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ORIGINAL RESEARCH

Metabolically Unhealthy Normal Weight: Prevalence and Associated Factors in an Adult Population from Northwest Colombia

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Background and Aim: Individuals with a normal weight may have metabolic alterations at risk for chronic non-communicable diseases. The prevalence of this condition and associated factors have not been reported in Latin American populations. We aimed to estimate the presence and associated factors of Metabolically Unhealthy Normal Weight (MUNW) in adults from a public program for the control and prevention of chronic diseases in Medellín, Colombia.

Methods: Cross-sectional study. Overweight and normal weight were characterized according to the absence or presence of one or more components of the metabolic syndrome, obtaining four phenotypes: Metabolically Healthy Normal Weight (MHNW), MUNW (phenotype of interest), Metabolically Healthy Overweight (MHO), and Metabolically Unhealthy Overweight (MUO). The association of these phenotypes with sociodemographic variables of lifestyles and increased waist circumference was conducted by using logistic regression.

Results: In 37,558 individuals (72.7% women), the prevalence of MUNW was 23.3%. Among the additional phenotypes, MUO was found to be more prevalent (71.6%), while MHNW and MHO were very slightly common, 2% and 3.1%, respectively. In a multiple model, the factors associated with MUNW were age over 60 years (trend [OR 1.56 95% CI 0.97–2.52] p-value = 0.066), living in a rural area ([OR 1.58 95% CI 1.09–2.29] p-value = 0.015), and increased waist circumference ([OR 1.68 95% CI 1.45–1.95] p-value < 0.001). Male gender was inversely associated with all phenotypes (P < 0.05).

Conclusion: Almost a quarter of the analyzed population presented MUNW. People living in a rural area and over 60 years old were more likely to present MUNW. Men were less likely to present the weight phenotypes studied, although they could have been underrepresented.

Keywords: normal weight, metabolism, risk factor, body mass index, metabolic profile, metabolic syndrome

Introduction

Excess adiposity in terms of overweight and obesity is a condition that is usually accompanied by metabolic and hemodynamic alterations.[1,2] This abnormal metabolic pattern appears to be at least partially explained by the deleterious effects of subclinical inflammation derived from adipose tissue on insulin sensitivity.[3] However, the combination of overweight/obesity status and metabolic health status leads to discordant phenotypes such as metabolically healthy overweight/obesity (MHO) and metabolically unhealthy normal weight (MUNW), and expectable phenotypes of metabolic unhealthy overweight/obesity (MUO) and metabolic healthy normal weight (MHNW).[4] There is some heterogeneity in definitions of these phenotypes, consisting of the absence or presence of metabolic syndrome criteria, hypercholesterolemia, and/or hyperinsulinemia or insulin resistance as components.[4,5]

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In recent years, discordant phenotypes MHO and MUNW have obtained growing attention due to the paradox they might represent in the management of risk for non-communicable chronic diseases. Despite individuals with MHO lack of main cardiometabolic risk factors, several prospective studies have shown associations between this phenotype and higher risk of diabetes and cardiovascular diseases when compared with MHNW.[6–8] Therefore, MHO seems to be a state in which normality of metabolic parameters is transitory and worsens throughout time in the individual with overweight or obesity, and thus excess body mass must be still a major criterion in risk management.[9,10] Meanwhile, MUNW has been associated with increased cardiovascular alterations and mortality by cardiovascular disease,[5,11] and the screening of these individuals is complex in clinical practice.

In Latin America, there have been scarce or null evaluations of MUNW. Particularly in Colombia, the need for estimation of discordant phenotypes and variables related to them is even more pertinent. According to a population-based study representative of urban individuals in the five major regions of Colombia, one of every two Colombians is affected by overweight or obesity (57.6%).[12] Moreover, diet habits are inclined toward hypercaloric meals according to a 2015 ENSIN survey analysis.[13] This increase might increase the chance of finding metabolic alterations either in normal or excess weight status. Therefore, we conducted a study to estimate the prevalence of MUNW and other weight status phenotypes and evaluate potential associated factors in a population attending a prevention and monitoring program of chronic diseases in Medellin, Colombia.

Methods

Study Population

This cross-sectional study consisted of the analysis of data from individuals linked to a program of public health for control of chronic diseases implemented by the health provider institution E.S.E Metrosalud, of the city of Medellín, in 2019. The original database contained 69,883 records of individuals over 18 years of age, with voluntary participation. The data were generated from electronic medical records. We included adults (18 years or older) with medical records linked to the program with active participation and screening compliance. We excluded cases with missing or out-of-range values for those anthropometric and cardio-metabolic risk variables that defined the discordant phenotypes. These extreme or out-of-range values, in addition to the criteria to define the values, are set out in Supplemental Table S1. Individuals with a diagnosis of diseases that already defined the individual with a pathology related to cardio-metabolic risk were excluded: diabetes (ICD-10 CODES E-110-149; E-100-109), kidney disease (ICD-10 CODES N170-179), and cerebrovascular (ICD-10 I600-679; G-450-459) and cardiovascular disease (ICD-10 I200-I259). The above exclusion criteria were based on 2 reasons: 1 - these disorders already define individuals with a cardio-metabolic pathology and not individuals at risk; and 2 - These pathologies, due to their metabolism, might bring associated complications, added to the effect of medications and treatment that could bias the cardio-metabolic factors values to define phenotypes of weight status. The consolidation process of the final sample of 37,558 individuals for the analysis is described step by step in Supplemental Table S2.

Study Outcomes

Determination of MUNW and other weight status phenotypes was based on the presence of Overweight or Normal Weight in combination with the presence or absence of cardio-metabolic risk factors. Overweight including obesity, was determined based on a BMI (calculated as weight/height^2) equal to or greater than 25 kg/m2, and a normal weight as a BMI below that cut-off point and above 18 kg/m^2.

Cardio-metabolic risk factors were taken from the criteria described in the harmonized definition of metabolic syndrome:[14] Triglycerides >150 mg/dl; High-density lipoprotein cholesterol (HDL-C) level of <40 mg/dl in men and <50 mg/dl in women; systolic blood pressure (SBP) of ≥130 mm/Hg and/or diastolic blood pressure (DBP) of ≥85 mm/Hg; and glucose levels of ≥100 mg/dl. The low-density lipoprotein cholesterol (LDL-C) levels were calculated according to the Friedewald equation, and levels >110 mg/dL were an additional cardiometabolic risk factor. Although this latter factor is not part of the definition of metabolic syndrome, high levels are associated with atherogenesis and cardiovascular risk.[15] We complement the dyslipidemia-related criteria and the increased blood pressure criterion by using information on clinical diagnosis of dyslipidemia and hypertension as part of those criteria.

