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Prevalence and risk factors associated with the metabolic syndrome and dyslipidemia in White, Black, Amerindian and Mixed Hispanics in Zulia State, Venezuela

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Abstract

Studies have highlighted the association between insulin resistance (IR) and several cardiovascular (CV) risk factors, including hypertension (HTN), obesity, dyslipidemia (i.e. high triglyceride and low HDL-cholesterol) and glucose intolerance, in a cluster known as the metabolic syndrome (MS). There are few data on the frequency of the MS and dyslipidemia in developing countries, and none in South America. To estimate the prevalence of the MS and its components in Zulia State, Venezuela, and to establish associated demographic and clinical factors, we evaluated 3108 Hispanic men and women aged 20 years or older from a cross-sectional survey of a random representative sample from each health district in Zulia State, Venezuela (1999–2001). Prevalence of the MS and dyslipidemia was defined according to the National Cholesterol Education Program (NCEP)/Adult Treatment Panel III (ATP III) criteria. The age-adjusted prevalence of MS and dyslipidemia was 31.2% and 24.1%, respectively, with higher rates in men than in women. Prevalence rates increased with age and with the degree of obesity. MS prevalence was lower in Amerindian (17.%) compared to Black (27.2%), White (33.3%) and Mixed (37.4%) men, but no differences were found among women. Overall, low HDL-cholesterol (65.3%), abdominal obesity (42.9%) and HTN (38.1%) were the most frequent MS components. After adjusting for age, sex and race groups, family history of diabetes, obesity and HTN were associated with the MS. Sedentary lifestyle also increased the risk of MS, event after adjusting for the same covariates, obesity and the degree of IR. These results suggest that MS is found in approximately one-third of the Venezuelan adult population in Zulia State, with higher prevalence in men related to the presence of dyslipidemia. Lifestyle interventions in MS subjects are needed in Venezuela to halt the burden of CV disease and diabetes.

Keywords: Dyslipidemia; Metabolic syndrome; HOMA-insulin resistance; Hispanics

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1. Introduction

The tendency for certain cardiovascular (CV) risk factors to cluster, such as obesity, insulin resistance (IR), glucose intolerance, dyslipidemia and hypertension, has been recognized for many years and has been variously termed as syndrome X [1], IR syndrome [2,3], and more recently as the metabolic syndrome (MS) [4].

Several mechanisms have been suggested to explain the clustering of metabolic disturbances and CV risk factors described in connection with the MS [5,6]. IR is an important factor linking many features of this syndrome [1,2,7]. Weight gain and sedentary lifestyle are usually connected with the development of the MS [8,9]. The presence of abdominal obesity in IR subjects is a powerful risk factor for the development of type 2 diabetes (T2D) [10–12] and CV disease [13–16]. As the prevalence of obesity increases in developed and developing nations, the prevalence of the MS may be expected to increase markedly. In light of the current worldwide epidemic of obesity, the MS implies a serious and growing public health problem [17].

The differences in diagnostic criteria for this syndrome are partially responsible for variations in the reported prevalence among different studies [4,18,19]. The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) guidelines highlighted the key clinically relevant features of this syndrome and proposed a definition to facilitate diagnosis and preventive interventions [20].

Using the NCEP definition, the age-adjusted prevalence of the metabolic syndrome was 24% in men and 23.4% in women in U.S. adults [21]. In an analysis by race and ethnicity, African–American and Mexican–American women had higher prevalence of the syndrome than men from the same groups. In spite of the widely appreciated magnitude of this problem, there are few data on the frequency of the MS in developing countries, particularly in South America.

CV disease is the leading cause of morbidity and mortality in Venezuela [22], yet no study has examined this cluster of CV risk factors among the different Hispanic groups that comprise this South American country. Therefore, the aims for this study were to examine the prevalence of the MS and its components in Zulia State, Venezuela, and establish associated demographic and clinical risk factors for the MS in this population.

2. Subjects and methods

2.1. Study subjects

The Zulia Coronary Heart Disease Risk Factor Study was designed to evaluate risk factors for atherosclerosis in the state's adult population and to develop population-based strategies aimed at changing unhealthy lifestyles and halting the increasing trend of CV disease and T2D in Venezuela. Zulia is located in the northwest of Venezuela and has a population mixture and distribution considered to be reflective of this country [23]. The study protocol was approved by the National Foundation for Science and Research (FONACIT) in Venezuela.

A stratified random sampling technique within each health district in Zulia State was used. Household lists from each district's healthcare center were used for sample selection. A random sample of the households, stratified according to healthcare district to achieve a distribution similar to the original population, was chosen. The response rate was 85%, with 3% refusing to be assessed or who could not be contacted and 12% who did not have the laboratory examination. A total of 3108 men and women aged 20 years or older were evaluated between March 1999 and April 2001.

2.2. Clinical data

After giving written informed consent, all participants were evaluated in their home by trained health care providers according to a standard protocol. Demographic and clinical information was obtained using a standardized questionnaire. Race was self-defined and included White, Black, Amerindian and Mixed Venezuelans; with the degree of admixture for the latter group recently described as being predominantly White followed by contribution from Amerindian and small contribution by Blacks [23]. Sedentary lifestyle and family history were assessed as previously reported [24]. Body mass index (BMI: weight/height^2 (kg/m^2)) was used as an estimate of overall adiposity and individuals were classified as normal weight, overweight or obese according to their

BMI values (<25, 25–29.9 or ≥ 30, respectively). Waist circumference was measured at the level of the umbilicus. Blood pressure was measured twice after participants were seated for 5 min using a previously approved protocol [25]. The mean of two measurements was taken as the blood pressure.

2.3. Laboratory data

Blood samples were drawn after 12–14 h of overnight fasting and were centrifuged within 30–45 min of collection. Specimens were divided into aliquots and stored at –70 °C until assayed. All blood lipid and glucose analyses were undertaken at our research laboratory using an automated chemical analyzer (Dimension® Dade Behring). Glucose was assayed by the glucose-oxidase method. Total cholesterol and triglyceride were measured enzymatically. High density lipoprotein (HDL)-cholesterol was measured after precipitation of the apo B-containing lipoproteins with phosphotungstate reagent as previously reported [26]. Insulin was measured with a double-antibody radioimmunoassay technique (Diagnostic Products Corp.) [27].

The homeostasis model assessment (HOMA), an epidemiologic method for assessing IR across glucose tolerance categories {HOMA-IR = insulin (μU/ml) × glucose (mmol/l)/22.5} was used as surrogate measure of insulin sensitivity [28].

