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## Prevalence of the metabolic syndrome, insulin resistance index, leptin and thyroid hormone levels in the general population of Mérida (Venezuela).

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**Key words:** epidemiology, cholesterol panel, International Diabetes Federation, Latin American Diabetes Association, Venezuelan criteria.

**Abstract.** The metabolic syndrome (MetSyn) is a significant risk factor for cardiovascular events, but scarce information exists about its frequency in Venezuela. In this cross-sectional study, we quantified the prevalence of the MetSyn in a probabilistic, stratified sample of 274 subjects aged  $\geq 18$  years from the Libertador district in Mérida, Venezuela. Secondary outcomes were the measurement of thyroid hormones (free  $T_4$  and TSH), leptin levels, and insulin resistance index (HOMA2-IR). The frequency of MetSyn (percentage  $\pm$  95% confidence interval) according to several diagnostic criteria was as follows: National Cholesterol Education Panel (NCEP, original): 27.4% (22.1-32.7); modified NCEP: 31.8% (26.3-37.3); International Diabetes Federation: 40.9% (35.1-46.7); Latin American Diabetes Association: 27% (21.7-32.3), and Venezuelan criteria: 31.8% (26.3-37.3). The MetSyn was more frequent in males than in females with most diagnostic criteria. The estimated prevalence of type 2 diabetes mellitus was 2.9% either according to the patients' self reports or to fasting glucose level found to be above 126 mg/dL. Abnormal HOMA2-IR index, free  $T_4$  and TSH (above the 95<sup>th</sup> percentile) were detected in 4.5%, 4.4% and 5.1% of the sample, respectively. Free  $T_4$  and TSH levels below the 5<sup>th</sup> percentile were detected in 4.4% and 4.7% of subjects respectively. These values are presented for comparisons with forthcoming studies in specific clinical populations. While studies are being conducted about the different definitions of the MetSyn in Venezuela, we recommend

analyzing and publishing local research data with all the available criteria so as to allow comparisons with the results already reported in the literature.

**Prevalencia del síndrome metabólico, índice de insulino resistencia y niveles de leptina y hormona tiroidea en la población general de Mérida (Venezuela).**

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**Palabras clave:** epidemiología, panel para el colesterol, Federación Internacional de Diabetes, Asociación Latino-Americana de Diabetes, criterios venezolanos.

**Resumen.** El síndrome metabólico (SM) es un factor de riesgo significativo en la ocurrencia de eventos cardiovasculares. Sin embargo, existe poca información sobre su frecuencia en Venezuela. En la presente investigación transversal, cuantificamos la prevalencia del SM en una muestra probabilística de 274 sujetos con edad mayor o igual a 18 años provenientes del municipio Libertador de la ciudad de Mérida, Venezuela. Como resultados secundarios, se cuantificaron los niveles de leptina, hormonas tiroideas ( $T_4$  libre y TSH), y el índice de resistencia a la insulina (HOMA2-RI). La frecuencia de SM (porcentaje  $\pm$  intervalo de confianza del 95%) de acuerdo a varios criterios diagnósticos fue la siguiente: Panel para el Colesterol (original): 27,4% (22,1-32,7); Panel para el Colesterol (modificado): 31,8% (26,3-37,3); Federación Internacional de Diabetes: 40,9% (35,1-46,7); Asociación Latino-Americana de Diabetes: 27% (21,7-32,3) y criterios Venezolanos: 31,8% (26,3-37,3). Al utilizar la mayoría de los criterios, el SM fue más frecuente en hombres que en mujeres. La prevalencia estimada de diabetes mellitus tipo 2 fue 2,9% tanto mediante el auto-reporte como mediante la detección de glicemia en ayunas  $> 126$  mg/dL. Se detectaron niveles anormales (por encima del percentil 95) del índice HOMA2-IR,  $T_4$  libre y TSH en el 4,5%, 4,4% y 5,1% de la muestra respectivamente. Niveles de  $T_4$  y TSH por debajo del percentil 5 se detectaron en el 4,4% y 4,7% de sujetos respectivamente. Los valores del HOMA2-RI y hormonas tiroideas también se presentan con el fin de permitir comparaciones con futuros estudios en poblaciones clínicas específicas. Mientras se realizan estudios adicionales en Venezuela sobre las diversas definiciones del SM, recomendamos analizar y publicar los resultados científicos locales con todos los criterios disponibles con el fin de permitir la comparación con los estudios que ya están disponibles.

