Clinical characteristics and classification of Cameroonian with obesity and metabolically normal phenotype in the West region of Cameroon

Maxwell Wandji Nguedjo a,c, Judith Laure Ngondi a,b,*, Françoise Raïssa Ntentie b, Boris Gabin Kingue Azantsa a, Javeres Leonel Ntepe Mbah d,e, Julius Enyong Oben a

a Department of Biochemistry, Faculty of Sciences, University of Yaoundé 1, P. O. Box 812, Yaoundé, Cameroon
b Higher Teacher's and Training College, University of Maroua, P. O. Box 55, Maroua, Cameroon
c Centre for Food, Food Security and Nutrition Research, Institute of Medical Research and Medicinal Plant Studies, P. O. Box 13033, Yaoundé, Cameroon
d Laboratory of Human Metabolism and Non-Communicable Disease, Institute of Medical Research and Medicinal Plant Studies, P. O. Box 13033, Yaoundé, Cameroon
e Department of Biosciences, COMSATS University Islamabad, Chak Shouzad, Islamabad 45550, Pakistan

ARTICLE INFO

Keywords:
Obesity
Metabolically normal phenotype
Clinical characteristics
Classification

ABSTRACT

The objective of this study was to classify and suggest an adequate definition of the metabolically normal phenotype among Cameroonian with obesity in the western Region of Cameroon. A cross-sectional study was conducted in the West Cameroon Region from August 2016 to August 2017. A total of 324 subjects with BMI > 27 kg/m², aged of 20 years and older, and not treated for cardiometabolic diseases were included in the study. Sociodemographic and clinical parameters of the subjects were collected. Four definitions of metabolic status were tested to suggest the definition that best identifies the subjects with obesity but metabolically normal phenotype (MNO) in the study. The prevalence of the MNO phenotype varied from 2.50% to 29.60% according to the definitions used. According to the individual definitions, the prevalence of the MNO phenotype was 29.60% according to Hinnouho, 16.00% according to Mbanya, 7.40% according to Meigs and 2.50% according to Widman. Markers of inflammatory profile (high sensitivity C-reactive protein and tumor necrosis factor-alpha), carbohydrate homeostasis (fasting glucose and homeostasis model assessment), markers of lipid profile (total cholesterol and triglyceride), systolic blood pressure, nitric oxide, adiposity indices (Waist circumference and waist to hip ratio) were significantly lower in MNO subjects for the majority of definitions. The modified Hinnouho definition showed better specificity (60.90%) and sensitivity (12.10%) for an area under the ROC curve of 0.98. The degree of agreement was low between the different pairs of definition of the MNO phenotype (Kappa < 0.61). There is poor agreement between the different definitions of the MNO phenotype among Cameroonian with obesity. Therefore, the adoption of a universal definition of MNO phenotype should be proposed to facilitate the management of metabolic health in people with obesity.

1. Introduction

Obesity is a disease defined by an exaggerated accumulation of adipose tissue and is found to be detrimental to health (Bosomworth, 2019). In 2016, more than 1.9 billion of adults were overweight in the world, among which 650 million were obese. Recent estimations reveal that by 2035, 38% of adults will be overweight worldwide and 20% obese (Montzel et al., 2019). Sub-Saharan Africa is also concerned, with nearly 30% and 10% of adults overweight and obese, respectively (Agyemang et al., 2016; Adeloye et al., 2021). The intersecting phenomenon of urbanization and westernization of people's lifestyle marked by sedentary and unhealthy diet contributes to the increase of the prevalence of obesity in this region of the globe (Simo et al., 2021) and makes it a major public health problem. Obesity is associated to an increased risk of premature death, coronary heart disease, stroke, type 2 diabetes and physical disability (Decaria et al., 2012). The high rate of deaths and cardiovascular diseases observed in individuals with obesity are thought to be influenced by a constellation of metabolic abnormalities, including high blood pressure, hyperglycemia, dyslipidemia, insulin resistance, and a proinflammatory state (Ortega et al., 2016). The frequency of these biological risk factors varying considerably among obese subjects making this chronic disease a very heterogeneous
clinical situation (Stefan et al., 2013). Epidemiological data indicate that a significant proportion (10–30%) of individuals who are classified as obese are metabolically normal based on their metabolic profiles (Blüher, 2020). The existence of this paradox of obesity metabolic status in the population emerged a new concept involving a group of metabolically normal obese (MNO) phenotype individuals (Acharya and Shukla, 2018). These MNO phenotype individuals have a favorable metabolic profile and a lower risk of developing cardiovascular disease compared to their at-risk, metabolically abnormal phenotype (MAO) counterpart (Primiaux et al., 2011).

To date, the lack of consensus on how to define individuals with a metabolically normal phenotype makes their identification complex. Several classifications have been proposed to categorize obese individuals with good cardiometabolic health, each using various criteria to accurately identify this population (Elías-Lopez et al., 2021). The criteria for defining this MNO phenotype are generally based on the absence of metabolic disorders related to the metabolic syndrome and/or the presence of insulin sensitivity (Phillips, 2016). Several studies have been carried out in Europe, Asia, and the United States of America about the metabolic phenotypes of obesity (Adair et al., 2021; Velho et al., 2010; Liu et al., 2019). However, in Sub-Saharan Africa, very little specific data about these phenotypes have been generated. In Cameroon, the only study conducted on metabolic phenotypes of obesity focused only on the prevalence of body mass index (BMI) metabolic phenotypes in the rural-urban context (Mbanya et al., 2015). However, to the best of our knowledge, there are no studies that focus on the metabolic phenotypes of obesity according to several definitions to distinguish the metabolically normal phenotype among Cameroonians. Native population of West Region of Cameroon, the Bamileke are one of the major ethnic groups in Cameroon which have a high prevalence of overweight in rural areas and are three times more likely to develop obesity than other Cameroonians (Pasquet et al., 2003). Focusing on this Bamileke population, this study was designed to assess the clinical characteristics and classification of obese people with a metabolically normal phenotype in order to understand its evolution in the socio-cultural context.