2.4. Definition of the metabolic syndrome and dyslipidemia

The MS was defined as in the NCEP/ATP III [20], by the presence of three or more of the following abnormalities: waist circumference ≥102 cm in men or ≥88 cm in women; blood pressure ≥130/85 mmHg; fasting triglyceride ≥150 mg/dl; HDL-cholesterol level <40 mg/dl in men or <50 mg/dl in women; or blood glucose ≥110 mg/dl. Dyslipidemia, previously reported as frequent in high-risk population studies in Zulia State [26,29], was defined as the presence of both high triglyceride and low HDL-cholesterol, using the same cut-off from the NCEP/ATP III [20].

2.5. Statistical analysis

All calculations were performed using the NCSS™ 2000 statistical package. All tests were two-sided and an alpha level of 0.05 or less was considered to be statistically significant. Data for continuous variables are presented as mean ± standard error (S.E.). Differences between mean values were assessed by analysis of variance (ANOVA), with Bonferroni adjustment for multiple comparisons. For analysis of prevalence data, the study population was divided into six age groups (20–29, 30–39, 40–49, 50–59, 60–69 and 70 years and older). All prevalence rates were adjusted for the survey design as follows: age-specific prevalence rates, calculated in each of the third, fourth, fifth, sixth, seventh and eighth age decades, were multiplied by weights (number of subjects in Zulia State in each given category divided by the overall number of subjects older than 20 years of age) and summed to obtain the population-standardized rate. The data are presented as prevalence rates and 95% confidence intervals. Chi-square test was used to compare race- and gender-specific rates of MS, dyslipidemia and MS components. Sex-specific logistic regression analyses were used to estimate the odds ratios (ORs) of the MS by family history of diabetes, obesity, hypertension and sedentary lifestyle. Separate analyses for the MS and dyslipidemia were perfomed in each race group with the same risk factors and including age, gender, BMI and HOMA-IR.

3. Results

3.1. Subject characteristics

Overall, data from 3108 subjects were assessed (2162 women and 946 men). Their demographic and clinical characteristics are summarized in Table 1. Blood pressure was higher ($p < 0.01$) and HDL-cholesterol was lower ($p < 0.01$) in men relative to women. Mixed Venezuelans were slightly younger than White and Black Venezuelans, but no gender differences with respect to age, BMI, self-reported diabetes and coronary heart disease, and the degree of sedentary lifestyle were observed across race groups, with the exception of Amerindians, where men were slightly older than women. Compared to other race groups, family history of diabetes was lower in Black men and in Amerindian women, while family history of hypertension was lower in Amerindian men and women. Compared to women, only among Mixed and

Table 1
Demographic and clinical characteristics of study subjects in Zulia State by race and gender

	Mixed		White		Black		Amerindian	
	Men ($n = 662$)	Women ($n = 1512$)	Men ($n = 108$)	Women ($n = 277$)	Men ($n = 110$)	Women ($n = 174$)	Men ($n = 66$)	Women ($n = 199$)
Age (years)	43.3 ± 0.6[a,¶,W,B]	42.7 ± 0.4 [¶,W,B]	46.5 ± 1.5	45.4 ± 0.9	48.1 ± 1.5	46.9 ± 1.2	46.6 ± 1.9[†]	42.9 ± 1.1
Self-reported diabetes (%)	5.8 (4.1–0.8)[b]	6.8 (5.6–8.2)	7.5 (3.3–14)	6.9 (4.2–11)	3.6 (1–9)	5.2 (2.4–9.6)	6.1 (1.7–15)	4.5 (2.1–8.5)
Self-reported CHD (%)	7.9 (6–10.2)	7.8 (6.5–9.3)	6.6 (2.7–13)	9.5 (6.3–14)	9.1 (4.4–16)	7.5 (4–12.4)	4.5 (1–13)	4 (1.8–7.8)
Family history of diabetes (%)	39 (35–43)	44 (41–47)	37 (28–47)	44 (38–50)	17 (10–24)[‡,¶,M,W,AI]	35.9 (28–43)	29 (18–41)	30 (23–37)[¶,M,W]
Family history of obesity (%)	32 (28–36)	36.2 (33–39)	36.2 (27–46)	38 (32–44)	25.7 (18–35)	35.4 (28–43)	27 (16–40)	35 (28–42)
Family history of hypertension (%)	65 (61–69)	69 (67–71)	60 (50–70)	75.1 (69–80)	69 (59–79)[¶,W]	76 (69–83)[¶,M]	43 (30–57)[¶,M,W,B]	61 (53–68)[¶,M,W,B]
Sedentary lifestyle (%)	74.2 (70–78)	84 (82–86)	75 (66–83)	80 (75–85)	78 (69–85.4)	86.5 (80–91)	75.8 (64–86)	84.9 (79–90)
Body mass index (kg/m^2)	27.3 ± 0.2	27.1 ± 0.2	27 ± 0.6	27.6 ± 0.4	26.5 ± 0.6	27.3 ± 0.5	25.4 ± 0.7	26.7 ± 0.4
Waist circumference (cm)	97.2 ± 0.5[‡]	89.4 ± 0.4[¶,W,B]	97.1 ± 1.3[‡]	92.3 ± 0.8	91.9 ± 1.3[¶,M,W]	90.5 ± 1	91.8 ± 1.7[¶,M,W]	89.4 ± 1
Systolic blood pressure (mmHg)	133.6 ± 0.9[‡]	125.5 ± 0.6	137.5 ± 2.3[‡]	128.7 ± 1.5	141 ± 2.3[‡,¶,M,AI]	135.4 ± 1.8[¶,M,W,AI]	127.8 ± 3[‡,¶,B,W]	121.8 ± 1.7[¶,B,W]
Diastolic blood pressure (mmHg)	78.5 ± 0.5[‡]	72.5 ± 0.3	80.3 ± 1.3[‡]	72.4 ± 0.8	81.3 ± 1.2[‡]	76.9 ± 1[¶,M,W,AI]	74 ± 1.6[‡,¶,B,W]	71.6 ± 0.9
Fasting blood glucose (mg/dl)	97.1 ± 1.6	95.5 ± 1.1	96.5 ± 4	92.5 ± 2.5	105.4 ± 4[‡]	91.5 ± 3.2	103.9 ± 5.1[‡]	94.3 ± 2.9
Fasting insulin (mU/l)	25.7 ± 1.6	24 ± 1.1	27.4 ± 4.9	28 ± 2.8	18.9 ± 3.3	24.8 ± 2.7	15.7 ± 4.8[¶,M,W]	17.8 ± 2.9[¶,M,W]
Total cholesterol (mg/dl)	160.9 ± 1.9[‡]	170.7 ± 1.3	166.5 ± 4.8[‡]	174.3 ± 3	201.2 ± 4.7[¶,M,W,AI]	204.3 ± 3.8[¶,M,W,AI]	145.6 ± 6[‡,¶,B,W]	163.2 ± 3.5
HDL-cholesterol (mg/dl)	39.5 ± 0.5 [‡]	45.7 ± 0.3	41.9 ± 1.3[‡]	46.1 ± 0.8	39.8 ± 1.3[‡]	43.9 ± 1	35.7 ± 1.6 [‡,¶,W]	40.4 ± 0.9[¶,M,W]
Triglyceride (mg/dl)	160.6 ± 3.3[‡]	127.7 ± 2.2	153.7 ± 8.1	138.8 ± 5.1	116.8 ± 8.1[‡,¶,M,W]	99.9 ± 6.4[¶,M,W,AI]	156.1 ± 9.9	134.6 ± 6