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## INTRODUCTION

The metabolic syndrome (MetSyn) refers to the association of five factors (abdominal obesity, hypertension and abnor-

mal glucose, triglyceride and high density lipoprotein cholesterol [HDL-c] levels) associated with increased risk for the development of type 2 diabetes (Type 2 DM), heart disease and stroke (1). The MetSyn is a sig-

nificant predictive factor in relation to these diseases, even though the contribution of each of its constituting variables to elevated health risks is controversial (2, 3).

Some studies have evaluated the prevalence of MetSyn in the Venezuelan general population (GP) and in specific groups (4-12). In one early study conducted in Zulia state, Flórez *et al.* (4), reported an age-adjusted prevalence of MetSyn of 31.2% among 3.108 subjects aged 20 or over. In this study as in most of those conducted in Venezuela, the authors used the National Cholesterol Education Program (NCEP)/Adult Treatment Panel III (ATP III) (11) criteria to diagnose the MetSyn. These criteria have been criticized for using cut-off points too high in waist circumference (WC) and fasting glucose. In particular, the WC limits appeared inadequate for Hispanic populations. Therefore, new criteria for Latin-America, including Venezuela that lowered the cut-off points for WC and glucose levels have been formulated (13-17).

In the present study, we evaluated the prevalence of MetSyn and its constituting variables according to five diagnostic criteria (13-17) in a probabilistic sample of adults from the GP in Mérida, a university town up in the Venezuelan Andes. As secondary outcomes, in all the subjects we quantified the homeostatic model for the insulin resistance index (HOMA2-IR) (18, 19), and the serum levels of tetraiodothyroxine ( $T_4$ ), thyroid-stimulating hormone (TSH). We also assessed the serum leptin levels in a probabilistic subsample of the interviewed subjects. This secondary data aim to register normative data by including abnormal values located out of the 5-10<sup>th</sup> and 90-95<sup>th</sup> percentiles.

## SUBJECTS AND METHODS

This study was conducted in the main district of Mérida (Libertador Municipium)

and was approved by the Los Andes University Ethics Committee.

We used a multistage design to obtain a probabilistic sample out of a total of 204.879 subjects aged  $\geq 18$  years according to the 2001 Venezuelan National Census living at the Libertador municipality in Mérida city. The primary selection units were randomly selected segments of the Libertador borough, where individual houses were randomly selected as well.

Sample size was calculated according to a simple random model with a two-tailed 95% confidence interval, a sampling error of 5% and a 24% of estimated prevalence. A minimum sample size of 280 subjects was estimated and invited to enter the study.

For the assessment of leptin levels, we selected every fifth consecutive subject from a randomly organized list.

The basic sampling units were households that were randomly chosen in each selected district segment. In each basic unit, one subject out of all the adults that were present at the time of the visit was randomly selected. The inclusion criteria were: (1) the subjects had to be 18 or more years old and permanent residents in the area; and (2) they must have signed an informed consent for voluntary participation.

The selected subjects were assessed in a single session in fasting conditions where the following evaluations were conducted: a) anthropometric variables were measured in light clothes. Abdominal circumference was measured in an equidistant point to the lower ribcage border and the anterior-superior iliac spine, at the end of a normal expiration; b) blood pressure was calculated as the average of two measures in standing, sitting and horizontal positions in a calm environment; c) a cubital venous blood sample was taken and immediately processed for posterior serum analysis in a single assay, and d) a detailed interview for collecting personal, demographic and medical data.

### Analysis

Glucose and lipids levels were measured with an enzymatic method from Human (Berlin, Germany). Insulin and leptin levels were assessed in duplicate using enzyme-linked immunosorbent assay (DRG, Germany). Thyroid hormones were quantified in by chemiluminiscence (Siemens, Germany). All the analyses were conducted in a single assay, with *intra* essay variations  $\leq 10\%$ .

The body mass index (BMI) was calculated as follows: weight (kg)/height (m<sup>2</sup>). Obesity was defined as a BMI  $\geq 30$  kg/m<sup>2</sup>. The insulin resistance index (HOMA2-IR) was calculated with an online computer program (19).

The MetSyn was diagnosed according to the following criteria (Table I): 1) National Cholesterol Education Panel (NCEP, original and modified) (13, 15); 2) International Diabetes Federation (IDF, 14); 3) Latin-American Diabetes Association (ALAD, 16), and; 4) harmonized criteria of the Venezuelan Society of Endocrinology and Metabolism (17).