In this way, the phenotypes and their metabolic condition were estimated as follows:

- Metabolically Healthy Normal Weight (MHNW): Normal weight and not having any cardio-metabolic risk criteria
- Metabolically Unhealthy Normal Weight (MUNW) (main category of analysis): Normal weight and presenting one or more cardio-metabolic risk criteria
- Metabolically healthy overweight/Obesity (MHO): Overweight or obesity and not having any cardio-metabolic risk criteria
- Metabolically Unhealthy Overweight/obesity (MUO): Overweight or obesity and presenting one or more cardio-metabolic risk criteria

Regarding the criterion of increased waist circumference (WC) from the metabolic syndrome definition, this was not used as part of the cardio-metabolic risk criteria that defined the categories of metabolic status previously described. The rationale for this decision was based on the fact that individuals with overweight tend to have this criterion, and it was of particular interest for this analysis to verify the relationship of abdominal obesity with MUNW.

Exposures of the Study

Increased waist circumference was one of the exposure variables based on ≥90 cm in men and ≥80 cm in women, according to the regional cut-offs suggested for South American populations by the harmonized definition of metabolic syndrome.[14] Sociodemographic and lifestyle variables were also exposure variables in this analysis, and were: age (years), sex (male/female[Ref]), education level (illiterate[Ref], elementary, secondary, technical profession education, undergraduate, graduate), ethnicity (general population[Ref], Afro-descendant, Palenquero, Raizal, Roma, and Indigenous) area of residence (urban[Ref]/rural), marital status (single[Ref], divorced, free union, married, widowhood), alcohol intake habit (yes/no), and smoking (yes/no). For these exposure variables, having missing values was not a reason for exclusion.

Ethnicity was defined according to the self-perception of belonging to a specific ethnic group. The measurement of smoking and alcoholism was based on the patient's consumption in the last month, at least once a week. For regular physical activity, an individual who reported engaging in vigorous or moderate physical activity at least three times per week was classified as active, and below that frequency was classified as inactive

Data Analysis

The continuous variables were summarized by calculating the median and its interquartile range, regardless of their normal or non-normal distribution. The rationale to homogenize the description of all these variables with the same central trend measure was on the basis that for non-normal distributed variables, a mean does not represent the values distribution and a median is the best option, and in the case of normally distributed variables, median and mean tend to be similar. The categorical variables were described as frequency and percentage. The difference in the distribution of the proportion of cases with each phenotype throughout categories of the exposure variables was examined via χ^2 test. Continuous variables of anthropometric, clinical, and biochemical variables were additionally described by groups of weight status phenotypes, and the trend for difference throughout the groups was estimated by using the Jonckheere-Terpstra test.

Logistic regression was used to evaluate the association between exposure variables and each weight status phenotype (MUNW, MHO, MUO) using metabolically MHNW as the reference for the outcomes. We first conducted univariate analyses with each exposure variable vs the outcomes and selected those that showed a p-value <0.10 to be included in the multiple model, observing the change in odds ratio (OR), confidence interval (CI), and p-value. In the multiples models, we used a backward elimination, by progressively removing variables with the highest (non-significant) p-values till obtaining the best explanatory model.

We additionally conducted a subgroup analysis by sex to identify potential sex differences in association patterns. We did not carry out any sensitivity analysis since this study had an exploratory nature to find variables associated with MUNW and other phenotypes.

The analyses were carried out using Stata Software 14.0.

Results

Sociodemographic characteristics and some lifestyle variables are described in Table 1. Most of the adults studied were over 60 years old (68.9%), women (72.7%), and one out of every two (48.9%) individuals reported schooling up to the primary level. The predominant marital status was being single with 40.7% followed by married status with 34.7%. A vast majority (80–95%) of the individuals resided in the urban area and did not recognize themselves in an ethnic group, being classified as general population, and did not report tobacco or alcohol use. Physical activity was reported in around two-thirds of the individuals (65.4%) (Table 1).

Table 1 Description of Study Sociodemographic Variables in the Sample

Variables	***Valid n for variable****	**n**	**%**
Age (years)	n=37,558		
18–39		1010	2.7
40–60		10,653	28.4
> 60		25,895	68.9
Sex	n=37,558		
Female		27,289	72.7
Male		10,269	27.3
Education level	n=31,034		
Illiterate		4662	12.4
Elemental		18,366	48.9
Secondary		7536	20.1
Technical education		299	0.8
Undergraduate		142	0.4
Graduate		29	0.1
Marital status	n=37,062		
Single		15,269	40.7
Divorced		1548	4.1
Free union		4005	10.7
Married		13,017	34.7
Widow/Widower		3223	8.6

(*Continued*)

Table 1 (Continued).

Variables	*Valid n for variable**	n	%
Ethnicity	n=37,557		
General population		33,182	88.3
Afrodescendant		854	2.3
Indigenous		145	0.4
Palenquero		143	0.4
Raizal		3091	8.2
ROM		142	0.4
Residential area	n=37,556		
Urban		35,369	94.2
Rural		2187	5.8
Alcohol consumption	n=35,544		
Yes		1646	4.4
No		33,898	90.3
Smoking	n=35,544		
Yes		4193	11.2
No		31,351	83.5
Physical activity	n=35,544		
Yes		10,966	29.2
No		24,578	65.4

Notes: *Valid n means number of individuals with data available for that specific variable.

Prevalence of MUNW was around one-quarter of the individuals (23.3%, n = 8734). MHNW and MHO were present in only 2% (n = 767) and 3.1% (n = 1164) of the individuals, respectively, and MUO was the most prevalent phenotype, 71.6% (n = 26,893).

Continuous variables of anthropometric, clinical, and biochemical variables are described in the whole sample and by weight status phenotypes in Supplemental Table S3. As expected, medians of biochemical markers and blood pressure tended to be higher in MUNW and MUO than in MHO and MHNW because based on cut-offs for these markers the phenotypes were established. The BMI median in the whole sample was in the range of overweight [27.8 Interquartile range (24.9–31.3)]. Waist circumference was higher in overweight phenotypes and comparable between normal weight phenotypes [MHNW median 85 (78–90) and MUNW median 86 (81–91)].