CHD, coronary heart disease; HDL, high density lipoprotein. For race-specific sex comparison: [†]$p < 0.05$, [‡]$p < 0.01$. For sex-specific race comparison (reference vs. others: M, Mixed; W, White; B, Black; AI, Amerindian): [¶]$p < 0.05$.

[a] Mean ± standard error.

[b] 95% confidence interval.

Table 2
Age-specific prevalence for the metabolic syndrome and dyslipidemia in Zulia State among race groups

	Mixed ($n = 2174$)	White ($n = 385$)	Black ($n = 284$)	Amerindian ($n = 265$)	Total ($n = 3108$)
Metabolic syndrome					
20–29	16.0 (12.9–15.9)[a]	12.5 (6.2–21.8)	14.6 (6.1–27.8)	4.5 (0.9–12.5)	14.4 (11.9–17.2)
30–39	27.8 (23.9–31.9)	25.0 (15.9–35.9)	30.8 (18.7–45.1)	26.0 (14.6–40.3)	27.6 (24.3–31.0)
40–49	40.0 (35.5–44.7)	40.8 (29.3–53.2)	36.4 (24.9–49.1)	37.9 (25.5–51.6)	39.6 (35.8–43.5)
50–59	54.8 (49.2–60.4)	61.7 (48.2–73.9)	48.0 (33.7–62.6)	59.5 (42.1–75.3)	55.3 (50.7–59.9)
60–69	51.1 (44.5–57.6)	57.1 (42.2–71.2)	38.7 (21.8–57.8)	50.0 (31.3–68.7)	50.7 (45.3–56.1)
≥70	48.3 (39.8–56.8)	44.4 (29.6–60.0)	32.4 (18.0–49.8)	52.2 (30.6–73.2)	45.6 (39.3–51.9)
Total	35.4 (33.4–37.5)	37.4 (32.6–42.5)	35.5 (28–39.3)	32.8 (27.2–38.8)	35.3 (33.6–37)
p-value for a trend	<0.0001	<0.0001	<0.05	<0.0001	<0.0001
Dyslipidemia					
20–29	15.4 (12.4–18.8)	8.8 (3.6–17.2)	8.3 (2.3–20.0)	11.9 (5.3–22.2)	13.8 (11.4–16.6)
30–39	24.7 (21.0–28.7)	23.8 (14.9–34.6)	15.4 (6.9–28.1)	34 (21.2–48.8)	24.6 (21.4–28.0)
40–49	30.5 (26.3–35.0)	35.2 (24.2–47.5)	19.7 (10.9–31.3)[¶,AI]	37.9 (25.5–51.6)	30.6 (27.1–34.3)
50–59	35.5 (30.3–41.0)	36.7 (24.6–50.1)	20 (10.0–33.7)	54.1 (36.9–70.5)	35.5 (31.1–40.0)
60–69	30.6 (24.8–37.0)	38.8 (25.2–53.8)	12.9 (3.6–29.8)	30 (14.7–49.4)	30.1 (25.3–35.3)
≥70	35.7 (27.8–44.1)	20 (9.6–34.6)	10.8 (3.0–25.4)[¶,M]	30.4 (13.2–52.9)	28.6 (23.1–34.7)
Total	26.7 (24.8–28.6)	26.2 (21.9–30.9)	15.1 (11.2–19.8)[¶,M,W,AI]	31.3 (25.8–37.3)	26 (24.4–27.5)
p-value for a trend	<0.0001	<0.01	0.66	<0.01	<0.0001

For race comparison (reference vs. others: M, Mixed; W, White; B, Black; AI, Amerindian): [¶] $p < 0.05$.
[a] Percentage (95% confidence interval).

White Venezuelans was waist circumference larger in men, while fasting blood glucose was higher in Black and Amerindian men, and triglyceride was higher in Mixed and Black men.

3.2. Prevalence of the MS and dyslipidemia by age, gender and race

The unadjusted and age-adjusted prevalence of the MS in Zulia State, Venezuela was 35.3% and 31.2%, respectively. As shown in Table 2 and Fig. 1, the prevalence of the MS increased with age, with the lowest prevalence in the 20–29 age group (23.2% in men and 10.3% in women, $p < 0.001$), and the highest prevalence in the 50–59 age group (43.5% in men and 59.9% in women, $p < 0.01$). Overall, the age-adjusted prevalence of the MS was higher in men (35%) than in women (29.8%) (see Table 3). Similarly, dyslipidemia was higher in men (30.7%, 95% CI: 27.7–33.7) than in women (21.4%, 95%

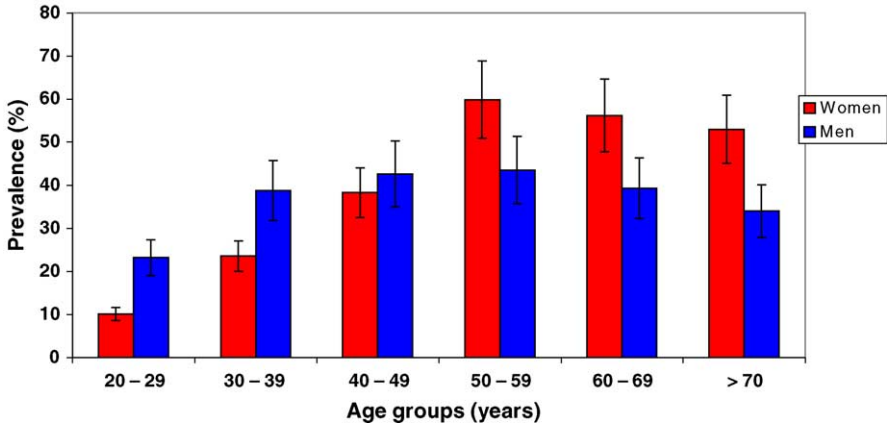

Fig. 1. Age-specific prevalence of the metabolic syndrome by gender in Zulia State, Venezuela.