### Statistical analysis

The frequency of the MetSyn and its constituting variables was expressed as percentage and 95% confidence interval. Crude and age-adjusted frequencies according to the most recent Venezuelan census and based on the procedure used by Florez *et al.*

**TABLE I**  
DIAGNOSTIC CRITERIA FOR THE METABOLIC SYNDROME

Variable	ATP III-AHA-NHLBI* (a,b)	IDF	ALAD	Venezuelan Society of Endocrinology and Metabolism (c)
Waist circumference (cm)	Females > 88; males > 102 cm (>94 for Hispanics)	Females $\geq 80$ ; males $\geq 90$	Females $\geq 88$ ; males $\geq 94$	Females $\geq 88$ ; males $\geq 94$
Fasting glucose (mg/dL)	$\geq 110$ (a) o $100$ (b) or under specific treatment	$\geq 100$ or previously diagnosed type 2 diabetes	$\geq 100$ , glucose intolerance or type 2 diabetes	$\geq 100$ or under specific treatment
Triglycerides (mg/dL)	$\geq 150$ or under specific treatment	$\geq 150$ or under specific treatment	$\geq 150$ or under specific treatment	$\geq 150$ or under specific treatment
HDL-c (mg/dL)	<40 (males), <50 (females) or under specific treatment	<40 (males), <50 (females) or under specific treatment	<40 (males), <50 (females) or under specific treatment	<40 (males), <50 (females) or under specific treatment
Blood pressure (mm/Hg)	Systolic pressure $\geq 130$ and/or diastolic pressure > 85	Systolic pressure $\geq 130$ and/or diastolic pressure $\geq 85$ or under specific treatment	Systolic pressure $\geq 130$ and/or diastolic pressure $\geq 85$ or under specific treatment	Systolic pressure $\geq 135$ and/or diastolic pressure $\geq 85$ or under specific treatment
Diagnosis	Three out of five	Abdominal obesity + two out of the remaining four criteria	Abdominal obesity + two out of the remaining four criteria	Three out of five

\* = Adult Panel Treatment III. (a) Original criteria (13). (b) Modified criteria (15). IDF = International Diabetes Federation (14). ALAD = Asociación Latino-Americana de Diabetes (Latin-American Diabetes Association) (16). (c) from reference 17.

(4), are provided. The influence of the demographic features on the prevalence of the syndrome was investigated by binary logistic regression analysis. Age and race were analyzed with the two-tailed *t* test for unrelated samples and chi-squared test, respectively. Bivariate correlation was conducted with the Pearson “*r*” coefficient analysis. Results were considered significant when  $p \leq 0.05$ .

## RESULTS

The study was conducted between January and March of 2006 in 274 subjects (63.9% females), representing 99.3% of the calculated sample size ( $n = 280$ ). Four individuals did not attend the examination session, and two were not included in the final analysis due to incomplete anthropometric data. The present sample had a 10.5 % excess of female representation (the local census reported 53.4% of

women). This was due to a higher proportion of women present at home when the survey was conducted.

Age, race, personal history of hypertension, dyslipidemia and sedentary life were similar in females and males, but alcohol abuse and tobacco consumption were significantly more frequent in males (Table II).

### Metabolic syndrome

The age-adjusted and unadjusted frequency of the MetSyn diverged according to the diagnostic criteria, ranging from 40.9% to 27% in the unadjusted figures, as follows (Table III): IDF > NECP (modified) > Venezuelan criteria > NECP (original) > ALAD. Glucose levels, WC and systolic pressure were the MetSyn constituting variables showing the highest variability, whereas triglyceride, HDL-c and blood pressure levels showed small or no variability (Table III).