When MUO and MUNW were compared in terms of individual metabolic components, both phenotypes were similar in proportions of cases with increased blood pressure, high LDL cholesterol, and a history of previous diagnosis of unspecified dyslipidemia (Table 2). However, high fasting glucose (HFG) high triglycerides levels (HTL), and low HDL-C were significantly more prevalent in MUO than in MUNW (Table 2).

The distribution of the weight phenotypes throughout categories of sociodemographic and lifestyle variables (exposures) is shown in Table 3. When compared with MHNW, the proportion of individuals with MUNW phenotype was significantly higher in female sex, and rural residence, and tended to be higher in the oldest individuals (p-value=0.074). Similarly, in comparison with the MHNW, cases with MHO and MUO were significantly more prevalent

Table 2 Individual Metabolic Components in the Unhealthy Metabolic Phenotypes (N = 37,558)

	MUO	MUNW	P-value
	n (%)	*n* (%)	
High fasting glucose (≥ 100 mg/dL)	11,102 (41.3)	2815 (32.2)	<0.001
High triglycerides level (≥ 150 mg/dL)	14,682 (54.6)	3925 (44.9)	<0.001
Low HDL-C	18,090 (67.3)	4589 (52.6)	<0.001
Increased blood pressure (SBP ≥ 130 or DBP ≥ 85 mg/dL) and/or diagnostic of hypertension	17,998 (66.9)	5755 (65.9)	0.075
Increased LDL-C (>110 mg/dL)	8657 (32.2)	2930 (33.5)	0.657
Dyslipidemia diagnostic	500 (1.9)	162 (1.1)	0.759

Abbreviations: MUO, metabolically unhealthy overweight/obesity; MUNW, metabolically unhealthy overweight/obesity.

Table 3 Distribution of Cases [n (%)] with Weight Status Phenotypes Throughout Categories of Exposure Variables

	MHNW	MUNW	MHO	MUO
Age group (years)				
18–39	20 (2.6)	139 (1.6)	33 (2.8)	818 (3.0)
40–60	165 (21.5)	1780 (20.4)	356 (30.6)	8352 (31.1)
>60	582 (75.9)	6815 (78)	775 (66.6)	177,723 (65.9)
*P-value**		*0.074*	*<0.001*	*<0.001*
Sex				
Female	446 (58.1)	5517 (63.2)	901 (77.4)	20,405 (75.9)
Male	321 (41.9)	3217 (36.8)	263 (22.6)	6468 (24.1)
*P-value**		*0.006*	*<0.001*	*<0.001*
Education level				
Illiterate	99 (15.9)	1159 (16.3)	145 (14.9)	3258 (14.6)
Elemental	373 (59.9)	4212 (59.2)	559 (57.4)	13,222 (59.2)
Secondary	143 (23)	1611 (22.7)	253 (26)	5529 (24.8)
Technical education	4 (0.6)	75 (1.1)	8 (0.8)	212 (0.9)
Undergraduate	3 (0.5)	47 (0.7)	7 (0.7)	85 (0.4)
Graduate	1 (0.2)	7 (0.1)	2 (0.2)	19 (0.1)
*P-value**		*0.904*	*0.762*	*0.745*
Marital status				
Single	350 (46)	3786 (43.9)	510 (44.1)	10,623 (40)
Divorced	27 (3.5)	352 (4.1)	40 (3.5)	1129 (4.3)
Free union	257 (33.8)	2977 (34.6)	363 (31.4)	9420 (35.5)
Married	69 (9.1)	681 (7.9)	146 (12.6)	3109 (11.7)

(Continued)

Table 3 (Continued).

	MHNW	MUNW	MHO	MUO
Widow/widower	58 (7.6)	820 (9.5)	98 (8.5)	2247 (8.5)
*P-value**		*0.272*	*0.148*	*0.011*
Ethnicity				
General population	684 (89.2)	7683 (88)	1032 (88.7)	23,783 (88.4)
Afro-descendant	15 (2.0)	181 (2.1)	45 (3.9)	613 (2.3)
Indigenous	2 (0.3)	33 (0.4)	3 (0.3)	107 (0.4)
Palenquero	4 (0.5)	35 (0.4)	6 (0.5)	98 (0.4)
Raizal	58 (7.6)	763 (8.7)	74 (6.4)	2196 (8.2)
ROM	4 (0.5)	39 (0.4)	4 (0.3)	95 (0.4)
*P-value**		*0.864*	*0.238*	*0.825*
Residence area				
Urban	736 (96)	8202 (93.9)	1125 (96.6)	25,306 (94.1)
Rural	31 (4.0)	532 (6.1)	39 (3.4)	1585 (5.9)
*P-value**		*0.021*	*0.427*	*0.031*
Alcohol intake (at least once a week)				
Yes	611 (94.3)	7760 (94.6)	998 (96.1)	24,529 (95.6)
No	37 (5.7)	443 (5.4)	40 (3.9)	1126 (4.4)
*P-value**		*0.738*	*0.076*	*0.106*
Smoking (at least once a week)				
Yes	546 (84.3)	6982 (84)	952 (91.7)	22,961 (89.5)
No	102 (15.7)	1311 (16)	86 (8.3)	2694 (10.5)
*P-value**		*0.872*	*<0.001*	*<0.001*
Physical activity				
Yes	479 (73.9)	5894 (72.7)	748 (72.1)	17,387 (67.8)
No	169 (26.1)	2239 (27.3)	290 (27.9)	8268 (32.2)
*P-value**		*0.504*	*0.404*	*<0.001*
Increased WC				
Yes	408 (53.2)	5746 (65.8)	1043 (89.6)	25,720 (95.6)
No	359 (46.8)	2988 (34.2)	121 (10.4)	1173 (4.4)
*P-value**		*<0.001*	*<0.001*	*<0.001*

Note: *Estimated via χ^2 test by using MHNW group as the reference.
Abbreviations: MUO, metabolically unhealthy overweight/obesity; MUNW, metabolically unhealthy overweight/obesity; MHO, metabolically healthy overweight/obesity; MHNW, metabolically healthy normal weight.

in the oldest group, female sex, and less prevalent in people who smoke vs non-smoking (Table 3). In addition, there were more cases of MUO among people reporting physical activity, and with residence in rural areas. All the phenotypes in comparison with MHNW were significantly more prevalent among individuals with increased WC (Table 3).