2. Materials and methods

2.1. Study design and sampling procedure

A cross-sectional survey was conducted during the period from August 2016 to August 2017 among Bamileke people residing in the West Cameroon region. Cameroonians participants of both sexes were recruited during free and voluntary health campaigns on cardiometabolic diseases, organized by the Cameroon Society of Nutritional Sciences. The study sites (03) were randomly selected and included secondary cities: Bafoussam (capital of Mifi department), Mbouda (capital of Bamboutos department) and Bangangte (capital of Nde department). The sample size was calculated according to the Magnani formula (Magnani, 1997), taking into account the 95% confidence level, the margin of error at 5% and the prevalence of metabolic syndrome in semi-urban Cameroon which is 17.4% (Ntandou et al., 2014). The required sample size was estimated at 221 individuals, but 324 individuals were retained after considering inclusion and exclusion criteria.

2.2. Inclusion and exclusion criteria

Participants of Bamileke ethnicity, from the western region of Cameroon, aged of 20 years and older, residing in the study site for at least 1 year, having a BMI >27 kg/m² and having given their informed consent were admitted to the study. Mentally handicapped persons and those diagnosed with hypertension, heart disease, diabetes or any other cardiometabolic diseases before being enrolled were excluded because of likely changes in dietary and lifestyle habits or possible drug treatments that may influence metabolism.

2.3. Ethical considerations

This study was approved by the National Ethics Committee of Cameroon under No. 2014/08/488/CE/CNERSH. The administrative authorities in charge of the cities selected for this study also gave their approval. The participants who agreed to participate freely in the study signed the free and informed consent form provided for this purpose. The Declaration of Helsinki on Human Medical Ethics was followed.

2.4. Questionnaire

After consenting to participate in the study, data on the participants were collected through a face-to-face interview. This was done via the administration of a questionnaire adapted from the WHO Stepwise approach for the surveillance of nutrition-related chronic diseases (WHO, 2017). The study questionnaire contained information on sociodemographic characteristics (age, sex, marital status, education, occupation and 12 items constituting possessions) and lifestyle (alcohol consumption, smoking etc…). Socioeconomic status (SES) was determined by using a household amenity score (NSAE/EDSB, 2001) as a proxy for income. This score was composed of the 12 items constituting the participants’ possessions, namely: wall and floor materials, type of fuel used for cooking, motorcycle, ownership of plot of land, television, car, electricity, mobile phone, line phone, water in the house, refrigerator. The first two items were dichotomous and coded ‘0’ for other materials and ‘1’ for a cement floor or wall. Fuel used for cooking was coded 1; 0.5 and 0 for oil or gas, charcoal and firewood, respectively. The last nine items were also dichotomous and coded ‘0’ if not present and ‘1’ if convenience was present. The sum of these items, for a maximum of 12, constituted the amenity score (or SES). The score values were grouped into three categories according to the method described by Ntandou et al. (2008). This classification included the SES: low [0–2], medium [3–4], and high [5–10], because no matter what, participants’ scores could not reach 12. Instead, in this study we grouped participants into two categories as defined by Ntandou et al. (2008) method, with slight modifications: low [0–2] and medium/high [3–9.5]. Medium and high SES were combined into one category because they are not always recognized as risk factors for obesity compared to low SES (Kuntz and Lampert, 2010). The level of education was classified into two categories namely: primary education (low) and, secondary and university education (high).

2.5. Physical examination

Weight was recorded to the nearest 0.1 kg using an electronic scale (The Tanita™ BC-418 Analyzer/Segmental Body Composition Scale) in moderately clothed participants. Height was measured to the nearest 0.1 cm using a stadiometer (Harpended™). Waist circumference was measured using a soft, non-stretchable tape measure on the midpoint between the lower edge of the ribs and the iliac crest in a plane perpendicular to the long axis of the body without restrictive clothing. Waist-to-height ratio (WHR) was determined by dividing the waist circumference (cm) by the hip circumference (cm). Body mass index (BMI) was calculated for all participants using the formula: BMI = Weight (kg)/Height² (m²) and expressed in kg/m². A BMI threshold >27 kg/m² has been used to diagnose obesity because comorbidities associated with obesity are typically seen in people with a BMI >27 kg/m² (or ≥30 kg/m²). Furthermore, current guidelines recommend that only people with a BMI >27 kg/m² (or ≥30 kg/m²) should be eligible for drug treatment for obesity (Colman, 2012). Besides this, many studies have characterised people with a BMI >27 kg/m² as obese (Said et al., 2010; Lin et al., 2022).

Two blood pressure measurements were taken using an OMRON electronic radial sphygmomanometer at rest. The participant was seated in a chair with the left arm parallel to the heart. The first measurement was taken after a 10-minute rest in the sitting position, and the second measurement one was after 10–15 min afterwards. The average of the
two measurements was used to assess the presence or absence of high blood pressure.

### 2.6. Laboratory measurements

In the morning, after a 12-hour overnight fast, approximately 5 ml of venous blood was collected into EDTA tubes, centrifuged, and the resulting plasma was stored in aliquots in the freezer at –20 °C for biochemical analyses. Samples were analyzed for total cholesterol (TC), high density lipoprotein cholesterol (HDLc) and triglyceride (TG) levels using Chronolab Diagnostic test kits under standard enzyme spectrophotometric methods. Plasma low density lipoprotein cholesterol (LDLc) level was estimated using the Friedewald's equation (Friedwald et al., 1972). Plasma nitric oxide levels were assessed by the method of Manish et al. (2006). Fasting blood glucose was measured by the glucose oxidase peroxidase (GOP-PD) method using a glucose meter and test strips (One-touch plus) directly on the participant’s fingertip. Fasting plasma insulin, high sensitivity C-reactive protein (hsCRP) and tumour necrosis factor (TNF) were determined by ELISA and microplate reader spectrophotometer. Assessment of the homeostatic model of insulin resistance (HOMA) was determined using the formula: HOMA = insulin (µU/L) x [glucose (mmol/L)/22.5] (Matthews et al., 1985).

