, K.R., Redden, D.T., Wang, C., Westfall, A.O., & Allison, D.B. (2003). Years of life lost due to obesity. *Journal of American Medical Association,* 289 (2): 187-193.

Hong, X., Zhang, X., You, L., Li, F., Lian, H., Wang, J., Mao, N., et al., (2023). Association between adiponectin and newly diagnosed type 2 diabetes in population with the clustering of obesity, dyslipidaemia and hypertension: a cross-sectional study. *BMJ Open*, 13:e060377. doi: 10.1136/bmjopen-2021-060377.

Ijeh, I.I., Okorie, U., Ejike, C.E.C.C. (2010). Obesity, metabolic syndrome and BMI-metabolic-risk sub-phenotypes: A study of an adult Nigerian population. *Journal of Medicine and Medical Sciences,* 1(6): 254-260.

Janiszewska, J., Ostrowska, J., Szostak-Węgierek, D. (2021). The Influence of Nutrition on Adiponectin-A Narrative Review. *Nutrients,* Apr 21, 13(5):1394. doi: 10.3390/nu13051394. PMID: 33919141; PMCID: PMC8143119.

Jiao, J. (2023). The Role of Nutrition in Obesity. *Nutrients,* May 30,15(11):2556. doi: 10.3390/nu15112556.

Jonas, M.I., Kurylowicz, A., Bartoszewics, Z., Lisik, W., Jonas, M., Domienik-Karlowics, J., & Puzianowska, K. (2017). Adiponectin/resistin interplay in serum and in adipose tissue of obese and normal-weight individuals. *Diabetology and Metabolic Syndrome*, 9:95.

Karelis, A.D., Brochu, M., & Rabasa-Lhoret, R. (2004) Can we identify metabolically healthy but obese individuals (MHO)? *Diabetes Metabolism*, 30(6):569–72.

Khanna, D., Khanna, S., Khanna, P., Kahar, P., & Patel, B.M. (2022). Obesity: A Chronic Low-Grade Inflammation and Its Markers. *Cureus*, Feb 28;14(2):e22711. doi: 10.7759/cureus.22711.

Khoramipour, K., Chadmari, K., Hekmatikar, A.A., Ziyaiyan, A., Taherkhani, S., Elguindy, N.M., & Bragazzi, N.L. (2021). Adiponectin: Structure, Physiological Functions, Role in Diseases, and Effects of Nutrition. *Nutrient,* Apr 2;13(4):1180. doi: 10.3390/nu13041180.

Kramer, C.K., Zinman, B., & Retnakaran, R. (2013). Are metabolically healthy overweight and obesity benign conditions?: A systematic review and meta-analysis. *Annal of Internal Medicine,* Dec 3;159(11):758-69. doi: 10.7326/0003-4819-159-11-201312030-00008.

Kruger, H.S., De Lange-Loots, Z., Kruger, I.M., & Pieters, M. (2022). The Metabolic Profiles of Metabolically Healthy Obese and Metabolically Unhealthy Obese South African Adults over 10 Years. *International Journal of Environmental Research and Public Health,* Apr 21;19(9):5061. doi: 10.3390/ijerph19095061.

Lee, H., Kim, J.S., & Shin, H. (2024). Predicting the Transition to Metabolically Unhealthy Obesity Among Young Adults With Metabolically Healthy Obesity in South Korea: Nationwide Population-Based Study. *JMIR Public Health Surveillence,* 10:e52103. doi: 10.2196/52103.

Magkos, F. (2019). Metabolically healthy obesity: what's in a name? *American Journal of Clinical Nutrition,* 110(3):533–539.

Marcus, Y., Segev, E., Shefer, G., Eilam, D., Shenkerman, G., Buch, A., Shenhar-Tsarfaty, S., Zeltser D., Shapira, I., Berliner, S., *et al.*(2023). Metabolically Healthy Obesity Is a Misnomer: Components of the Metabolic Syndrome Linearly Increase with BMI as a Function of Age and Gender. *Biology*, 12(5):719. https://doi.org/10.3390/biology12050719.

Millán, J., Pintó, X., Muñoz, A., Zúñiga, M., Rubiés-Prat, J., Pallardo, L. F., Masana, L., Mangas, A., Hernández-Mijares, A., González- Santos, P., Ascaso, J. F., & Pedro-Botet, J. (2009). Lipoprotein ratios: Physiological significance and clinical usefulness in cardiovascular prevention. *Vascular Health Risk Management,* 5:757–765.

Morrison, J.A., Glueck, C.J., Daniels, S., Wang, P., Horn, P., & Stroop, D. (2010). Paradoxically high adiponectin and the healthy obese phenotype in obese black and white 16-year-old girls. *Translational Research,* 156(5):302–308.

Moussa, O., Arhi, C., Ziprin, P., Darzi, A., Khan, O., & Purkayastha, S. (2019). Fate of the metabolically healthy obese-is this term a misnomer? A study from the Clinical Practice Research Datalink. *International Journal of Obesity* (London), May,43(5):1093-1101. doi: 10.1038/s41366-018-0096-z.