Table 4 describes multiple models with variables explaining MUNW, MHO, and MUO. Having a marital status of free union, residing in a rural area compared to an urban one, and having an increased WC were the variables that maintained their positive and significant association with MUNW in the final multivariable model. Being 60 years or older was also positively associated with MUNW in the final multivariable model but as a trend (p-value=0.068). Meanwhile, MHO and MUO had either positive or inverse determinants in their final models. As happened for MUNW, marital status involving conjugal union (married and/or free) and increased WC were positively associated with MHO and MUO, whereas for both overweight/obesity phenotypes being male was found to be a protective determinant. Smoking was inversely related to MHO, and the practice of physical activity increased the likelihood of MUO (Table 4).

Analyses by sex showed some differences in determinants of MUNW, MHO, and MUO (Supplemental Table S4). As occurred in the whole sample, in both men and women, increased WC was a significant associated factor for all three discordant phenotypes of weight status. Based on associated variables in the whole sample, for the case of MUNW, residence area was associated with women only, while age remained a significant predictor in men. Variables that did not reach final multiple models in the whole sample, were or tended to be associated with MHO or MUO in multiple models in a sex-specific way. Ethnicity was positively associated with MUO in women (ROM ethnic group vs general population) and men (Palenquero ethnic group vs general population) and with MHO only in men (Afro-descendant vs general population p-value=0.062). Marital status (free union vs single) tended to have an association with MHO in women. Particularly in women, alcohol intake was consistently found as a variable filtered in multiple models for all of the discordant phenotypes with a marginal statistical significance ($P \geq 0.05$ and < 0.1) in the multiple models. Educational level was positively associated with MUO (secondary education vs illiterate) but this paradoxical relationship might be a chance finding.

Discussion

In the present analysis, it was found that approximately one in four individuals presented MUNW (23.3%). Concerning the other phenotypes or categories of metabolic condition, the MUO presented the highest proportion of cases with 71.6%, and to a lesser extent the MHO with 3.1% and the MHNW with 2%. Regarding variables associated with these phenotypes in multivariate analysis, age over 60 years, residence in a rural area, and high waist circumference were positively associated with MUNW. Being male was inversely associated with the MHO and MUO overweight phenotypes, while marital status was positively related to the opportunity to present them. Smoking habits and physical activity were paradoxically, inversely, and positively associated with MHO and MUO, respectively. Living in a rural area was additionally associated with MUO. Having an increased WC had strong positive associations with the opportunity to present all the phenotypes with metabolic alteration and/or overweight.

Studies on the estimation of MUNW have been mostly conducted in Asian populations, and the criteria for the definition of this phenotype are not consistent across the studies (Table 5).

Although BMI has been the reference to establish normal weight, some studies, as our analysis, excluded underweight individuals (BMI < 18.5)[17,18,20–22,24,26] while other analyses used a broader classification based on <25 kg/mt2.[16,23,25] One of the studies reviewed, conducted exclusively in people older than 60 years used a cut-off of BMI < 23 kg/mt2 for normal weight, because of recommended guidelines for older adults.[19] Meanwhile, for the definition of metabolic obesity or unhealthy metabolic condition, previous research has mainly used the presence of metabolic syndrome (≥3 metabolic/clinical alterations) based on ATP III[3,4,6,11] and IDF[2,8] definitions. Other studies have implemented independent criteria, such as elevated HOMA-IR[1] and C-reactive protein.[5] We identified five studies that considered increased waist circumference as one of the possible criteria to establish metabolic unhealthy conditions[16–19,21] (Table 5). Unlike the studies previously mentioned, we did not use increased waist circumference among possible criteria because we aimed to verify its association with MUNW and to confirm whether other factors were independently associated with MUNW in the presence of such a strong predictor of cardiometabolic risk in multiple models.

Table 4 Multivariable Models Explaining Each Weight Status Phenotype Compared to Metabolically Healthy Normal Weight (MHNW)

Metabolically Unhealthy Normal Weight (MUNW)

Variables	Preliminary Model		Final model	
	OR (CI95%)	P-value	OR CI95%	P-value
Sex				
Female	1.0 (REF)	0.423	–	–
Male	0.93 (0.79–0.109)			
Marital status				
Single	1.0 (REF)			
Divorced	0.86 (0.46–1.59)	0.636	0.84 (0.45–1.56)	0.588
Free union	1.50 (1.02–2.21)	0.039	1.52 (1.03–2.24)	0.032
Married	1.01 (0.78–1.30)	0.913	1.00 (0.78–1.28)	0.986
Widow/Widower	0.84 (0.56–1.25)	0.394	0.83 (0.56–1.24)	0.377
Residential area				
Urban	1.0 (REF)		1.0 (REF)	
Rural	1.58 (1.09–2.29)	0.015	1.58 (1.09–2.29)	0.015
Age group				
18–39	1.0 (REF)		1.0 (REF)	
40–59	1.46 (0.89–2.41)	0.132	1.47 (0.89–2.41)	0.129
≥ 60	1.56 (0.97–2.52)	0.066	1.56 (0.96–2.51)	0.068

Metabolically Healthy Overweight/obesity (MHO)

Variables	Preliminary model		Final model	
	OR (CI95%)	P-value	OR (CI95%)	P-value
Sex				
Female	1.0 (REF)	<0.001		<0.001
Male	0.64 (0.50–0.82)		0.65 (0.51–0.82)	
Marital status				
Single	1.0 (REF)			
Divorced	0.86 (0.46–1.59)	0.636	0.84 (0.45–1.56)	0.588
Free union	1.50 (1.02–2.21)	0.039	1.52 (1.03–2.24)	0.032
Married	1.01 (0.78–1.30)	0.913	1.00 (0.78–1.28)	0.986
Widow/Widower	0.84 (0.56–1.25)	0.394	0.83 (0.56–1.24)	0.377
Ethnicity				
General population	1.0 (REF)		–	–
Afrodescendant	1.66 (0.86–3.21)	0.129		
Indigenous	0.87 (0.12–6.20)	0.893		
Palenquero	1.11 (0.24–5.08)	0.891		
Raizal	0.80 (0.51–1.24)	0.327		
ROM	0.42 (0.10–1.80)	0.245		
Smoking				
No	1.0 (REF)	0.001		0.001
Yes	0.53 (0.37–0.76)		0.56 (0.4- −0.79)	

Metabolically Unhealthy Overweight/obesity (MUO)

Variables	Final model	
	OR (CI95%)	P-value
Sex		
Female	1.0 (REF)	0.013
Male	0.79 (0.37–0.52)	
Marital status		
Single	1.0 (REF)	
Divorced	1.29 (0.84–1.99)	0.236
Free union	1.54 (1.16–2.06)	0.003
Married	1.23 (1.03–1.47)	0.022
Widow/Widower	1.03 (0.76–1.39)	0.821
Residential area		
Urban	1.0 (REF)	
Rural	1.46 (0.98–2.17)	0.060
Physical activity		
No	1.0 (REF)	0.003
Yes	1.30 (1.09–1.56)	

(*Continued*)

Table 4 (Continued).