### 2.7. Diagnosis of cardiometabolic risk factors and determination of the normal metabolic status

Cardiometabolic risk factors such as abdominal obesity (waist circumference (WC) > 102 cm (men) and >88 cm (women)), hyper-triglyceridemia (TG > 150 mg/dL), hypercholesterolemia (TC > 200 mg/dL), high blood pressure (Systolic blood pressure (SBP) > 130 mmHg and/or diastolic blood pressure (DBP) > 85 mmHg), hyperglycemia (fasting blood glucose (FBG) > 100 mg/dL) and insulin resistance (HOMA > 2.6) were diagnosed according to the criteria of NCEP (2001) and Matthews et al. (1985). Chronic low-grade inflammation defined by a high-sensitivity C-reactive protein (hsCRP) level ≥ 3 mg/L, was diagnosed according to the criteria of Widman et al. (2008). Considering the lack of a standardized definition and the number of non-standard metabolic abnormalities used to distinguish obesity-associated metabolic phenotypes, 4 modified definitions (Meigs et al., 2006; Wildman et al., 2008; Hinnouho et al., 2014 and Mbanya et al., 2015) based on the total absence of metabolic abnormalities to define the metabolically normal phenotype were adopted. Metabolic anomaly values and threshold values commonly validated on multiple occasions in the Cameroonian population (TC ≥ 200 mg/dL replacing HDL-C (<40 mg/dL (men)) or (<50 mg/dL (women)) and HOMA > 2.6 replacing HOMA > 90th percentile) were used as a component of the criteria for defining metabolic phenotypes of obesity (Table 1). The obesity phenotypes were classified into 2 groups of subjects namely: “Metabolically Normal Obese” subjects (MNO) which suggests no metabolic abnormalities and “Metabolically Abnormal Obese” subjects (MAO) with at least one metabolic abnormality. The Cardiometabolic Index (CMI) was calculated by the following formula: CMI = [(TG/HDL-c) x (Waist circumference/Height)] (Wakabayashi and Daimon, 2015). A CMI ≥ 0.80 in women and a CMI ≥ 1.748 in men reflected impaired carbohydrate homeostasis (Wakabayashi and Daimon, 2015).

### 2.8. Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0 for Windows. The results of the descriptive analysis were expressed as frequency (%) for categorical variables and as mean ± standard error for continuous variables. Chi-square test was performed to assess the difference in proportion between the categorical variables. Student’s t test was used to detect differences in means between two groups of a continuous dependent variable. The metabolic phenotypes of obesity were classified according to the linear discriminant model and the areas under the Receiver Operating Characteristic (ROC) curves were compared using the method of Hanley and McNeil (1983). ROC values less than 0.70 indicated low accuracy, ROC values between 0.70–0.90 indicated useful applications and ROC values above 0.90 indicated high accuracy (Manel et al., 2001). The kappa coefficient (K) was used to assess the degree of agreement between the definitions used and these degrees of agreement were categorized as follows: If K < 0.61 the degree of agreement is poor, if K is between 0.61 and 0.80 the degree of agreement is good, and if K ≥ 0.81 the degree of agreement is more than perfect (Manel et al., 2001). The significance level used was p < 0.05.

### 3. Results

As shown in Table 2 women represented 70.40% of the 324 study participants. Subjects with medium and high education levels (92.00%), those living in couples (70.40%), unemployed subjects (69.10%) and those with medium and high socioeconomic levels (51.90%) were predominantly represented. With regard to the lifestyle of the study population, 14.80% of the subjects drank alcohol and 6.20% were smokers.

The study population had an average age of 46.28 ± 0.68 years and an average BMI of 32.21 ± 0.21 kg/m²; with an average lean body mass of 54.07 ± 0.21 kg and a body fat of 40.08 ± 0.52 %. The average values of waist circumference and waist to hip ratio were 99.04 ± 0.73 cm and 0.89 ± 0.007 respectively. The average values of SBP and DBP were 122.41 ± 1.01 mmHg and 71.05 ± 0.67 mmHg in the general population. Regarding lipid profile markers, plasma triglyceride (122.85 ± 3.39 mg/dL) and total cholesterol (177.86 ± 4.26 mg/dL) average values were below the diagnostic cut-off values for hyperlipidemia. While the average HDL cholesterol value (45.33 ± 1.82 mg/dL) was above the diagnostic value for HDL hypercholesterolemia in men but below the diagnostic value for HDL hypercholesterolemia in women but below the diagnostic cut-off values for hyperlipidemia. The study population had an average age of 46.28 ± 0.68 years and an average BMI of 32.21 ± 0.21 kg/m²; with an average lean body mass of 54.07 ± 0.21 kg and a body fat of 40.08 ± 0.52 %. The average values of waist circumference and waist to hip ratio were 99.04 ± 0.73 cm and 0.89 ± 0.007 respectively. The average values of SBP and DBP were 122.41 ± 1.01 mmHg and 71.05 ± 0.67 mmHg in the general population. Regarding lipid profile markers, plasma triglyceride (122.85 ± 3.39 mg/dL) and total cholesterol (177.86 ± 4.26 mg/dL) average values were below the diagnostic cut-off values for hyperlipidemia. While the average HDL cholesterol value (45.33 ± 1.82 mg/dL) was above the diagnostic value for HDL hypercholesterolemia in men but below the diagnostic value for HDL hypercholesterolemia in women but below the diagnostic cut-off values for hyperlipidemia.