TABLE II  
UNWEIGHTED SOCIODEMOGRAPHIC CHARACTERISTICS

	Females (n = 175, 63.9%)	Males (n = 99, 36.1%)	Total (n = 274, 100%)
Age (mean $\pm$ S.D)	41.3 $\pm$ 15.3 (a)	44.1 $\pm$ 15.3	42.3 $\pm$ 15.3
Race [n (%)]			
White	86 (49.1) (b)	48 (48.5)	134 (48.9)
Admixed	6 (3.4)	9 (9.1)	15 (5.5)
Afro-American	44 (25.1)	23 (23.2)	67 (24.5)
Native (Indian)	39 (22.3)	19 (19.2)	58 (21.2)
Conditions [n (%)]			
Hypertension*	26 (14.9) (c)	16 (16.2)	42 (15.3)
Dyslipidemia*	33 (18.9) (d)	16 (16.2)	49 (17.9)
Alcohol abuse	21 (12) (e)	49 (49.5)	70 (25.5)
Tobacco use	32 (18.3) (f)	31 (31.3)	63 (23)
Sedentary life	89 (50.9) (g)	47 (47.5)	136 (49.6)

t (272) = 1.4,  $p = 0.15$ . (b)  $\chi^2$  (3) = 4.1,  $p = 0.25$ . (c)  $\chi^2$  (1) = 0.005,  $p = 0.9$ . (d)  $\chi^2$  (1) = 0.4,  $p = 0.5$ . (e)  $\chi^2$  (2) = 51.1,  $p = 0.000$ . (f)  $\chi^2$  (1) = 4.8,  $p = 0.02$ . (g)  $\chi^2$  (1) = 0.9,  $p = 0.4$ . \* = the subject reports abnormal values and/or specific pharmacological treatment.

**TABLE III**  
CRUDE (C) AND AGE-ADJUSTED (A) PREVALENCE OF THE METABOLIC SYNDROME  
AND ABNORMAL VALUES OF ITS CONSTITUTING VARIABLES

	International Diabetes Federation	Cholesterol panel (modified)	Venezuelan criteria	Cholesterol panel (original)	Latin American Diabetes Association
Metabolic syndrome					
C	40.9 (35.1-46.7)	32.5 (27.0-38.0)	31.8 (26.3-37.3)	27.4 (22.1-32.7)	27.0 (21.7-32.3)
A	34.4 (28.8-40.0)	26.9 (21.6-32.2)	26.4 (21.2-31.6)	22.4 (17.5-27.3)	23.7 (18.7-28.7)
Waist circumference					
C	65.7 (60.1-71.3)	41.2 (36.7-45.7)	41.2 (36.7-45.7)	30.3 (24.9-35.7)	41.2 (36.7-45.7)
A	60.2 (54.4-66.0)	37.7 (32.0-43.4)	37.7 (32.0-43.4)	27.5 (21.9-33.1)	37.7 (32.0-43.4)
Glycaemia					
C	9.1 (5.7-12.5)	9.1 (5.7-12.5)	9.1 (5.7-12.5)	5.8 (3.0-8.6)	9.1 (5.7-12.5)
A	7.5 (4.4-10.6)	7.5 (4.4-10.6)	7.5 (4.4-10.6)	4.9 (2.3-7.5)	7.5 (4.4-10.6)
HDL cholesterol					
C	84.7 (80.9-89.0)	84.7 (80.9-89.0)	84.7 (80.9-89.0)	84.7 (80.9-89.0)	84.7 (80.9-89.0)
A	84.2 (79.9-88.5)	84.2 (79.9-88.5)	84.2 (79.9-88.5)	84.2 (79.9-88.5)	84.2 (79.9-88.5)
Triglycerides					
C	38.7 (32.9-44.5)	39.8 (34.0-45.6)	39.8 (34.0-45.6)	39.8 (34.0-45.6)	38.7 (32.9-44.5)
A	35.7 (30.0-41.4)	36.4 (30.7-42.1)	36.4 (30.7-42.1)	36.4 (30.7-42.1)	35.7 (30.0-41.4)
Systolic pressure					
C	24.1 (19.0-29.2)	24.1 (19.0-29.2)	18.2 (13.6-22.8)	24.1 (19.0-29.2)	24.1 (19.0-29.2)
A	19.3 (14.6-24.0)	19.3 (14.6-24.0)	14.3 (10.2-18.4)	19.3 (14.6-24.0)	19.3 (14.6-24.0)
Diastolic pressure					
C	27.7 (22.4-33.0)	27.7 (22.4-33.0)	27.7 (22.4-33.0)	27.7 (22.4-33.0)	27.7 (22.4-33.0)
A	23.3 (18.3-28.3)	23.3 (18.3-28.3)	23.3 (18.3-28.3)	23.3 (18.3-28.3)	23.3 (18.3-28.3)
Systolic or diastolic pressure					
C	32.1 (22.6-37.6)	32.1 (22.6-37.6)	30.7 (25.2-36.2)	32.1 (22.6-37.6)	32.1 (22.6-37.6)
A	26.6 (21.4-31.8)	26.6 (21.4-31.8)	25.5 (20.3-30.7)	26.6 (21.4-31.8)	26.6 (21.4-31.8)

Values represent percentage and 95% confidence interval. C = crude prevalence; A = age-adjusted prevalence.