Metabolically Unhealthy Normal Weight (MUNW)					Metabolically Healthy Overweight/obesity (MHO)					Metabolically Unhealthy Overweight/obesity (MUO)		
Variables	**Preliminary Model**		**Final model**		**Variables**	**Preliminary model**		**Final model**		**Variables**	**Final model**	
	OR (CI95%)	**P-value**	**OR CI95%**	**P-value**		**OR (CI95%)**	**P-value**	**OR (CI95%)**	**P-value**		**OR (CI95%)**	**P-value**
Increased WC No Yes	 1.0 (REF) 1.65 (1.41–1.93)	 <0.001	 1.0 (REF) 1.65 1.41–1.93	 <0.001	**Alcohol consumption** No Yes	 1.0 (REF) 1.27 (0.73–2.22)	 0.393			**Increased WC** No Yes	 1.0 (REF) 17.7 (14.8–21.1)	 <0.001
					Increased WC No Yes	 1.0 6.55 (5.04–8.51)	 <0.001	 6.55 (5.04–8.50)	 <0.001			

Abbreviations: OR, Odds ratio; CI, Confidence interval; REF, Reference category; WC, Waist circumference.

Table 5 Selected Studies on Metabolically Unhealthy Normal Weight (MUNW)

Authors (year)[Ref.]	n	Design Cross sectional/ Prospective	% Male	How MUNW was Estimated	MUNW Prevalence/ Incidence	Associated factors			
						Associations with	**No Associations with**	**Analysis was Adjusted (Yes/No)**	**Covariates used**
Lee et al (2009)[16]	5267	Cross-sectional		BMI < 25 kg/m2) + Metabolic syndrome: ≥ 3 abnormal metabolic components. WC of ≥ 90 cm for men and ≥ 85 cm for women; blood pressure (BP) of ≥ 130/85 mmHg; glucose of ≥ 100 mg/dL; high density lipoprotein cholesterol (HDL) of <40 mg/dL for men or < 50 mg/dL for women; and triglyceride (TG) of ≥ 150 mg/dL.	8.7%	**Age**: 40–59 OR 4.7 (CI 95%: 3.2–6.9), ≥60 OR 9.0 (CI 95%: 5.8–13.8) vs 20–39 years. **Education**: >High school OR 0.5 (CI 95%:0.4–0.7), High school OR 0.7 (CI 95% 0.6–0.9) vs ≤ Middle school. **Time spent for high intensity exercise** OR 0.8 (CI 95%:0.7–0.9)	Gender Smoking Drinkers Total energy intake Carbohydrate simple Fat intake Protein intake	Yes	Adjusted to each other
Lee et al (2011)[17]	8987	Cross-sectional	48.1	BMI ≥18.5 and <23 kg/m2 + HOMA-IR in the highest Quartile or having MetS or hypertriglyceridemic waist (HTGW) phenotype (TG >1.69 mmol/L and WC >90 cm for men or >80 cm for women).	14.2% for men and 12.9%for women	**Men**: Total cholesterol levels over 5.17 mmol/L OR 1.481 (CI 95% 1.086–2.021). TG over 1.69 mm OR 1507 (CI 95% 1.093–2.077). HDL levels lower than 1.03 mmol/L OR 1.580 (CI 95% 1.053–2.371). **Women**: BMI over 21.5 kg/m2 OR 1405; (CI 95% 1034–1909). TC levels over 5.17 mmol/L (OR 1524 (CI 95% 1.112–2.090) TG levels over 1.69 mmol/L OR 1.799 (CI 95% 1.302–2.487).	Age BMI WC	Yes	Adjusted to each other

(*Continued*)

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Table 5 (Continued).

Authors (year)Ref.	n	Design Cross sectional/ Prospective	% Male	How MUNW was Estimated	MUNW Prevalence/ Incidence	Associated factors			
						Associations with	**No Associations with**	**Analysis was Adjusted (Yes/No)**	**Covariates used**
Choi et al (2012)[18]	3050	Cross-sectional	40.3	BMI ≥18.5 and <25.0 kg/m2 + Syndrome metabolic IDF criteria, presence of three or more of the following components in the presence of central obesity (90 cm for men and 80 cm for women): TG >150 mg/dL, HDL-C <40 mg/dL for men and <50 mg/dL for women, a high blood pressure (BP) (systolic BP 130 or diastolic BP 85 mmHg), high fasting blood glucose (FBG 100 mg/dL).	14.3%.	Protein intake (% of energy) OR 0.96 (CI 95% 0.93–0.99). Frequency of Snacks 3/day OR 0.5 (CI 95% 0.31–1.00) vs 0–1/day.	Fat, carbohydrates total energy (% of energy), regular diet, kind of snacks.	Yes	Age, gender, BMI, daily alcohol consumption, smoking status, income, education and variables of diet (fat, carbohydrates total energy).
Choi et al (2013)[19]	2317	Prospective observational cohort study during 10 years of follow-up.	22.1	BMI < 23 kg/m2 + Presence of MetS. MetS was determined NCEP ATP III criteria, 3 or more of the following components: high blood pressure (systolic blood pressure 130 or diastolic blood pressure 85 mmHg or known treatment for hypertension), hypertriglyceridaemia (fasting plasma triglycerides 1.69 mmol/l), low HDL cholesterol (fasting HDL cholesterol <1.04 mmol/l in men, <1.29 mmol/l in women), and hyperglycaemia (fasting plasma glucose 5.6 mmol/l or 2hPG 7.8 mmol/l or known treatment for diabetes).	18.3%	Highest risk of death from all causes HR 2.2 (CI 95% 1.4–3.4) and CVC HR 3.02 (1.39–6.6) vs MHO.	No data	Yes	Age, sex, smoking, alcohol drinking and presence of diabetes, hypertension and CVD.