#### Table 1. Criteria used to define the metabolically normal obese phenotype.

| Definitions | Meigs et al. (2006) | Widman et al. (2008) | Hinnouho et al. (2014) | Mbanya et al. (2015) |
|-------------|---------------------|----------------------|------------------------|----------------------|
| SBP > 130 mmHg and/or DBP > 85 mmHg | SBP > 130 mmHg and/or DBP > 85 mmHg | SBP > 130 mmHg and/or DBP > 85 mmHg | SBP > 130 mmHg and/or DBP > 85 mmHg |
| TG > 150 mg/dL | TG > 150 mg/dL | TG > 150 mg/dL | TG > 150 mg/dL |
| HDL-C (<40 mg/L (men)) or (<50 mg/L (women)), replaced by TC ≥ 200 mg/dL | HDL-C (<40 mg/L (men)) or (<50 mg/L (women)), replaced by TC ≥ 200 mg/dL | HDL-C (<40 mg/L (men)) or (<50 mg/L (women)), replaced by TC ≥ 200 mg/dL | HDL-C (<40 mg/L (men)) or (<50 mg/L (women)), replaced by TC ≥ 200 mg/dL |
| FBG ≥ 100 mg/dL | FBG ≥ 100 mg/dL | FBG ≥ 100 mg/dL | FBG ≥ 100 mg/dL |
| HOMA > 90th percentile, replaced by hscRP ≥ 2.6 | - | HOMA > 90th percentile, replaced by hscRP ≥ 2.6 | - |
| WC > 102 (men); WC > 88 (women) | - | - | - |
| hscRP ≥ 3 mg/L | - | - | - |

* = Modified parameters; WC: waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; TG: Triglyceride; TC: Total cholesterol; HDLc: high density lipoprotein cholesterol; FBG: fasting blood glucose; HOMA: Homeostasis Model Assessment; hsCRP: high sensitivity C-reactive protein.

* The above criteria have been replaced by the complete absence of metabolic abnormalities.
Table 2. Socio-demographic and clinical characteristics of 324 subjects with obesity living in the West Cameroon region.

| Parameters | General population | P value |
|------------|--------------------|---------|
| Sex, % (n) | Woman              | 70.40 (228) | <0.001 |
|            | Man                | 29.60 (96)   |         |
| Level of education, % (n) | Low          | 8.00 (26) | <0.001 |
|            | High               | 92.00 (298) |         |
| Marital status, % (n) | Unmarried | 29.60 (96) | <0.001 |
|            | Married            | 70.40 (228) |         |
| Profession, % (n) | Unemployed | 69.10 (224) | <0.001 |
|            | Employed           | 30.90 (100) |         |
| Socio-economic level, % (n) | Low     | 48.10 (156) | 0.505  |
|            | Medium and High    | 51.90 (168) |         |
| Alcohol consumption, % (n) | No     | 85.20 (276) | <0.001 |
|            | Yes                | 14.80 (48)  |         |
| Smoking, % (n) | No     | 93.80 (304) | <0.001 |
|            | Yes                | 6.20 (20)   |         |
| Age, M ± SE | Age (years) | 46.28 ± 0.68 | n.a.   |
|            | Body mass index (kg/m²) | 32.21 ± 0.21 | n.a.   |
|            | Body fat (%)       | 40.08 ± 0.52 | n.a.   |
|            | Lean body mass (kg) | 54.07 ± 0.53 | n.a.   |
|            | Waist circumference (cm) | 99.04 ± 0.73 | n.a.   |
|            | Hip circumference (cm) | 112.13 ± 0.63 | n.a.   |
|            | Waist-to-hip ratio  | 0.89 ± 0.10  | n.a.   |
| Blood pressure, M ± SE | Systolic blood pressure (mmHg) | 122.41 ± 1.01 | n.a.  |
|            | Diastolic blood pressure (mmHg) | 71.05 ± 0.67 | n.a.  |
|            | Pulse (beats/min)   | 77.81 ± 0.74  | n.a.   |
| Marker of endothelial function | Nitric oxide (μmol/L) | 12.35 ± 0.48 | n.a. |
| Lipid profile, M ± SE | Triglycerides (mg/dL) | 122.85 ± 3.39 | n.a. |
|            | Total cholesterol (mg/dL) | 177.86 ± 4.26 | n.a. |
|            | High density lipoprotein | 45.33 ± 1.82 | n.a.  |
|            | Low density lipoprotein | 91.65 ± 11.1 | n.a.  |
| Carbohydrate homeostasis, M ± SE | Fasting blood glucose (mg/dL) | 110.86 ± 1.62 | n.a. |
|            | Insulin (μU/mL)     | 13.35 ± 0.34  | n.a.   |
|            | Homeostasis model assessment | 3.56 ± 0.11 | n.a. |
| Inflammatory profile, M ± SE | High sensitivity C-reactive protein (mg/L) | 4.58 ± 0.08 | n.a. |
|            | Tumor necrosis factor α (pg/ml) | 18.46 ± 0.15 | n.a. |
| Cardiovascular index, M ± SE | Cardiometabolic index | 1.35 ± 0.21 | n.a. |

Descriptive analyses of the general population were performed and the results are presented as frequency (%) and mean ± standard error. Chi-square test was used to compare proportions between categorical variables. n.a: not applicable.

Table 3. Prevalence of cardiometabolic risk factors in 324 subjects with obesity living in the West Cameroon region.

| Cardiometabolic risk factors | Prevalence % (95% CI) |
|-----------------------------|-----------------------|
| Abdominal obesity (Waist circumference >102 cm (men); Waist circumference >88 cm (women)) | 80.20 (75.50-84.40) |
| Inflammation (High sensitivity C-reactive protein ≥3 mg/L) | 80.20 (75.50-84.40) |
| Insulin resistance (Homeostasis model assessment ≥2.6) | 64.20 (58.70-69.40) |
| High blood pressure (Systolic blood pressure ≥130 mmHg and/or Diastolic blood pressure ≥85 mmHg) | 60.20 (54.60-65.60) |
| Hyperglycemia (Fasting blood glucose ≥100 mg/dL) | 50.60 (45.00-56.20) |
| Hypercholesterolemia (Total cholesterol ≥200 mg/dL) | 27.20 (22.40-32.40) |
| Hypertriglyceridemia (Triglyceride ≥150 mg/dL) | 17.30 (13.30-21.80) |