The percentage of subjects with abnormal values of the MetSyn constituting variables who were aware or under specific pharmacological treatment was: fasting glucose (0/24 = 0.0%); HDL-c (41/231 = 17.7%); triglycerides (21/105 = 20%); hypertension: 41/87 = 47.21%). In the whole sample, 2.9% reported being treated for type 2 diabetes mellitus or were found with fasting glucose levels above 126 mg/dL. This may be cautiously considered as an estimation of the prevalence of that disease.

#### **Influence of demographic variables**

The MetSyn frequency was higher in males than in females, but the figures did not reach statistical significance after adjusting for the other co-variables: IDF (45.5% vs. 38.3%), NECP modified (42.4% vs. 26.9%), Venezuelan criteria (40.4% vs. 25.1%), NECP original (29.3% vs. 26.3%), ALAD (34.3% vs. 22.9%) (Table IV). The frequency increased with age and BMI, and such a difference was statistically significant with almost all the diagnostic criteria (Table IV). For example, with the Venezue-

**TABLE IV**  
INFLUENCE OF DEMOGRAPHIC AND CLINICAL VARIABLES IN THE FREQUENCY OF METABOLIC SYNDROME

Variable	Diagnostic criteria	Wald (df)	P
Gender	IDF	0.7 (1)	0.9
	NECP (modified)	2.1 (1)	0.1
	Venezuelan criteria	2.4 (1)	0.12
	NECP (original)	0.2 (1)	0.7
	ALAD	0.9 (1)	0.4
Age	IDF	19.0 (5)	0.002
	NECP (modified)	14.7 (5)	0.001
	Venezuelan criteria	13.9 (5)	0.01
	NECP (original)	16.9 (5)	0.005
	ALAD	8.6 (5)	0.1
Ethnicity	IDF	1.6 (3)	0.7
	NECP (modified)	3.6 (3)	0.3
	Venezuelan criteria	4.2 (3)	0.2
	NECP (original)	2.8 (3)	0.4
	ALAD	3.4 (3)	0.3
Body mass index	IDF	35.7 (4)	0.000
	NECP (modified)	43.5 (4)	0.000
	Venezuelan criteria	44.7 (4)	0.000
	NECP (original)	46.9 (4)	0.000
	ALAD	36.0 (4)	0.000

The analysis was binary logistic regression analysis with MS (according to specific criteria) as Dependent variable, and sex, age, BMI and ethnicity as covariates.

lan criteria, the age-related figures were: 18-29 yrs. (21.2%), 30-39 yrs. (15.8%), 40-49 yrs. (34.6%), 50-59 yrs. (47.3%), 60-69 yrs. (59.1%), >70 yrs. (61.5%). As regards BMI, the MetSyn frequencies were: <20 (0.0%), 20-24.9 (6.6%), 25-29.9 (36.5%), 30-34.9 (63.5%),  $\geq 35$  (85.7%). As for race, no significant differences were observed with any criteria (Table IV).

#### Leptin levels, insulin resistance index (HOMA2-IR), and thyroid hormones

These data are presented as references for future comparative studies. Leptin levels were separately analyzed in females and males because the values are significantly higher in women even after correcting for BMI (20). The expected positive correlation between leptin levels and BMI was highly

significant (Table V). Since leptin levels were measured in a subset of the whole sample, the association between leptin and MetSyn was not explored.

When considering the HOMA2-IR and thyroid hormone levels, values above the 90 or 95<sup>th</sup> percentiles were considered as abnormal.

Abnormal values of the HOMA2-IR (>90<sup>th</sup> and 95<sup>th</sup> percentiles) were observed in 9.5% and 4.7% respectively of the total sample). The HOMA2-IR descriptive statistics are displayed in Table VI. The HOMA2-IR was significantly higher in subjects with MetSyn according to the ALAD criteria than those without it, even after controlling for BMI ( $1.2 \pm 0.07$  vs.  $0.9 \pm 0.04$ ,  $F(1, 272) = 10.3$ ,  $p = 0.001$ ).