Kim et al (2013)[20]	1846 Only women	Cross-sectional	–	BMI 18.5–24.9 kg/m2 + MetS, was defined by ATP III criteria [7, 8]. Having 3 or more of criteria: waist circumference (>80 cm), serum triglycerides ≥150 mg/dL, HDL-cholesterol <50 mg/dL, blood pressure (BP) ≥130/85 mmHg or use of antihypertensive medications, and fasting glucose ≥100 mg/dL. Therefore, the four categories were 1) the normal weight subjects without MetS, 2) the normal weight subjects with MetS, 3) the overweight/obese subjects without MetS, and 4) the overweight/obese subjects with MetS.	16%	MUNW had greater odds of having ox-LDL OR 2.42 (CI 95% 1.65–3.55) and 8-epi-PGF2α OR 1.49 (CI 95% 1.03–2.4) vs MHNW.	No data	Yes	Age, alcohol consumption, smoking status, total- and LDL-cholesterol, and hs-CRP
Yoo et al (2014)[21]	1012	Cros-sectional	56,8	BMI ≥ 18.5 and <25.0 kg/m2 + Syndrome metabolic ATP III criteria, Presence of three or more of the following components: abdominal obesity by waist circumference (90 cm for men and 80 cm for women); high blood pressure (systolic blood pressure 130 or diastolic blood pressure 85 mmHg or known treatment for hypertension); hypertriglyceridemia (1.69 mmol/l); low HDL cholesterol (< 1.04 mmol/l in men, <1.29 mmol/l in women); hyperglycemia (glucose 5.6 mmol/l or known treatment for diabetes).	6.4%	Higher brachial-ankle pulse wave velocity and maximal carotid intima-media thickness values than those with MHO, adjusting for age and gender (p value 0.026 and p value 0.018, respectively) vs MHO. Arterial stiffness and carotid atherosclerosis OR 2.98 (CI 95% 1.54–5.73) p value 0.011).	No data	Yes	Age, gender, smoking habits, alcohol intake, LDL cholesterol, AST, ALT, hsCRP, history of diabetes and anti-hyperlipidemic agents.

(*Continued*)

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Table 5 (Continued).

Authors (year)[Ref.]	n	Design Cross sectional/ Prospective	% Male	How MUNW was Estimated	MUNW Prevalence/ Incidence	Associated factors			
						Associations with	No Associations with	Analysis was Adjusted (Yes/No)	Covariates used
Mark-Park et al (2016)[22]	2103	Cros-sectional	43	IBM 18.5 to <25 kg/m2 + having 2 or more of the following: high glucose, blood pressure, triglyceride, C-reactive protein, and insulin resistance values and low high-density lipoprotein cholesterol levels.	24.3%	Increment 1-DS in adherence to a DASH diet or HEI was significantly associated with reductions in the risk of all-cause mortality 17.2% HR, 0.83 (CI 95% 0.72–0.97) and 22% HR, 0.78 (CI 95% 0.68–0.90), respectively. Cardiovascular disease mortality HR 0.72 (CI 95%, 0.55–0.94) and HR 0.79 (CI 95%, 0.65–0.97), respectively. Cancer mortality was observed with 1-SD increment of HEI HR 0.63 (CI 95% 0.46–0.88).	No data other variables	Yes	Age, sex, race/ethnicity, educational attainment, income, smoking status, alcohol consumption, level of physical activity, and total calorie intake.
Zhang et al (2017)[23]	22,376	Cros-sectional	61.4	BIM < 25 kg/m2 +Metabolic syndrome, criteria IDF: having three or more of WC ≥ 90 cm for male and ≥ 80 cm for female; triglycerides (TG) concentration ≥ 150 mg/dL; high-density lipoprotein cholesterol (HDL-C) concentration < 40 mg/ dL for male and < 50 mg/dL for female or taking anti-hyperlipidemic medications; BP ≥ 130/85 mmHg or taking antihypertensive medications; fasting plasma glucose >100 mg/dL or taking anti-diabetic medications, insulin or oral agents.	4.4%	No data	–	–	–

Hajian-Tilaki et al (2018)[24]	986	Cros-sectional	45	BMI > 18.5 and <25 kg/m2 + 2 of 4 components ATP III criteria: TG > 150 mg/dl, HDL < 50 mg/dl women, HDL <40 mg/dl men, FBS > 110 mg/dl and SBP/DBP > 130/85 mmHg).	17.2%	**Age**: 50–59 OR 3.83 (CI 95% 1.71–8,57) 60–70 OR 4.74 (CI 95% 1.79–12.54) vs 20–29 years. **Current smoking** OR 2.91 (CI 95% 1.18–7.18).	MUNW Sex, Educational level, Physical activity, WC.	Yes	Adjusted to each other
Buscemi et al (2017)[25]	1019	Cros-sectional	40.2	BMI <25 kg/m2 + presence of 2 or mores the following conditions: prediabetes/type 2 diabetes, hypertension, hypertriglyceridemia or low HDL cholesterolemia, and hypercholesterolemia.	9.5%	No data	No data	No data	No data
Zheng et al (2020)[26]	17,876	Cros-sectional	41.9	BIM 18.5–23.9 kg/m2. + two or more metabolically abnormal traits: (1) TG ≥1.7 mmol/L; (2) HDL-C < 1.03 mmol/L for men and < 1.29 mmol/L for women; (3) SBP ≥130 mmHg or DBP ≥85 mmHg, or using antihypertensive drug therapy; and (4) FPG ≥5.6 mmol/L or using anti-diabetic treatment.	16.1%	**Waist circumference (WC)**: WC 70–79 cm: OR 1.33 (CI 95% 1.19–1.48) vs CC < 70 cm. WC 80–89 cm: OR 2.05 (CI 95% 1.79–2.34). WC ≥ 90 cm: OR 3.29 (CI 95% 2.51–4.32) **Central obesity** OR 1.44 (CI 95% 1.31–1.60) **Education level**: Secondary OR 0.71 (CI 95% 0.62–0.83), College or upper OR 0.30 (CI 95% 0.21–0.42) vs primary school. **Regular alcohol drinking** (3 or more 3 time/week) OR 0.83 (CI 95% 0.74–0.91) vs no or less. **Foot preference balanced** OR 0.59 (CI 95% 0.46–0.75), vegetarian OR 0.65 (CI 95% 0.51–0.83) vs meet based. **Family history of diseases** OR 1.45 (CI 95% 1.26–1.67) **Menopause**: OR 2.06 (IC 95%: 1.62–2.58)	Smoking status, Regular tea drinking, Sedentary time, fruit and milk intake.	Yes	Age Sex BIM WC

Note: ox-LDL and 8-epi-PGF2α are indicators for oxidative stress.