Descriptive analysis of cardiometabolic risk factors in the general population was performed and the results are presented as a percentage. %: Percentage; CI: Confidence interval.
| Parameters                     | Definitions                                                                 |
|-------------------------------|----------------------------------------------------------------------------|
| M.Eins (mg/dL)                | MNO 0.00 (0)                                                               |
| Widman M.Banya M.Himouho      | MNO 0.00 (0)                                                               |
| M.Himouho                     | MNO 0.00 (0)                                                               |
| % (n)                         | % (n)                                                                       |
| Alcohol drinker, (n)          | 0.00 (0)                                                                   |
| Smoker, (n)                   | 0.00 (0)                                                                   |
| Age (years)                   | 44.67 ± 0.78                                                               |
| BMI (kg/m²)                   | 29.60 ± 0.33                                                               |
| Body fat (%)                  | 30.80 ± 0.85                                                               |
| LBM (kg)                      | 57.96 ± 1.90                                                               |
| WC (cm)                       | 68.68 ± 1.37                                                               |
| Man                           | 7.70 ± 0.01                                                                |
| HC (cm)                       | 100.66 ± 1.37                                                             |
| WHR                           | 0.68 ± 0.09                                                                |
| SBP (mmHg)                    | 123.33 ± 1.37                                                              |
| DBP (mmHg)                    | 75.00 ± 0.29                                                               |
| Pulse (beats/min)             | 80.67 ± 4.52                                                               |
| NO (μmol/L)                   | 24.93 ± 0.51                                                               |
| TG (mg/dL)                    | 75.78 ± 3.15                                                               |
| TC (mg/dL)                    | 120.82 ± 2.10                                                              |
| HDLc (mg/dL)                  | 46.24 ± 0.06                                                               |
| LDLc (mg/dL)                  | 59.39 ± 0.02                                                               |
| Blood glucose (mg/dL)         | 86.67 ± 0.49                                                               |
| Insulin (μIU/mL)              | 14.70 ± 1.34                                                               |
| HOMA                          | 3.18 ± 0.31                                                                |
| hsCRP (mg/L)                  | 3.03 ± 0.01                                                                |
| TNFα (pg/mL)                  | 13.33 ± 0.27                                                               |
| CMI                           | 0.69 ± 0.07                                                                |

Values are presented as percentage (frequency) and mean ± standard error. The descriptive analysis was used to determine the proportions of MNO and MAO subjects for each definition. Chi-square and Student’s t-tests were performed to assess the difference between MNO and MAO subjects. On the same line, values marked with * are significantly different at p < 0.05. BMI: Body Mass Index; LBM: Lean Body Mass; WC: Waist circumference; HC: Hip circumference; WHR: waist-to-hip ratio; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; NO: Nitric Oxide; TG: Triglyceride; TC: Total cholesterol; HDLc: High density lipoprotein cholesterol; LDLc: Low density lipoprotein cholesterol; TNFα: Tumor Necrosis Factor; hsCRP: high sensitivity C-reactive protein; HOMA: Homeostasis Model Assessment; CMI: Cardio-metabolic Index.

As shown by Figures 1 and 2, the areas under the ROC curves as defined by Meigs (Figure 1a), Widman (Figure 1b), Mbanja (Figure 2a) and Himouho (Figure 2b) were 1.00, 1.00, 0.99 and 0.98, respectively. Table 5 shows that all areas under the ROC curves were > 0.90, which reflects a high precision for the different definitions used. However, the definition of MNO phenotype according to Himouho had the highest precision.
sensitivity (60.90%) and specificity (12.10%), followed by the Mbanya definition with a sensitivity of 55.00% and a specificity of 6.90%. On the other hand, the Meigs and Widman definitions had a sensitivity of less than 55.00% and a specificity of less than 1.00%.

The degree of agreement was low between the different MNO phenotype definition pairs (Table 6). The degree of agreement between the MNO phenotype definitions pairs ranged from -0.03 for the definition pair (Meigs-Widman) to 0.48 for the definition pair (Hinnouho-Mbanya).

4. Discussion

Not all people are subject to obesity-related metabolic complications in the same way (Primaux et al., 2011). This difference is due to their metabolic status. Thus, there are several phenotypes in individuals with

| Definition pairs       | Kappa ± Standard error |
|------------------------|------------------------|
| Hinnouho –Meigs        | 0.31 ± 0.05            |
| Hinnouho –Mbanya       | 0.48 ± 0.05            |
| Hinnouho –Widman       | 0.11 ± 0.03            |
| Meigs–Mbanya           | 0.35 ± 0.07            |
| Meigs–Widman           | −0.03 ± 0.01           |
| Mbanya–Widman          | 0.23 ± 0.06            |
obesity depending on their metabolic status. In this work, we were interested in people with obesity but metabolically normal phenotype (MNO) in the West Region of Cameroon. Four definitions of the MNO phenotypes (Meigs, Widman, Mbanya, and Hinnouho) were selected and their adjustment to clinical characteristics of the MNO subjects were assessed. The four definitions were tested, based on the presence of preserved insulin sensitivity and/or the absence of disturbances related to the metabolic syndrome associated with a CRP level indicative of an inflammatory state. Since there is no standardized definition of cardiometabolic health in people with obesity, this study used the modified Meigs, Widman, Mbanya and Hinnouho definitions. The prevalence of metabolic phenotypes of obesity ranged from 2.50% to 29.60% for MNO subjects and from 70.40% to 97.50% for MAO subjects. With regard to individual definitions, analysis of the data showed that the prevalence of the MNO phenotype was 29.60% according to Hinnouho, 16.00% according to Mbanya, 7.40% according to Meigs and 2.50% according to Widman. This disparity in the prevalence of the MNO phenotype could be explained by the number of abnormalities in each of the definitions tested. In addition, the presence of abnormalities such as high waist circumference, inflammatory state and insulin resistance in the definition of the MNO phenotype tends to decrease the prognosis of obese subjects to present a healthy cardiometabolic profile. The prevalences in this study are also different from those reported by Phillips et al. (2013) who found a proportion of metabolically normal subjects of 23.2% (Widman), 30.2% (Meigs) and 36.6% (HOMA) among participants with obesity in Ireland. Using the same definition of Hinnouho, the prevalence of the MNO phenotype of 42.5% recorded amongst the English population in 2015 is higher than that obtained in this study (29.6%) (Hinnouho et al., 2014). These differences in variation observed in the prevalence of the metabolically normal phenotype among people with obesity would be explained by the type of population studied, the components of the definitions, the presence or absence of the number of abnormalities required to identify MNO subjects but also the threshold values of the metabolic abnormalities. In addition, the lack of agreement between the different definitions of the MNO phenotype observed in general in our study (kappa=0.61) would be evidence of this. This is in line with the work of Velho et al. (2010) who noted that the heterogeneity of the definitions used made it difficult to compare studies conducted on the prevalence of MNO subjects. The research of Tian et al. (2018) had also noted a disparity in the risk of developing hypertension in MNO subjects according to 5 definitions of cardiometabolic status. This demonstrates that the criteria for distinguishing the metabolically normal phenotype according to the different definitions used do not predispose MNO subjects to the same risk of developing cardiovascular disease.