Table 3
Age-adjusted prevalence rates for the metabolic syndrome and its components in Zulia State by race and gender

	Mixed ($n = 2174$)	White ($n = 385$)	Black ($n = 284$)	Amerindian ($n = 265$)	Total ($n = 3108$)
Metabolic syndrome					
Total	31.9 (30.0–33.9)[a]	31.3 (26.8–36.3)	29.4 (24.0–34.9)	28.1 (22.6–33.7)^{¶,M}	31.2 (29.6–32.9)
Women	29.6 (27.3–32.0)	30.9 (25.6–36.9)	30.9 (24.3–38.5)	29.9 (23.9–37.0)	29.8 (27.9–31.8)
Men	37.4 (33.8–41.3)‡	33.3 (24.6–43.1)	27.2 (19.2–36.6)^{¶¶,M}	17.1 (8.6–27.9)^{¶¶,M,W,B}	35.0 (32.0–38.1)‡
High WC					
Total	42.7 (40.6–44.8)	47.4 (42.4–52.7)^{¶,B,AI}	40.1 (34.4–46.1)	41.2 (35.1–47.3)	42.9 (41.2–44.6)
Women	46.3 (43.8–48.8)	52.5 (46.3–58.4)^{¶¶,M}	54.2 (46.3–61.6)^{¶¶,M}	47.6 (40.6–54.9)	47.9 (45.8–50.0)
Men	34.1 (30.5–37.9)^{‡,¶¶,B,AI}	34.0 (25.4–44.0)^{‡,¶¶,B,AI}	18.4 (11.5–26.7)‡	15.7 (7.5–26.1)‡	31.4 (28.4–34.4)‡
High BP					
Total	38.1 (36.0–40.2)	36.6 (31.8–41.7)	48.6 (42.6–54.6)^{¶¶,M,W,AI}	28.5 (23.3–34.5)^{¶,M,W,B}	38.1 (36.4–39.9)
Women	31.4 (29.1–33.8)	30.6 (25.3–36.5)	40.0 (32.9–47.9)^{¶,M,W,AI}	27.0 (21.1–33.9)^{¶,B,M}	31.5 (29.6–33.5)
Men	53.1 (49.3–57.0)‡	53.1 (42.9–62.5)‡	63.9 (53.9–72.6)^{‡,¶,M,W,AI}	33.5 (22.2–46.0)^{¶,M,W,B}	53.3 (50.1–56.5)‡
High BG					
Total	10.7 (9.4–12.1)	9.6 (6.9–13.0)	14.1 (10.3–18.7)	12.5 (9.3–16.2)	10.9 (9.8–12.0)
Women	10.0 (8.5–11.6)	10.0 (6.8–14.3)	10.1 (6.2–15.9)	9.9 (6.2–15.1)	10.0 (8.8–11.3)
Men	12.1 (9.7–14.8)	8.0 (3.9–15.2)	20.2 (13.0–28.7)^{†,¶¶,M,W}	16.8 (8.6–27.9)^{†,¶,M,W}	13.1 (11.1–15.4)‡
High TG					
Total	33.9 (31.9–35.9)	31.2 (26.6–36.1)	17.4 (13.0–22.2)^{¶¶,M,W,AI}	34.5 (28.6–40.4)	32.3 (30.7–34.0)
Women	28.7 (26.4–31.1)	28.3 (22.9–33.9)	13.1 (8.6–19.2)^{¶¶,M,W,AI}	33.6 (27.1–40.7)	27.8 (25.9–29.7)
Men	46.5 (42.7–50.4)‡	39.8 (30.5–49.7)†	24.5 (16.8–33.7)^{‡,¶,M,W}	34.7 (23.5–47.6)	43.1 (39.9–46.3)‡
Low HDL-C					
Total	64.3 (62.3–66.3)	61.9 (56.8–66.7)	68.5 (62.9–74.0)	77.8 (72.2–82.6)^{¶¶,M,W,B}	65.3 (63.6–67.0)
Women	66.0 (63.6–68.4)	64.8 (58.7–70.2)	74.1 (67.0–80.5)	78.9 (72.6–84.3)^{¶¶,M,W}	67.5 (65.5–69.4)
Men	59.9 (56.1–63.7)‡	54.3 (44.8–64.2)†	59.1 (49.3–68.4)‡	75.2 (63.6–85.5)^{¶¶,M,W,B}	59.9 (56.8–63.0)‡

WC, waist circumference; BP, blood pressure; BG, blood glucose; TG, triglycerides; HDL-C, high density lipoprotein cholesterol. For sex comparison: $^{†}p < 0.05$, $^{‡}p < 0.01$. For race comparison (reference vs. others: M, Mixed; W, White; B, Black; AI, Amerindian): $^{¶}p < 0.05$, $^{¶¶}p < 0.01$.

[a] Percentage (95% confidence interval).

CI: 19.7–23.2), with prevalence rates increasing across age strata (see Table 2). The overall age-adjusted prevalence of dyslipidemia was 24.1% (95% CI: 22.6–25.6).

Among men, a lower age-adjusted prevalence of the MS was seen in Amerindian (17.1%) and Black (27.2%) compared to Mixed Venezuelans (37.4%), while in women there were no significant differences across race groups. In contrast, Black Venezuelans showed lower age-adjusted prevalence of dyslipidemia in men (19.1% in Blacks versus 32.6% in Mixed, 29% in Whites, and 31.5% in Amerindians, $p < 0.01$) and women (11.3% in Blacks versus 21.8% in Mixed, 21.8% in Whites, and 28.6% in Amerindians, $p < 0.01$).

3.3. Effect of BMI on MS and dyslipidemia prevalence

The relationship between BMI and MS prevalence is presented in Fig. 2. A steep rise in the prevalence of the MS is observed in women and men from all race groups. Overall, 15.5%, 37.1% and 61.6% of normal weight, overweight and obese women met MS diagnostic criteria ($p < 0.001$). Similarly in men, the corresponding prevalence rates were 12.2%, 38.4% and 70.3% ($p < 0.001$).