Abbreviations: MUNW, Metabolically unhealthy normal weight; MHO, metabolically healthy overweight/obesity; BMI, Body mass index; MetS, Metabolic syndrome; HOMA-IR, Homeostatic model insulin resistance; WC, Waist circumference; HDL, HDL cholesterol; LDL, LDL cholesterol; IDF, International diabetes federation; OR, Odds ratio; CI, Confidence interval; HR, hazard ratio; DBP, Diastolic blood pressure; SBP, Systolic blood pressure; TG, Triglycerides; TC, Total cholesterol; FBS, Fasting blood sugar test; FPG, Fasting plasma glucose test.

In the group of individuals studied, it was found a prevalence of 23% that is higher than that reported in most of the studies reviewed for this discussion, which describe prevalence estimates around 18%[17–20,24,26] or much lower, below 10%.[16,21,23,25] This discrepancy might be due to some methodological differences. We set a cut-off of ≥ 1 MetS criteria to establish metabolic obesity in normal weight, thus a cut-off of ≥3 MetS criteria may underestimate an unhealthy metabolic classification by accepting the presence of one or two criteria as a normal status of metabolic health. We also excluded underweight status because the opportunity to detect cardiometabolic alterations in the BMI range of underweight might be too low, and the presence of individuals with underweight may dilute cases with MUNW. Our prevalence of MUNW was comparable to that described by Park et al, 24.3% in the NHANNES population, and in that study underweight condition was excluded and the cut-off of MetS criteria for unhealthy metabolic classification was restricted to having two or more instead of three or more.[22] Another potential explanation for our higher prevalence is the use of increased LDL-C levels as an additional criterion for unhealthy metabolic status. None of the reviewed studies included this dyslipidemia alteration because metabolic alterations to estimate MUNW have been regularly adopted from metabolic syndrome definitions which do not take into account LDL-C levels. Increased cholesterol or LDL-C levels are part of the Framingham Score for cardiovascular risk, and thus it represents a complementary criterion to detect people with atherogenic risk. We re-estimated the prevalence of MUNW in our sample without considering increased LDL-C as a metabolic abnormality criterion, and the proportion of MUNW minimally decreased to 20.8%, although it approximated to prevalence findings in population-based studies by Choi et al (18.3%) and Hajian –Tilaki et al (17.2%) in elderly Korean adults and adults from Northern Iran, respectively.[19,24] Similarly, it seems that studies with elderly populations or that had a broader age range with old age individuals included, as our study, tend to report higher proportions of MUNW cases.[19,22]

Similar to our study, Zheng et al found an association between waist circumference and MUNW.[26] In contrast, Hajian-Tilaki et al found no association between WC and MUNW, however, the sample of this study was much smaller (n=986).[24] Regarding age, two studies found that the older, the greater the presence of MUNW.[16,24] These studies included people older than 60 years, and none used different criteria for the classification of weight status in older adults. The age-MUNW association is consistent with the trend previously mentioned about the higher prevalence of MUNW in studies that included older individuals. Possible mechanisms could involve aging-related epigenetic changes that have been associated with traditional CVD risk factors in a cohort with a high prevalence of hypertension,[27] and with endothelial alterations that interact with the development of cardiovascular disease such as arteriosclerosis.[28]

There was also an increased opportunity to present MUNW by being a resident of a rural area (vs urban area). In contrast, several studies have shown rural residence as a protective factor for cardiometabolic risk when compared to living in urban environments which are linked to higher physical inactivity and higher caloric intakes.[29,30] Our positive association might be related to a local context of differences in access to services and health inequities in health. In Colombia, some authors have exposed the barriers that rural residents deal with such as long distances between health centers and homes, transportation problems, and the lack of primary and preventive care, in addition to the fact that some areas are vulnerable to armed conflict, which makes access difficult.[31,32] In agreement with what was found in our analysis, a study in Colombia conducted by Ashner-Montoya found that individuals who lived in rural areas (vs urban areas) had 1.48 times higher odds (95% CI: 1.30–1.56) of presenting metabolic syndrome.[33]

Increased WC was a factor associated with MUNW and the other phenotypes, and it was the only non-sociodemographic or lifestyle variable that was used as an exposure variable in this analysis, not only to confirm its expectable relationship with MUNW but also to verify if other variables associated remained significantly associated in the presence of increased WC in the multiple models. Thus, age-MUNW and rural residence-MUNW relationships appear to be neither confounded nor mediated by increased waist circumference. Therefore, each variable in the model would have a different mechanism of relationship with MUNW. Particularly, increased WC is an indicator of visceral-type fat accumulation, which is found between the organs and digestive parts in the abdominal axis. This visceral fat has harmful biological properties based on its subclinical inflammatory effects that decrease the effect of insulin, predispose to dyslipidemia, and increase the risk of diabetes and cardiovascular disease.[34,35]

In the present study, subjects with MUNW showed a considerable prevalence of high waist circumference, 65%. The finding of high waist circumference as a variable positively associated with MUNW reinforces the concept that localized adiposity is a good predictor of cardio-metabolic risk. Several studies have reported waist circumference as a strong predictor of diabetes and cardiovascular disease independently of body mass index.[36,37]

The MHO phenotype has a very low prevalence in the sample of subjects analyzed (3.1%), which reinforces the concept that the trend for metabolic health in individuals with overweight or obesity is a rare event, and should be considered a transitory state towards the alteration of metabolic markers.[9,10] Consistently, it was observed that MUO was the most prevalent phenotype, as it was highly likely that individuals with excess adiposity would have a negative metabolic profile. The sum of the overweight phenotypes prevalence in the analyzed population (74.7%) exceeds the global Colombian prevalence of 56.1% according to the National Survey of the Nutritional Situation 2015 (ENSIN 2015).[38] However, the presence of middle-aged and older subjects included in the investigation predisposes to find more cases of overweight.[39] In light of the above, the prevalence of MUNW is likely much higher in the Colombian general population in which normal weight is more prevalent than in individuals from the Metrosalud chronic disease prevention program.