The variability in cut-off values of adiposity markers such as body mass index used to diagnose obesity in MNO and MAO subjects could also explain the difficulty in comparing the results of our study with other studies. Indeed, the cut-off values for the diagnosis of obesity varied in many studies, i.e. BMI ≥30 kg/m² (Roberson et al., 2014; Mbanya et al., 2015), BMI ≥28 kg/m² (Zheng et al., 2015) and BMI ≥25 kg/m² (Geetha et al., 2011). These observed differences between the diagnosis of obesity in our population (BMI ≥27 kg/m²) and that of other studies reveal that BMI would not be a predictive factor for the MNO phenotype since subjects with MAO and MNO phenotypes are present within the same BMI category. Moreover, the BMI ≥27 kg/m² used to define obesity in our study population is categorized by the World Health Organization as overweight encompassing pre-obese (BMI 27–29.9 kg/m²) and obese (BMI ≥30 kg/m²) individuals. On the other hand, the definition of adiposity such as waist circumference or waist-hip ratio which are indicators of fat distribution would be more suitable as predictors of cardiometabolic health in obesity. This study’s results revealed that waist circumference and waist-hip ratio were lower in MNO subjects compared to MAO subjects. The work of Fezeu et al. (2006) had also shown that central obesity defined by waist circumference is a determinant strongly associated with a constellation of metabolic abnormalities in Cameroonian. Indeed, it is recognized that an increase in waist circumference indicative of abdominal body fat accumulation has a deleterious effect on the cardiometabolic profile with consequent elevation of blood pressure, blood glucose, total cholesterol and triglycerides (Lukics et al., 2019). These observations are in line with the results obtained in our study which have shown that plasma triglycerides, total cholesterol, LDL cholesterol and blood glucose values in MAO subjects were significantly higher compared to MNO subjects for all definitions of metabolic status used. Study results may indicate health complications related to alteration in adipocyte function marked by an increase in triglyceride lipolysis in hypertriglyceridemic adipose tissue, leading to an excess of free fatty acids in the blood, which will be preferentially used over glucose by the various tissues of the body, thus leading to an increase in blood glucose via the installation of insulin resistance, hence the hyperglycemia (Longo et al., 2019). Consequently, the reuptake and storage of free fatty acids in the liver could lead to an increase in the production of hepatic triglycerides which may result in hypertriglycerideremia (Klopf et al., 2013). Hypertriglycerideremia may also be the main cause of other lipid abnormalities since the overproduction of triglyceride-rich lipoproteins in the liver would lead to an increase in the activity of esterified cholesterol transfer protein (CETP) and hepatic lipase, thus contributing to a reduction in circulating HDL particles and an overproduction of small and dense LDL particles (Fisher and Cohen, 2013). The significantly elevated nitric oxide content observed in the MNO subjects in this study for the definitions of Hinnouho, Meigs and Mbanya could account for the presence of lower blood pressure in these individuals free from metabolic abnormalities. Since the vascular endothelium plays a major role in the regulation of vascular resistance via the bioactivation of endothelium derived nitric oxide which is an important determinant of vascular relaxation. Therefore, vascular alteration would lead to endothelial dysfunction with a consequent decrease in the release of vasodilators such as nitric oxide in favor of increased production of endothelin-1 considered as a vasoconstrictor thus contributing to the increase in blood pressure (Brandes, 2014). Brant et al. (2017) had shown that MNO subjects have impaired vascular function but less markedly than in MAO subjects. The obtained results of this study also revealed that for 3 of the definitions used (Hinnouho, Mbanya and Widman), insulin resistance (HOMA) was significantly lower in subjects with MNO phenotype than their counterparts at risk for MAO phenotype. This corroborates the work of Achille et al. (2014) who had noted that low insulin resistance was predictive of the development of MNO phenotype. Similarly, the study by Yangoua et al. (2010) had revealed that nearly half of obese Cameroonian had insulin resistance. On the other hand, chronic low-grade inflammation has been recognized as a key element in the pathogenesis of insulin resistance, with elevated circulating levels of CRP and proinflammatory cytokine such as TNFα (Tangvarasittichai et al., 2015). Indeed, TNF-α inhibits lipoprotein lipase and stimulates lipolysis in adipocytes, thus contributing to the development of insulin resistance (Tangvarasittichai et al., 2015). This study’s results showed that hsCRP and TNF-α levels were lower in MNO subjects compared with their MAO counterparts. This observation is consistent with the work of Marques-Vidal et al. (2011) who had shown that MNO individuals have reduced levels of CRP and TNFα depending on the definition used. However, the results of this study showed that the averages values of hsCRP and TNFα observed in MNO and MAO subjects were generally higher than the diagnostic values of inflammation (hsCRP ≥3 mg/L and TNFα ≥12 pg/mL) defined by Widman et al. (2008) and Darko et al. (2015). This analysis shows that both MNO and MAO subjects are prone to inflammation. Furthermore, the higher averages values of hsCRP and TNFα observed in MNO subjects compared to MAO subjects could be explained by the maintenance of the capacity of adipose tissue to meet the metabolic needs of the body, thus mitigating visceral body fat accumulation and the risk of developing cardiovascular diseases (Chait and den Hartigh, 2020). In contrast, the higher averages values of hsCRP and TNFα in MAO subjects compared to MNO subjects could be explained by the loss of metabolic flexibility of adipose tissue thus leading to adipocyte hypertrophy with a consequent change in the inflammatory profile characterised by elevated production...
of hsCRP and pro-inflammatory adipokines such as TNF-α (Fuster et al., 2016). The resulting inflammation is thought to increase the risk of developing metabolic disorders such as insulin resistance, hypertension, dyslipidemias and dysglycaemias (Barber et al., 2021). In this study, the cardiometabolic index obtained by the product of the waist-to-height ratio and the triglyceride/HDL cholesterol ratio was significantly higher in MAO subjects compared with MNO subjects. This result could be explained by lower levels of HDL cholesterol, higher triglycerides, and higher waist circumference in MAO subjects compared with MNO subjects. A higher cardiometabolic index in MAO subjects would thus reflect a higher risk of developing cardiovascular disease in them. Similar results reported by Abolnezhadian et al. (2020) showed that individuals with a metabolically abnormal phenotype had higher levels of triglycerides and cardiometabolic index than individuals with a metabolically normal phenotype. According to the literature, a waist-to-height ratio >0.5 indicates a high cardiometabolic risk while a TG/HDL ratio ≥2.0 reflects small, dense LDL particles and therefore the alteration of adipose tissue function and the installation of dyslipidemias which lead to an increase in the risk of developing cardiovascular diseases (Di Bonito et al., 2012; Shi et al., 2018; Alzeidan et al., 2020). The results obtained in this study show that cardiometabolic index, waist-to-height ratio and TG/HDL ratio can be used in clinical practice as efficient tools to diagnose cardiometabolic risk factors and preclinical signs of liver and heart abnormalities as well as to detect MNO patients and those with an aggravated cardiometabolic profile who require monitoring to prevent cardiovascular diseases.