National Cholesterol Education Program (NCEP) (2022). Expert Panel on Detection, Evaluation, Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation,* 106(25):3143–3421.

Nezhadali, M., Mesbah-Namin, S.A., Hedayati, M., AKbarzadeh, M., Bonab, L.N.H., & Daneshpour, M.S. (2022). Serum adiponectin and cortisol levels are not affected by

studied ADIPOQ gene variants: *Tehran lipid and glucose study*, 22,104: doi.org/10.1186/s12902-022-01020-8.

Nri-Ezedi, C., Okpara, H., Okeke, K., Nwaneli, E., Edokwe, E., Echendu, S. & Ulasi, T. (2022). Exploring the Relationship between Adiponectin and Blood Pressure in Nigerian Children. *Open Journal of Endocrine and Metabolic Diseases*, 12, 9-19. doi: 10.4236/ojemd.2022.122002.

Nwagha, U.I., Ikekpeazu, E.J., Ejezie, F.E., Neboh, E.E., & Maduka, I.C. (2010). Atherogenic index of plasma as useful predictor of cardiovascular risk among postmenopausal women in Enugu, Nigeria. *African Health Sciences*, 10(3):248–252.

Olamoyegun, M.A., Oluyombo, R., & Asaolu, S.O. (2016). Evaluation of dyslipidemia, lipid ratios, and atherogenic index as cardiovascular risk factors among semi-urban dwellers in Nigeria. *Annals of African medicine*, 15(4):194–199. doi: 10.4103/1596-3519.194280.

Ramakrishnan, N., Auger, K., Rahimi, N. & Jialal, I. (2024). Biochemistry, Adiponectin. [Updated 2023 Jul 30]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537041/.

Rey-López, J.P, de Rezende, L.F., Pastor-Valero, M., & Tess, B.H. (2014). The prevalence of metabolically healthy obesity: a systematic review and critical evaluation of the definitions used. *Obesity Review*, 15(10):781–790.

Schulze, M.B., Stefan, N. (2024) Metabolically healthy obesity: from epidemiology and mechanisms to clinical implications. *Nature Review Endocrinology*, 20, 633–646. https://doi.org/10.1038/s41574-024-01008-5.

She, Y., Mangat, R., Tsai, S., Proctor, S.D., & Richard, C. (2022) The Interplay of Obesity, Dyslipidemia and Immune Dysfunction: A Brief Overview on Pathophysiology, Animal Models, and Nutritional Modulation. *Frontier of Nutrition*, 9:840209. doi: 10.3389/fnut.2022.840209.

Smith, G.I., Mittendorfer, B., & Klein, S. (2019). Metabolically healthy obesity: facts and fantasies. *Journal of Clinical Investigation*, 129(10):3978-3989. doi:10.1172/JCI129186.

Telle-Hansen, V.H., Christensen, J.J., Formo, G.A., Holven, K.B., & Ulven, S.M. (2020). A comprehensive metabolic profiling of the metabolically healthy obesity

phenotype. *Lipids in Health and Diseases,* 19, 90. https://doi.org/10.1186/s12944-020-01273-z.

Tomono, Y., Hiraishi, C., &Yoshida, H. (2018). Age and sex differences in serum adiponectin and its association with lipoprotein fractions. *Annal of Clinical Biochemistry,* 55, 165–171.

Vague, J. (1956). The degree of masculine differentiation of obesities: a factor determining predisposition to diabetes, atherosclerosis, gout, and uric calculous disease. *American Journal of Clinical Nutrition,* 4(1):20-34.

Vekic, J., Stefanovic, A., & Zeljkovic, A. (2023). Obesity and Dyslipidemia: A Review of Current Evidence. *Current Obesity Report*, 12, 207–222. https://doi.org/10.1007/s13679-023-00518-z.

Wang, G., Wang, Y., & Luo, Z. (2022). Effect of Adiponectin Variant on Lipid Profile and Plasma Adiponectin Levels: A Multicenter Systematic Review and Meta-Analysis. *Cardiovascular Therapeutics*, https://doi.org/10.1155/2022/4395266.

Wurtz, P., Havulinna, A.S., Soininen, P., Tynkkynen, T., Prieto-Merino, D., Tillin, T., *et al.* (2015). Metabolite profiling and cardiovascular event risk: a prospective study of 3 population-based cohorts. *Circulation,* 131(9):774–85.

Yanai, H., & Yoshida, H. (2019). Beneficial Effects of Adiponectin on Glucose and Lipid Metabolism and Atherosclerotic Progression: Mechanisms and Perspectives. *International Journal of Molecular Sciences*, 20(5):1190. https://doi.org/10.3390/ijms20051190.

Zheng, R., Zhuo, D., & Zhu, Y. (2016). The long-term prognosis of cardiovascular disease and all-cause mortality for metabolically healthy obesity: a systematic review and meta-analysis. *Journal of Epidemiology and Community Health,* 70(10):1024-1031.