**TABLE V**  
LEPTIN SERUM LEVELS (pg/mL)

Females (n = 32)					Males (n = 13)				
Mean ± S.D	Range	Correlation with BMI, Pearson coefficient (p)	Percentile		Mean ± S.D	Range	Correlation with BMI, Pearson coefficient (p)	Percentile	
			10	90				10	90
16.9 (8.1)	3.7-38.9	0.69 (0.000)	8.3	31.5	7.9 (5.6)	1-16	0.89 (0.000)	1.5	15.5

**TABLE VI**  
INSULIN RESISTANCE INDEX AND THYROID HORMONE LEVELS

Variable	Females (n = 175)				Males (n = 99)				Total (n = 274)			
	Mean ± S.D	Range	Percentile		Mean ± S.D	Range	Percentile		Mean ± S.D	Range	Percentile	
			10	90			10	90			10	90
Insulin resistance index (HOMA2-IR)	0.97 ± 0.63	0.35- 4.4	0.39	1.73	1.1 ± 0.60	0.33- 3.0	0.41	1.9	1.01 ± 0.62	0.33- 4.37	0.40	1.8
Tetraiodothyro xine (ng/dL)	1.10 ± 0.17	0.55- 2.19	0.92	1.29	1.14 ± 0.23	0.02- 1.85	0.92	1.47	1.11 ± 0.20	0.02- 2.19	0.92	1.34
Thyroid stimulating hormone mIU/mL	1.65 ± 0.69	0.05- 6.0	1.05	2.24	2.04 ± 3.87	0.54- 38.45	0.93	2.65	1.79 ± 2.39	0.05- 38.45	0.99	2.43

No subject had either a previous diagnosis of, or was under treatment for a thyroid disease. Abnormally low T<sub>4</sub> levels (below the 10<sup>th</sup> or 5<sup>th</sup> percentiles) were detected in 24 (8.8%) and 12 (4.4%) subjects of the whole sample respectively. Abnormally high T<sub>4</sub> levels (above the 90<sup>th</sup> or 95<sup>th</sup> percentiles) were detected in 26 (9.5%) and 12 (4.4%) subjects respectively. Abnormally low TSH levels (below the 10<sup>th</sup> or 5<sup>th</sup> percentiles) were detected in 24 (8.8%) and 13 (4.7%) subjects of the whole sample respectively. Abnormally high TSH levels (above the 90<sup>th</sup> or 95<sup>th</sup> percentiles) were detected in 27 (9.9%) and 14 (5.1%) subjects respectively.

When combining both data sets analyzed with the 5-95<sup>th</sup> percentile cut-off limits, hyperthyroidism was detected in ap-

proximately 4.4-4.7% of the population, whereas hypothyroidism was observed in approximately 4.4-5.1% of the sample. Seven out of fourteen subjects with high TSH levels (50% of the abnormal TSH group and 2.5% of the whole sample) had normal T<sub>4</sub> levels. Therefore, this value should be considered with caution as an estimation of subclinical hypothyroidism.

The frequency of MetSyn was similar in subjects with or without abnormal TSH levels: 25.9% vs. 27.1 %,  $\chi^2 (1) = 0.000$ ,  $p = 1.0$ .

### Correlation analysis

Several positive and negative correlations were observed among the anthropometric and biochemical variables (Table VII). This information is presented for comparative analysis in future studies.



TABLE VII  
CORRELATION ANALYSIS MATRIX

	Waist circumference	Glucose	Triglycerides	HDL-c	Systolic pressure	Diastolic pressure	HOMA-IR	Free T4	TSH
Waist circumfer.	-	0.22 (0.000)*	0.08 (0.2)	0.01 (0.9)	0.43 (0.000)*	0.52 (0.000)*	0.52 (0.000)*	-0.03 (0.7)	0.15 (0.01)*
Glucose	-	-	0.06 (0.3)	-0.07 (0.2)	0.21 (0.00)*	0.16 (0.001)*	0.43 (0.000)*	0.04 (0.5)	0.04 (0.5)
Triglycerides	-	-	-	0.38 (0.000)*	0.01 (0.8)	0.002 (0.9)	0.093 (0.1)	0.001 (0.9)	-0.01 (0.8)
HDL-c	-	-	-	-	0.006 (0.9)	0.02 (0.7)	-0.05 (0.4)	0.09 (0.1)	-0.11 (0.7)
Systolic pressure	-	-	-	-	-	0.79 (0.000)*	0.34 (0.000)*	0.000 (0.99)	0.09 (0.1)
Diastolic pressure	-	-	-	-	-	-	0.29 (0.000)*	0.03 (0.6)	0.11 (0.08)
HOMA-IR	-	-	-	-	-	-	-	-0.03 (0.6)	0.14 (0.02)*
Free T4	-	-	-	-	-	-	-	-	-0.5 (0.000)*
TSH	-	-	-	-	-	-	-	-	-

Values represent Pearson coefficient and associated probability. (\*) statistically significant,  $p < 0.05$ .  $n = 274$  for all analysis.