Dyslipidemia prevalence also increased across BMI categories (14.9% in normal weight, 27.9% in overweight, and 40.4% in obese subjects, $p < 0.001$), with similar rise in both genders and all race groups.

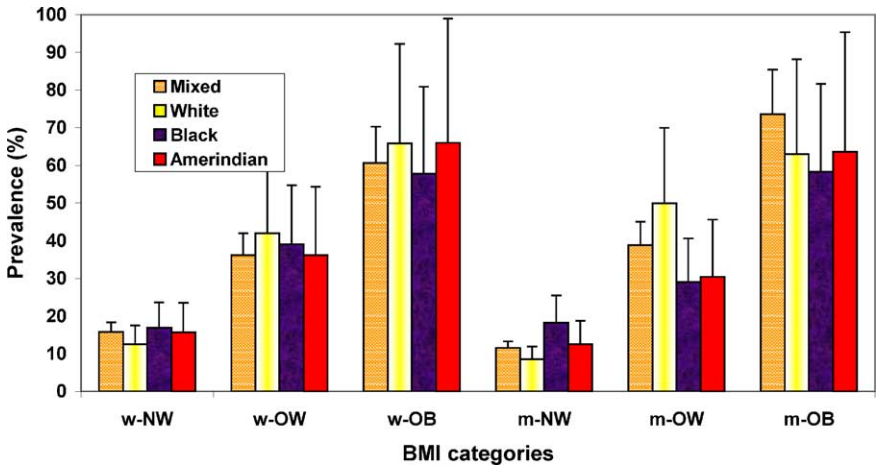

Fig. 2. Prevalence of the metabolic syndrome in normal weight (NW), overweight (OW) and obese (OB) women (w) and men (m) by race groups.

3.4. Components of the MS by gender and race

Despite some gender differences, low HDL-cholesterol was the most common metabolic abnormality (67.5% in women versus 59.9% in men, $p < 0.01$), followed by high blood pressure (53.3% in men versus 31.5% in women, $p < 0.01$) and large waist circumference (47.9% in women versus 31.4% in men, $p < 0.01$).

There were also racial differences in the frequency of MS components. Low HDL-cholesterol was more common in Amerindians (77.8%) than in the other race groups (68% in Blacks, 64.3% in Mixed and 61.9% in Whites, $p < 0.01$). Blacks had a higher prevalence for HTN (48.6%) than Mixed (38.1%) and Whites (36.6%) ($p < 0.01$), while the lowest HTN prevalence was seen in Amerindians (28.5%). Among men, Whites (34.1%) and Mixed (34%) had larger waist circumference than Blacks (18.4%) and Amerindians (15.7%) ($p < 0.01$). Conversely in women, Blacks (54.2%) and Whites (52.5%) had more abdominal obesity than Mixed (46.3%). Elevated triglyceride was predominantly higher in men (43.1%) than in women (27.8%) ($p < 0.01$), with the exception of the Amerindian group. In addition, hypertriglyceridemia was significantly lower among Blacks (17.4%) than in other race groups (34.5% in Amerindians, 33.9% in Mixed, 31.2% in Whites, $p < 0.01$).

Overall, elevated fasting blood glucose (FBG) was more frequent in men (13.1%) than in women (10%) ($p < 0.01$), even when the new cut-off for impaired glucose regulation (FBG $\geq$ 100 mg/dl), proposed in 2003 by the American Diabetes Association [30], was used (27.4% in men and 22.3% in women, $p < 0.01$). Consequently, men had more prediabetes (19.6%) than women (14.9%) ($p < 0.001$), but no gender difference was seen among those reaching a diabetic FBG ($\geq$126 mg/dl) (7.8% in men and 7.4% in women). In addition, among men, Blacks (20.2%) and Amerindians (16.8%) had higher prevalence of elevated FBG than Mixed (12.1%) and Whites (8%), while no significant differences were observed in women across race groups.

Most subjects with MS had three abnormalities (60.3%), while 32.1% had four, and 7.6% had five. It is noteworthy that HOMA-insulin resistance increased with the number of abnormalities found within a single individual in all race groups ($p < 0.0001$) (Fig. 3), with mean values higher among Whites (9.7) and Mixed (9.4) than in Amerindians (5.9) ($p < 0.05$).

Among MS subjects, the combination of dyslipidemia (i.e., high triglyceride and low HDL-cholesterol) with abdominal obesity and high blood pressure was the most common presentation (20.4%). This was followed by the cluster of abdominal obesity, high blood pressure and low HDL-cholesterol (18%) and the combination of abdominal obesity and dyslipide-

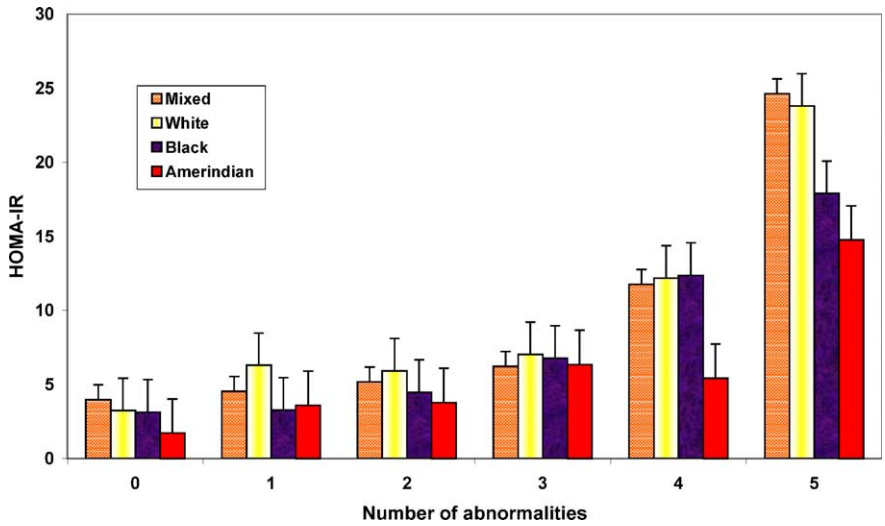

Fig. 3. HOMA-insulin resistance (IR) stratified by the number of metabolic syndrome abnormalities across race groups in Zulia State, Venezuela.

mia (15.8%), with the former combination more frequent among Blacks (33.7%) and the latter one predominantly found in Amerindians (28.7%) (Fig. 4).