In addition, the areas under the ROC curve according to the definition of Meigs, Widman, Mbanya and Hinnouho showed good discrimination. However, a large variability in specificity and sensitivity values was observed for the different definitions of the MNO phenotype. These observations sufficiently revealed that sensitivity and specificity were linearly related to the prevalence of the MNO phenotype among subjects with obesity. The Hinnouho definition had the highest sensitivity and specificity values. The results of this study suggest the Hinnouho definition of the MNO phenotype as the most efficient measure of the metabolic status of subjects with obesity amongst the Cameroonian Bamileke ethnic group. Indeed, Trevethan (2017) had noted that sensitivity and specificity can be used for screening decisions regarding if they are high.

This study is the first of its kind to examine the obesity phenotype paradox in an African population that is socio-culturally predisposed to develop obesity. This is done using several definitions of the metabolically healthy obese phenotype involving the complete absence of metabolic abnormalities. The main limitation of this study may be that the study was conducted on only one ethnic group of the Cameroonian population. Thus, an in-depth study taking into account other ethnic groups of the Cameroonian population will allow for improved management of obesity according to the ethnocultural context.

5. Conclusion

The disparity in the prevalence of the MNO phenotype would be attributed to the components of various definitions used, as well as the specificity of the criteria of each (or particular) definition. The importance of standardizing the definition of the MNO phenotype is crucial for the therapeutic management of subjects with obesity. The modified Hinnouho definition could be an appropriate definition to distinguish MNO subjects from MAO subjects among Bamileke with obesity. The results of this study demonstrate that people with obesity without metabolic abnormalities exist in the Cameroonian population. They suggest that measures for prevention, screening and management of metabolic abnormalities in individuals with obesity by the government must take into account the ethnocultural aspect and the area of residence of the populations. Hence the need to extend this study to other regions and ethnic groups of the Cameroonian population. In addition, further studies on the contribution of sociodemographic characteristics, lifestyle, food consumption profile, food security status and genetics on the cardiometabolic profile of Cameroonian populations with obesity should be conducted.

Declarations

Author contribution statement

Maxwell Wandji Nguedjo: Conceived and designed the experiments; Performed the experiments; Wrote the paper.

Judith Laure Ngondi: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

François Raissa Ntente: Performed the experiments.

Boris Gabin Xingue Azantsa; Javeres Leonel Ntepe Mbah: Analyzed and interpreted the data.

Julius Enyong Oben: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data.

Funding statement

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

Supplementary content related to this article has been published online at https://doi.org/10.1016/j.heliyon.2022.e11652.

Acknowledgements

The authors thank the population of the West Cameroon region for consenting to participate in this study.

References

Abolnezhadian, F., Hosseini, S.A., Alipour, M., Zakerkhsh, M., Cheraghian, B., Ghandil, P., Cheraghpour, M., 2020. Association metabolic obesity phenotypes with cardiometabolic index, atherogenic index of plasma and novel anthropometric indices: a link of FTO-rs9999609 polymorphism. Vasc. Health Risk Manag. (16), 249–256.

Acharya, S., Shukla, S., 2018. Metabolic healthy obesity—A paradoxical fallacy? J. Clin. Diagn. Res. 12, OE07–OE10.

Achille, I., Hazuda, H.P., Fowler, S.P., Aung, K., Lorenzo, C., 2014. Predicting the development of the metabolically healthy obese phenotype. Int. J. Obes. 39 (2), 226–234.

Adair, K.E., Bowden, R.G., Funderburk, L.K., Forse, J.S., Ylitalo, K.R., 2021. Metabolic health, obesity, and renal function: 2013–2018 national health and nutrition examination surveys. Life 11 (9), 886.

Adoloye, D., Ige-Elebede, J.O., Ezeimofo, M., Owolabi, E.O., Ezeigwe, N., Omosuye, G., Adebiyi, A.O., 2021. Estimating the prevalence of overweight and obesity in Nigeria in 2020: a systematic review and meta-analysis. Ann. Med. 53 (1), 495–507.

Agyemang, C., Boatemaa, S., Agyemang/Frempong, G., De-Graft Aikins, A., 2016. Obesity in sub-saharan Africa. Metabolic Syndrome 41–53.