## DISCUSSION

This study described the frequency of MetSyn and related variables according to several diagnostic criteria in Merida city. On the one hand, it will allow comparisons with studies conducted in other countries and in Venezuelan cities with different ethnic and nutritional features. On the other hand, the results presented in this GP sample will be compared with those obtained in a set of studies conducted in specific clinical populations in this city, particularly in drug-treated subjects with psychiatric and/or neurological disorders.

The study has the limitation of a higher proportion of females than that reported in the local census (63.9% vs. 53.4%). Besides, the blood pressure quantification included standing and lying down measures in addition to the sitting position, the formers not being included in previous

studies. And lastly, the sample was not adjusted by race and socioeconomic status. These features hinder the strict comparison of this data with previous studies.

The MetSyn is a pathological condition affecting almost one third of the general population in Latin America (11). By including anthropometric, blood pressure, lipid and carbohydrate variables in its definition and given its predictive value for cardiovascular and metabolic disorders, the MetSyn is the focus of numerous preventive and therapeutic strategies.

We report here that the frequency of MetSyn varies considerably according to the definition adopted. For example, in the present study, the top value (IDF, 34.4%) was almost one third higher than those reported at the bottom ranges (NCEP original [22.4%] and ALAD [23.7%]). These disparities are mainly due to the different cut-off points adopted for abdominal obesity (WC):

in the IDF criteria, the cut-off points are 8 (in women) and 4 cm (in men), i.e. lower than those required by the ALAD criteria. The waist cut-off point for the original NECP is 12 cm higher than the one used in the IDF model. The differences in the other MetSyn constituting variables among the diagnostic criteria are less conspicuous.

The age-adjusted prevalence of MetSyn in our study according to the NECP original criteria was 22.4 % (17.5-27.3). This figure is lower than those reported by Flórez *et al.*, (4) in a probabilistic sample of 3108 subjects from the GP in the Venezuelan state of Zulia (31.2%, 95% CI = 29.6–32.9), by Ruiz-Fernandez *et al.* in a non-probabilistic sample of 100 subjects in Valencia, capital of the Venezuelan Carabobo state (57%) (7), by Becerra-Leal *et al.*, in a probabilistic sample of 109 ethnically mixed subjects in rural Mucuchies (Mérida state) (38%) (9), and by Escobedo *et al.*, in 1836 subjects in Barquisimeto city (Lara state) (26%) in the CARMELA study (8).

The age-adjusted frequency of abnormal values of the following variables of the MetSyn was higher in the Zulia state (4) than in Mérida: WC (42.9% vs. 27.5%), glycaemia (10.9% vs. 4.9%) and blood pressure (38.1% vs. 26.6%), whereas triglycerides (32.3% vs. 36.4%) and HDL-c levels (65.3% vs. 84.2%) were higher in our sample.

Like Flórez *et al.* (4), we found that the MetSyn was more frequent in males, but sex differences did not reach statistical significance after covariate analysis. In fact, the difference reached its lowest value in the analysis using the original NECP criteria (29.3% vs. 26.3%, see Results section).

Flórez *et al.*, (4) indeed reported that the frequencies of abnormal WC and HDL-C levels were significantly higher in women than in men, whereas an opposite pattern was reported for glucose, triglyceride and

blood pressure values. In our analysis with the original NCEP criteria and age and BMI as covariates in the logistic regression, the following figures were observed (females vs. males): triglycerides (38.9% vs. 41.1%,  $p = 0.9$ ), HDL-c (86.3% vs. 81.8%,  $p = 0.3$ ), blood pressure (26.9% vs. 41.4%,  $p = 0.06$ ), WC (35.4% vs. 21.2%,  $p = 0.000$ ) and glycaemia (2.3% vs. 12.1%,  $p = 0.005$ ).