Only 11.2% of the study population was free from any of the MS abnormalities. Within the 20–29-year-old group of the general population, 20.5% had no abnormality, while this figure dropped to 2.7% in people above 70 years of age. In younger individuals, low HDL-cholesterol was the most frequent abnormality without significant changes across age strata (from 62.8% in those aged 20–29 to 67.9% in those 40–49 years of age). In contrast, high triglyceride increased from 20.3% in the younger age group to 46% in those aged 50–59, while elevated fasting blood

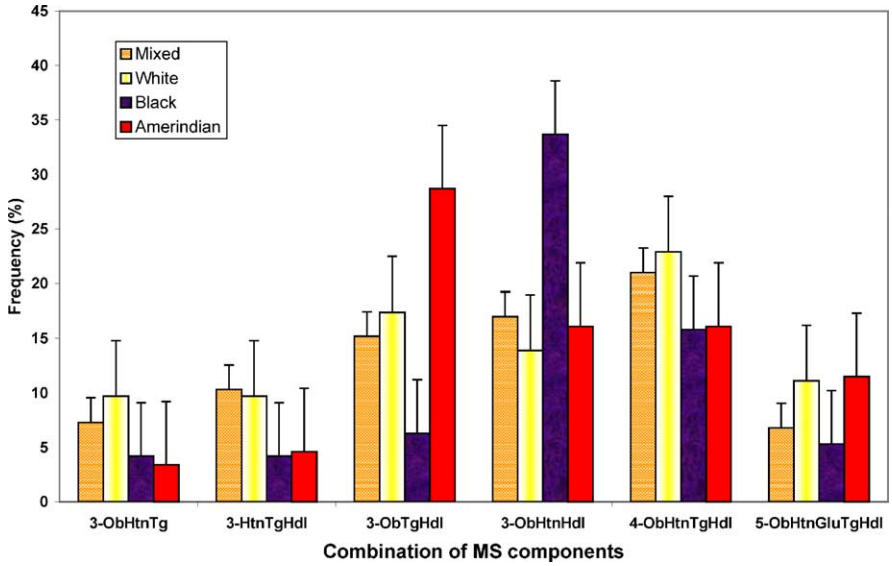

Fig. 4. Most frequent combination among metabolic syndrome subjects by race in Zulia State, Venezuela.

Table 4
Distribution of risk factors and logistic regression analyses for the metabolic syndrome in Zulia State by gender

	In those without MS (%)	In those with MS (%)	Crude OR (95% CI)	Adjusted OR (95% CI)	
				Model 1	Model 2
Family history of diabetes					
Overall	38.0	43.7	1.29 (1.10–1.51)	1.46 (1.23–1.73)	1.23 (0.97–1.56)
Women	41.0	43.6	1.12 (0.93–1.35)		
Men	31.0	44	1.85 (1.38–2.48)		
Family history of obesity					
Overall	31.8	40.4	1.44 (1.23–1.69)	1.58 (1.33–1.87)	1.18 (0.93–1.50)
Women	33.4	41.8	1.43 (1.18–1.73)		
Men	28.1	37.5	1.50 (1.11–2.03)		
Family history of hypertension					
Overall	66.4	70.7	1.23 (1.04–1.45)	1.30 (1.09–1.56)	1.02 (0.79–1.32)
Women	68.3	72.7	1.23 (1.01–1.51)		
Men	62.0	66.1	1.22 (0.91–1.64)		
Sedentary lifestyle					
Overall	78.7	85.1	1.55 (1.26–1.90)	1.42 (1.17–1.80)	1.37 (1.01–1.88)
Women	81.6	86.9	1.47 (1.14–1.91)		
Men	71.8	81	1.72 (1.22–2.42)		

MS, metabolic syndrome; OR, odds ratio; CI, confidence interval. Model 1: adjusted for age, sex and race groups. Model 2: adjusted for body mass index, homeostasis model assessment (HOMA)-insulin resistance and model 1 variables.

glucose increased from 4% in younger subjects to 28.3% in those age 60 and above. Abdominal obesity also increased from 25.8% in those aged 20–29 to a peak of 63.5% (72.8% in women) in those 50–59 years. High blood pressure rose from 21.7% in those 20–29 years to become the most common abnormality in those aged 60–69 and 70 and above (71.4% and 78.5%, respectively).

3.5. Risk factors for the MS and dyslipidemia

Crude and adjusted ORs for each risk factor are presented in Table 4. Family history of obesity was associated with higher risk for the MS in both men and women. In contrast, family history of diabetes increased the risk for the MS only in men, while family history of hypertension was associated with higher risk of MS in women. Overall, these relationships remained significant after adjusting for age, gender and race groups, but disappeared when elevated BMI ($\geq$25 kg/m^2) and higher HOMA-IR (median split) were entered in each model. Conversely, sedentary lifestyle was significantly associated with higher risk for the MS in both men and women, even after adjusting for these demographic and metabolic variables.

Separate multiple logistic regression analyses for MS and dyslipidemia with the same covariates are shown in Table 5. Age increased the risk for MS in all race groups, particularly in Amerindian subjects. In contrast the effect of age on dyslipidemia was only evident among Mixed and White subjects. Male gender was a risk factor for dyslipidemia only in the Black group. The effect of family history of diabetes on the MS and dyslipidemia was evident only in Mixed subjects, while sedentary lifestyle significantly increased the risk for both MS and dyslipidemia in the White group. The effect of overweight/obesity on the MS was similar in all race groups, while the effect on dyslipidemia was somewhat stronger in White and weaker in Mixed subjects. Insulin resistance (HOMA-IR) was associated with the presence of the MS in all race groups, but the effect on dyslipidemia was only evident in Mixed and Amerindian subjects. In fact, in the Amerindian race, insulin resistance was associated with the presence of dyslipidemia when all the other risk factors were taken into account.