Alzeidan, R., Fayed, A., Rabiee, F., Heri, A., Elmorshedy, H., 2020. Diagnostic performance of waist-to-height ratio in identifying cardiovascular risk factors and metabolic syndrome among adult Saudis. Saudi Med. J. 41 (3), 253–260.

Barber, T.M., Kyrour, I., Randeva, H.S., Weickert, M.O., 2021. Mechanisms of insulin resistance at the crossroad of obesity with associated metabolic abnormalities and cognitive dysfunction. Int. J. Mol. Sci. 22 (546), 1–16.

Blüher, M., 2020. Metabolically healthy obesity. Endocr. Rev. 41 (3), 405–420.

Bosomworth, N.J., 2019. Normal-weight central obesity. Unique hazard of the toxic waist. Can. Fam. Physician 65 (6), 399–408.

Branden, R.P., 2014. Endothelial dysfunction and hypertension. Hypertension 64 (5), 924–928.
M.W. Nguedjo et al. Heliyon 8 (2022) e11652

Klop, B., Elte, J., Cabezas, M., 2013. Dyslipidemia in obesity: mechanisms and potential

Hinnouho, G.-M., Czernichow, S., Dugravot, A., Nabi, H., Brunner, E.J., Kivimaki, M.,

Fuster, J.J., Ouchi, N., Gokce, N., Walsh, K., 2016. Obesity-induced changes in adipose

Hanley, J.A., McNeil, B.J., 1983. A method of comparing the areas under receiver-

Matthews, D.R., Hosker, J.P., Rudenski, A.S., Naylor, B.A., Teacher, D.F., Turner, R.C.,

Fezeu, L., Balkau, B., Kengne, A.-P., Sobngwi, E., Mbanya, J.-C., 2006. Metabolic

Elías-L...

Manel, S., Williams, H.C., Ormerod, S.J., 2001. Evaluating presence

Luk...

Colman, E., 2012. Food and drug administration

Chait, A., den Hartigh, L.J., 2020. Adipose tissue distribution, in

Brant, L.C.C., Wang, N., Ojeda, F.M., LaValley, M., Barreto, S.M., Benjamin, E.J.,

2022. Factors related to overweight and obese populations maintaining metabolic

targets. Nutrients 5 (4), 1218

107 (30), 517

387. Cotonou, Institut National de Statistique et d...

2164.

Ntandou, G., Delisle, H., Agueh, V., Fayomi, B., 2008. Physical activity and socioeconomic

status explain rural-urban differences in obesity: a cross-sectional study in Benin

(west Africa). Ecol. Food Nutr. 47 (4), 313–337.

Ntirengay, F.R., Ngonzi, J.L., Azanta, K.B.G., San, E.V., Dimo, H.T., Mbong, A.M.A.,

Chakok, N.R.M., Ngumkgem, S.B., Zambah, O., Oben, E.J., 2014. Urbanization and metabolic

syndrome in Cameroon: alertness on less urbanised areas. Endocrinol. Metab. Syndrome 3, 127.

Ortega, F.B., Lave, J.C., Blair, S.N., 2016. Obesity and cardiovascular disease. Circ. Res. 118 (11), 1752–1770.

Pasquet, P., Tsegoua, L.S., Melaman-Seg, F., Froment, A., Rikong-Adie, H., 2003.

Prevalence of overweight and obesity for urban adults in Cameroon. Amn. Hum. Biol. 30, 551–562.

Phillips, C.M., 2016. Metabolically healthy obesity across the life course: epidemiology, determinants, and implications. Ann. N. Y. Acad. Sci. 1391 (1), 85–100.

Phillips, C.M., Dillon, C., Harrington, J.M., McCarthy, V.I.C., Kearney, P.M., Fitzgerald, A.P., Perry, J.I., 2013. Defining metabolically healthy obesity: role of dietary and lifestyle factors. PLoS One 8 (10), e76188.

Primeau, V., Codere, L., Karelis, A.D., Brochu, M., Lavoie, M.E., Meslier, V., Sladek, R., Lahont-Lahreht, R., 2011. Characterizing the profile of obese patients who are metabolically healthy. Int. J. Obes. 35, 971–981.

Roberson, L.L., Aneri, E.C., Maziak, W., Agaston, A., Feldman, T., Roussef, M., Nasir, K., 2014. Beyond BMI: the “Metabolically healthy obese” phenotype & its association with clinical/subclinical cardiovascular disease and all-cause mortality - a systematic review. BMJ Public Health 14 (1), 14.

Said, Q., Marx, C.M., Schwartz, J.S., Ben-Joseph, R., Brinxer, D.L., 2010. Impact of body mass index on the incidence of cardiometabolic risk factors in ambulatory care settings over 5 years or more. Value Health 13 (2), 265–272.

Shi, W.-R., Wang, H.-Y., Chen, S., Guo, X.-F., Li, Z., Sun, Y.-X., 2018. Estimate of prevalent diabetes from cardiometabolic index in general Chinese population: a community-based study. Lipids Health Dis. 17 (236), 1–19.

Simo, P., Agbor, V.N., Tsegoua, P.F., Fezeu, L.C.F., Bonghae, D.T., Mbonda, A.G.N.,

Mbanya, D., 2021. Prevalence and factors associated with overweight and obesity in

Cameroon: alertness on less urbanised areas. Endocrinol. Metab. Syndrome 3, 127.

9

World Health Organization, 2017. The WHO STEPswise approach to noncommunicable disease risk factor surveillance (STEPS). Available at: http://www.who.int/chp/steps/en/ (Accessed 30 June 2022). Accessed.

Yangou, M.C.H., Azanta, K.R.G., Ntirengay, F.R., Ngonzi, J.L., Oben, E.J., 2010. Prevalence of insulin resistance in obese Cameroonian women. J. Diabetes. Metab. Endocrinol. 1 (12), 1–26.

Zheng, R., Yang, M., Bao, Y., Li, H., Shan, Z., Zhang, B., Lai, M., 2015. Prevalence and determinants of metabolic health in subjects with obesity in Chinese population. Int. J. Environ. Res. Publ. Health 12 (11), 13662–13677.