The phenotypes related to a BMI≥25 (MHO and MUO) shared similar associations with the exposure variables of sex and marital status of common-law marriage. Previous studies have found married status positively associated with higher opportunity of obesity when compared with unmarried categories.[40,41] Although the explanation for this relationship is still unclear, some hypotheses have been provided. One lays on the fact that unmarried people might prioritize physical activity and the control of their diet to look more attractive with the expectation of building couple relationships.[40] Another reason is related to the stress-triggered weight loss effects in individuals who deal with separated/divorced status vs married status.[40] In addition, married individuals cope with either work or domestic duties that limit their time for physical activity and predispose them to consume fast food/processed food-based diets. In the case of sex being a man compared to being a woman was associated with a 35% and 66% reduction in the chance of having MHO and MUO, respectively. This agrees with reports of a higher global prevalence of obesity in women than in men.[42,43] In this pattern, gender inequalities and vulnerability conditions are involved.[43] For instance, in Mexico, Araujo et al described gender inequities, in terms of high prevalence of hypertension, overweight, and increased WC in mothers who are heads of households from vulnerable sectors, compared to men of the same age (average 40 years) and with women from high socioeconomic status.[44] However, the analysis of this study lacks proper variables to evaluate the vulnerability of the women in the sample.

Two lifestyle variables, smoking habit and physical activity presented presumably contradictory associations with phenotypes characterized by overweight. Smoking and its inverse relationship with MHO (OR 0.56 p-value = 0.001), initially could be seen as an unexpected finding, in terms that two risk factors for NCDs, smoking and overweight, are not aligned in a positive sense of association. However, this pattern has an epidemiological and biological background that supports it. Wang, in a population sample of 70,394 subjects from the Chinese Health and Nutrition Survey, found a lower chance of being overweight in smokers (−6.5%) and a 2.7% greater likelihood of being underweight in the same individuals, compared to non-smokers.[45] Similarly, Jitnarim et al reported a significantly lower BMI in smokers vs non-smokers (21.6 kg/m2 vs 22.2 kg/m2) in 7858 Thai adults recruited from 17 provinces.[46] However, when strong, moderate, and light smoking habits were compared within the group of smokers, a higher average BMI was found in those with a strong habit.[46] Nicotine and its effect of increasing caloric expenditure could explain a lower weight in smokers.[47] Meanwhile, the self-reported practice of physical activity also had a paradoxical positive association with the chance that an individual presented MUO. This paradoxical association might be explained by the fact that individuals affected by overweight and obesity reported more practice of physical activity to lose weight.

The sub-analysis by sex revealed only alcohol intake as a sex-specific associated factor for MUNW different from those factors described in the whole sample, and sex-specific associations between ethnicity and overweight/obesity phenotypes. In women, alcohol consumption was associated with a higher likelihood of having MUNW. The link between sex, alcohol, and cardiometabolic risk is still controversial. While some studies report higher odds of cardiovascular disease risk by alcohol intake in men,[48] others have found this in women,[49] and others describe significant risk in both sexes.[50] The conflicting findings also arise in terms of frequency of alcohol consumption, with suggestions of moderate intake protective factor for cardiometabolic risk[48,51] vs observations on the harmfulness of either moderate or heavy intakes of alcohol for cardiovascular health.[50] Our finding needs to be interpreted with caution given that no structured questionnaires were used to estimate alcohol consumption habits. Similarly, differences by sex might be attributed to residual confounding in terms of covariates not measured or available in this analysis. There were also particular associations between a few ethnic groups and obesity/overweight phenotypes. It is unclear why ROM ethnicity was a significant determinant of MHO only in women, and Palenquero/Afro-descendant groups increased the opportunity to present MUO only in men. However, these findings altogether are consistent with previous studies reporting a higher risk of cardiometabolic disease in ethnic minority groups.[52,53] Although genetic factors might be implied in differences by ethnicity in cardiometabolic risk,[54] vulnerability, and social marginalization seem to be strong determinants in this relationship.[55]

Strengths and weaknesses

One of the strengths of this study is that it appears to be the first to be carried out in a Latin-American population on the characterization of MUNW and other metabolic phenotypes, and it serves as a baseline for future research. Likewise, a robust sample size was used and multiple associated factors were evaluated, and the independence of these factors was explored in a multivariate analysis. On the other hand, the analysis also presents weaknesses that should be highlighted. First, the information collected on lifestyle variables such as smoking, alcohol consumption, and physical activity was not based on structured questionnaires with international validity, but rather based on general frequency questions in the last month. Second, the findings of this analysis cannot be easily extrapolated to the general population since the sample was users of a program for the prevention and management of chronic diseases, in which young individuals are underrepresented. In terms of relative comparison with women in the sample, male sex individuals (27%) might also have been underrepresented and this could have influenced protective associations with MHO, MUO, and MUNW. Nevertheless, our large sample of 10,269 men might have attenuated this potential limitation. Another limitation is the multi-testing nature of univariate and multivariate analyses to find determinants of the outcome variables, which can lead to chance findings. Another limitation was the lack of information on socioeconomic status to explore inequities. Similarly, aggregate information on medications was not available and this variable may have helped complement dyslipidemia-related criteria and increased blood pressure criterion.

Conclusions

Almost a quarter (23.3%) of the population analyzed presents the metabolically discordant metabolically Obese normal weight (MUNW) phenotype. The sum of the two phenotypes with BMI $\geq$ 25 (MHO and MUO) show a prevalence of overweight of 74.7% of the total sample, indicating that only the 2% represented presented an ideal state for NCD prevention goals. The rural area of residence and being older than 60 years (as a trend) were associated with presenting MUNW. Being a man reduces the opportunity to present the MHO and MUO phenotypes. The age-MUNW and rural residence-MUNW relationships appear to be neither confounded nor mediated by increased waist circumference. Increased waist circumference, as expected, was a variable consistently associated with overweight phenotypes, but its association with MUNW reaffirms the high relevance of localized fat, particularly visceral fat, in cardiometabolic risk beyond general adiposity.

Future studies should be carried out in the general population to corroborate the findings of our study. Likewise, research should be carried out that describes, through relevant methodologies, to what extent metabolic alterations are not being detected in individuals with a normal BMI in the current Colombian health system, and whether the measure of waist circumference is being used in clinical practice routine.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

The study applied the guidelines of the Declaration of Helsinki and Resolution 8430 of the Colombian Ministry of Health, which state that this is a risk-free investigation. The participating institutions were endorsed, and the project was endorsed by the scientific committee of Metrosalud. The information was collected based on medical records; therefore, informed consent was not obtained.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare that they have no competing interests in this work.

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