Additional logistic regression analyses for each MS component showed that age, male gender, family history of hypertension and obesity and Black race were associated with the presence of high blood pressure. In contrast, for abdominal obesity the main risk factors

Table 5
Multiple logistic regression analyses for the metabolic syndrome and dyslipidemia in Zulia State among race groups

	Mixed	White	Black	Amerindian	Overall
Metabolic syndrome					
Age $\geq$ 45 years	3.84 (2.90–5. 09)[a]	3.32 (1.39–7.94)	2.94 (1.44–5.99)	7.26 (2.93–18.04)	3.82 (3.01–4.84)
Sex (male)	0.92 (0.68–1.25)	0.75 (0.28–1.92)	0.58 (0.28–1.21)	0.54 (0.20–1.47)	0.85 (0.65–1.09)
Family history of hypertension	0.85 (0.62–1.17)	1.20 (0.49–2.98)	1.65 (0.74–3.72)	1.04 (0.42–2.59)	0.97 (0.75–1.26)
Family history of diabetes	1.39 (1.02–1.89)	1.03 (0.43–2.44)	0.59 (0.26–1.30)	1.17 (0.44–3.13)	1.21 (0.94–1.56)
Family history of obesity	1.14 (0.84–1.54)	0.94 (0.41–2.20)	0.86 (0.39–1.89)	1.08 (0.44–2.64)	1.11 (0.86–1.43)
Sedentarism	1.38 (0.94–2.02)	3.26 (1.22–8.68)	0.81 (0.32–2.00)	0.92 (0.29–2.90)	1.39 (1.01–1.91)
BMI $\geq$ 25 kg/m^2	4.11 (2.98–5.66)	5.44 (2.18–13.52)	4.12 (1.91–8.88)	5.15 (2.06–12.84)	4.24 (3.25–5.54)
High HOMA-IR[b]	2.36 (1.78–3.13)	2.37 (1.04–5.40)	2.77 (1.35–5.65)	3.04 (1.26–7.33)	2.44 (1.93–3.09)
Race (Amerindian)[c]					1.11 (0.73–1.68)
Dyslipidemia					
Age $\geq$ 45 years	2.08 (1.58–2.75)	2.02 (1.17–3.50)	1.66 (0.67–4.07)	1.89 (0.87–4.14)	2.03 (1.60–2.58)
Sex (male)	1.32 (0.98–1.78)	1.28 (0.70–2.35)	2.61 (1.08–6.33)	0.89 (0.37–2.17)	1.33 (1.03–1.72)
Family history of hypertension	0.95 (0.69–1.29)	0.93 (0.50–1.71)	1.66 (0.56–4.93)	0.95 (0.41–2.21)	0.97 (0.74–1.26)
Family history of diabetes	1.59 (1.17–2.16)	1.05 (0.59–1.87)	0.82 (0.30–2.27)	1.31 (0.53–3.21)	1.41 (1.09–1.83)
Family history of obesity	0.80 (0.59–1.10)	1.25 (0.71–2.23)	0.85 (0.31–2.35)	0.93 (0.41–2.15)	0.80 (0.61–1.03)
Sedentarism	1.17 (0.80–1.72)	2.31 (1.11–4.80)	1.38 (0.41–4.65)	0.67 (0.23–1.93)	1.16 (0.84–1.60)
BMI $\geq$ 25 kg/m^2	1.82 (1.33–2.49)	3.16 (1.18–8.43)	2.47 (0.93–6.62)	2.55 (1.13–5.75)	1.99 (1.52–2.60)
High HOMA-IR	1.85 (1.39–2.46)	1.67 (0.73–3.80)	2.44 (0.93–6.35)	2.70 (1.23–5.92)	1.93 (1.51–2.46)
Race (Amerindian)					1.40 (1.03–1.90)

BMI, body mass index; HOMA, homeostasis model assessment; IR, insulin resistance.
[a] Data presented as odds ratio (95% confidence interval).
[b] Upper half (median split).
[c] Only for the overall model.

were: female gender, age, family history of obesity and diabetes and sedentary lifestyle. Finally, age older than 45 years, male gender, family history of obesity and diabetes and lack of exercise were significantly associated with higher risk of elevated fasting blood glucose.

4. Discussion

We found that using the NCEP/ATP III criteria, approximately one-third of the Venezuelan subjects in this study have the MS. Since the population studied was representative of Zulia State, this finding can be generalized to the whole population of this western state in Venezuela, suggesting that the MS is widespread among Venezuelan adults. In addition, our study showed that prevalence rates are highly variable among age and BMI groups; that MS prevalence is similar across race groups in women, but varies among men. Using the NCEP/ATP III cut-off values for triglyceride and HDL-cholesterol, we report that approximately one-fourth of the study subjects had dyslipidemia. The slightly higher MS prevalence found in men was probably related to higher dyslipidemia and high blood pressure rates in men than in women. Finally, we found that risk factors such as family history of obesity and diabetes and sedentary lifestyle are linked with the presence of the MS and dyslipidemia in this population, but with differences in their effect according to race group and gender. These results provide the foundation for prevention initiatives directed to diabetes and CV disease.

The prevalence of the MS in this study is higher than previous reports in other populations [3,19,21,31–35] and similar to the recently published study on adults from Tehran [36]. However, some of these differences might arise from variations in the MS definition used in each study. For instance, Trevisan et al. [31] reported a prevalence of 3–3.5% in Italy, but MS was diagnosed based on the presence of all metabolic abnormalities. We found that 7.6% of our subjects had all five metabolic components, while the recent report in an Iranian population showed that 9% met all criteria [36]. Reports in the US population aged

20 and older [21,37] showed that approximately one-fourth meet the NCEP/ATP III MS criteria. Using the World Health Organization (WHO) diagnostic criteria for the MS, the reported prevalence in the US population was 25.1% [38]. However, applying the WHO definition requires an abnormal oral glucose tolerance test (OGTT) (i.e., diabetes or impaired glucose tolerance) or the presence of IR (in normoglycemic subjects), plus two additional abnormalities: obesity, dyslipidemia, hypertension or microalbuminuria. In contrast, the NCEP/ATP III definition can be easily applied without OGTT or actual IR measurement.

Several limitations are related to the most commonly accepted definitions of the MS (NCEP/ATP III, WHO and European Group for the study of IR (EGIR)), as recently reviewed [5]. First, the suggested components are continuous variables; therefore, cut-off values chosen may be different. For instance, a recent report using different criteria for abdominal obesity (waist circumference $\geq$90 cm in males and $\geq$80 cm in women) showed larger MS prevalence among Koreans than using the NCEP/ATP III waist cut-off [33]. Second, these variables are interrelated and the pathophysiology of the proposed clusters (lipids, body mass, insulin/glucose and blood pressure) is not clear. Third, the prevalence of each of the MS components may be different across race groups, as shown in our study, particularly among Amerindian and Black Venezuelans. Finally, if the MS is used to predict diabetes [12,39] or CV disease [15,16,40], neither the NCEP/ATP III nor the WHO definitions exclude subjects with diabetes or previous CV disease, therefore limiting the ability to identify subjects suitable for primary prevention with the strategies currently available [41,42]. Only the EGIR group restricts the definition to non-diabetic subjects [43]. If subjects with prior history of diabetes and/or CV disease were excluded, the age-adjusted prevalence of the MS in Zulia State would have been 25.7% (26.7% in women and 23.6% in men).