The study of Becerra *et al.*, (9) reported a higher frequency of MetSyn than we did (38% and 43% according to the ATP-III and IDF criteria respectively) and a slightly higher frequency in females than in males is worth discussing, because it was conducted in the same state of this investigation. However, that study was carried out in a rural area, of a high altitude (more than 2,000 meters of difference between both villages) and with a higher proportion of ethnically mixed subjects (100% vs. 5.5% in our study). It is thus possible that these differences in methods explain the studies' discrepancies.

While it is not the objective of this study, it is worthwhile comparing the Venezuelan and the Latin-American criteria to enrich the discussion about which criteria should be adhered to in future comparative studies. The cut-off points for WC, glucose and HDL-c levels are similar in both lists, whereas the systolic pressure has a higher cut-off point ( $\geq 135$  vs.  $\geq 130$  mm/Hg), and the triglyceride definition includes 150 mg/dL in the Venezuelan criteria. An important difference between the two criteria is that the Latin-American criteria require abdominal obesity to be mandatory in order to diagnose MetSyn. Since the difference in the triglyceride criteria is negligible, and since the diastolic pressure criteria, in contrast to the systolic ones, are similar, it appears that it is the abdominal obesity requirement that better discriminates between both sets of criteria. Therefore, the Venezuelan criteria consider abdominal

obesity as having the same diagnostic weight as the lipid level, carbohydrate and blood pressure abnormalities, whereas the ALAD criteria propose a more prominent role for the WC status.

To clarify which set of criteria predicts the highest health risk is a major scientific and clinical issue. A robust finding is that the risk of type 2 diabetes and CVD significantly increases as more components of the MetSyn definitions are included, for example from 3 to 4 or more (21).

According to most MetSyn definitions, the relative risk for incident diabetes is higher than for cardiovascular diseases (CVD) (22). Impaired fasting glucose (IFG) is the strongest predictor for type 2 diabetes development; the other criteria components are similar or better than IFG to predict CVD (23).

An index of central obesity (WC/height) was tested in China as a substitute for the single WC assessment according to the NECP and IDF criteria, but its risk predictive value for CVD was not better than that of the standard WC criteria (24). Besides, empirically-derived MetSyn criteria were not better predictors of CVD than did the already existing definitions (25). These last authors concluded that "the existing metabolic syndrome definitions will be sufficient for use in clinical practice and research studies should the MetSyn debate conclude in a recommendation for its continued use" (25).

Several significant correlations were observed in the bivariate analysis of the MetSyn constituting variables. This reinforces the postulated physiological association among them and indirectly supports the conceptual validity of the syndrome.

As expected, the serum leptin levels were higher in women than in men and the well-known positive correlation between hormone levels and BMI (20) was observed in both genders.

The thyroid hormone and the HOMA-IR data presented here are expected to be used for future comparisons in ongoing studies. By combining the frequencies of abnormal TSH and T4 levels, we report an estimated prevalence of hypothyroidism of 4.4-4.7% (2.5% of the subclinical type) and hyperthyroidism of 4.4-5.1%. These values must be cautiously interpreted because they were based only on laboratory data and no clinical examination was conducted. Unfortunately, there are no other published data about thyroid dysfunction in the Venezuelan adult GP that would allow a comparison with the results reported here. The third National Health and Nutrition Examination Survey in the United States reported hypothyroidism in 4.6% of the sample (0.3% clinical and 4.3% subclinical) and hyperthyroidism in 1.3% (0.5% clinical and 0.7% subclinical) (26). We expect to compare our data with future studies conducted in Venezuela.

Finally, 2.9% of the subjects either reported type 2 diabetes mellitus or were found to have glucose levels similar or above 126 mg/dL. Hoffman *et al.*, (27) reported newly diagnosed type 2 diabetes in 6.5% of Hispanic subjects but only 46% of these subjects had fasting glucose levels  $\geq 126$  mg/dL. Hence, the values reported here may underestimate the actual prevalence of that disease.

This descriptive study corroborates that significant differences exist in the frequency of MetSyn and its constituting variables according to the diagnostic criteria selected. The Latin American Diabetes Association criteria give a prominent status to abdominal obesity, whereas the Harmonized Venezuelan criteria attribute the same weight to the five MetSyn variables. This may account for the differences observed between both criteria schedules. This is why the authors recommend analyzing the MetSyn frequency data with both (or more)

diagnostic criteria in the research about the construct validity of the MetSyn that is currently being conducted in Venezuela.

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