The age-adjusted prevalence of the MS in this Venezuelan population was higher in men (35%) than in women (29.8%). In a previous report in the U.S. population [21], there was little overall difference between men and women (24% versus 23.4%, respectively) while in a recent study in the Iranian population, higher rates were reported in women (42%) than in men (24%), mainly due to differences in the prevalence of abdominal obesity (10% in men versus 46% in women) [36]. In contrast, a report in a French population showed a higher prevalence of MS in men (23%) than in women (12%), with higher prevalence of dyslipidemia in men (30%) than in women (14%) [44]. In similar fashion, the difference in MS prevalence in our study may be related to dyslipidemia prevalence, which was higher in men (30.7%) than in women (21.4%).

Epidemiologic studies have shown that the prevalence and characteristics for this syndrome vary among different race/ethnic groups [21,33–36,45–47]. We found lower age-adjusted prevalence rates for the MS among Amerindian (17.1%) and Black (27.2%) Venezuelans. Similarly, reports in the U.S. have found lower rates in African Americans (16.4%) [21], but higher rates in Native Americans (31%) [12]. The lower MS prevalence in Amerindian men was surprising given the higher prevalence of dyslipidemia in these subjects (31.5%). However, the lower prevalence of abdominal obesity (15%) and elevated blood pressure (20%) among younger Amerindian men could partially explain the reported difference in MS prevalence. In fact, dyslipidemia and abdominal obesity was the only MS combination in those $<$40 years, while in those aged 40–60 dyslipidemia and high blood pressure were more frequent, and in those age 60 and above the cluster of dylipidemia, high blood pressure and elevated fasting blood glucose were more common.

The prevalence of the MS increased with age in both genders and all race groups. Other studies have found an age effect on the prevalence of the MS [21,34–36]. Most MS components had a similar age-related trend, with a two-fold increase in high triglyceride, near three-fold for abdominal obesity and high blood pressure, and a several-fold increment in high fasting blood glucose. In addition, age-related worsening in IR has been previously reported [2,48]. Age-related difference in the degree of clustering of risk variables has been shown in some [49], but not in all studies [36].

The single most common abnormality was low HDL-cholesterol. In this sample of Venezuelan adults, 65.3% had low HDL-cholesterol (67.5% in men and 59.9% in women), which is more than what had previously been reported from the U.S. [50], Canada

[51], Mexico [52], Turkey [53,54] and Iran [36]. Similar methodology to measure HDL-cholesterol (i.e., after precipitation of apo B-containing lipoproteins with phosphotungstic acid) has been used in these large population-based studies by Mahley et al. [54] and Aguilar-Salinas et al. [52]. Prior reports in Venezuelan subjects have shown low HDL-cholesterol levels in individuals at high risk for diabetes [26,29] using the same methodology, as well as using lipoproprotein ultracentrifugation in subjects at high risk for CV disease [55] and in obese and non-obese patients [56]. In addition, a study in adolescents from Zulia State has recently shown that low HDL-cholesterol is associated with low apolipoprotein A-1 levels [57].

Several factors including obesity, insulin resistance, smoking, lower physical activity or inherited genetic defects may be responsible for low HDL-cholesterol levels in this population. Studies have suggested that genetic polymorphisms in apolipoprotein E, hepatic lipase and cholesteryl ester transfer protein loci are associated with low HDL-cholesterol levels [58–61]. Differences in allele frequency and hepatic lipase activity have been reported across race groups [62]. Since HDL-cholesterol was much lower among Amerindian men (75.2%) and women (78.2%), studies are needed to evaluate the role of these polymorphisms in the development of dyslipidemia in this population.

Obesity is thought to be an important modulator of the metabolic syndrome [2]. Visceral adiposity has been proposed to lead to IR, which results in hypertension and other metabolic abnormalities in the same individual [63]. Nearly one-third of the population in Zulia State was overweight and an additional one-fourth was obese. In addition, abdominal obesity was more frequent in women (47.9%) than in men (31.4%), and in particular was higher among White and Black women.

In this study, the prevalence of elevated blood pressure was 38.1%, with an important age-related trend in both men and women. It has been reported that about half of the patients with hypertension have IR and hyperinsulinemia [64]. A significant correlation between blood pressure and fasting insulin has been reported in some [65–67], but not all studies [68]. High blood pressure was more frequent in the elderly, among men, in Black Venezuelans, and in those with family history of obesity and hypertension. Elevated fasting blood glucose was more frequent in men than in women and among Black and Amerindian men. Similarly, prediabetes was more common in men (19.6%) than in women (14.9%), but there were no gender differences in the prevalence of those in the diabetic range (7.5%). This rate is slightly higher that the estimated prevalence for Venezuela in 2000 (between 5.1% and 6.0%) [69]. As expected, those older than 45 years, with family history of diabetes and obesity, and with sedentary lifestyle were at higher risk for elevated fasting blood glucose. Therefore, prevention strategies should focus on these high-risk subjects, to reduce the risk of diabetes [41,42], and even prevent the development of the MS [9].

Some study limitations should be noted. First, this was a cross-sectional study; therefore, causal pathways underlying the reported relationships cannot be inferred. Second, the assessment of insulin resistance was estimated by the HOMA-IR method, which indirectly estimates the degree of insulin sensitivity, but is not as accurate as the euglycemic–hyperinsulinemic clamp. Third, sample size was smaller in Amerindians and Black Venezuelans, and this may have prevented us from properly assessing risk factors for MS and dyslipidemia in these race groups.

In summary, this first report of the metabolic syndrome in Venezuela shows a high prevalence of this disorder. Our findings indicate that approximately one in three patients meets ATP III metabolic syndrome criteria and harbors risk for CV disease and diabetes. Although for many obese patients the risk is already evident, our findings reveal abnormalities even in normal weight and overweight individuals. Since patients with this syndrome may develop diabetes and CV disease, with a burden on the country's healthcare system, efforts are needed to promote a healthy diet, increase physical activity, achieve weight reduction and reverse dyslipidemia and other metabolic abnormalities.

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