he Maracaibo city metabolic syndrome prevalence study: primary results and agreement level of 3 diagnostic criteria

Estudio de Prevalencia de Síndrome Metabólico: resultados preliminares y nivel de concordancia de 3 criterios diagnósticos

Valmore Bermúdez, MD, MPH, PhD¹*, Joselyn Rojas, MD, Msc¹, Juan Salazar, MD1, María José Calvo, Bsc¹, Jessenia Morillo, Bsc¹, Wheeler Torres, Bsc¹, Carmen Chávez, Bsc¹, Luis Olivar, Bsc¹, Milagros Rojas, Bsc¹, María Sofía Martínez, Bsc¹, Maricarmen Chacín, MD1, Roberto Añez, MD¹, Clímaco Cano-Ponce, PharmD¹ ¹Endocrine-Metabolic Research Center, "Dr. Félix Gómez," Faculty of Medicine, University of Zulia, Maracaibo 4004, Venezuela.

Abstract

Objetivo: El propósito de esta investigación fue determinar la prevalencia de Síndrome Metabólico (SM) y factores asociados en la población adulta del Municipio Maracaibo.

Materiales y métodos: Estudio descriptivo, transversal, con muestreo aleatorio multietápico, con 2.230 individuos de ambos sexos, mayores de 18 años de edad. Para el diagnóstico de SM se utilizaron los criterios propuestos por ATPIII-2005, IDF-2005 e IDF-2009, utilizando la prueba kappa de Cohen y la escala de valoración Landis y Koch para evaluar el nivel de concordancia entre las tres clasificaciones. Se construyeron 3 modelos de regresión logística para la evaluación de factores de riesgo relacionados a SM.

Resultados: La prevalencia de SM fue de 42,4%, 41,6% y 35,5% según IDF-2009, IDF-2005 y ATPIII-2005 respectivamente. El grado de concordancia entre IDF-2009 y ATPIII-2005: k=0.86 (p<0,00001); entre IDF-2005 y ATPIII-2005: k=0.84 (p<0,0001); y entre IDF-2005 e IDF-2009: k=0.98 (p<0,00001). Los componentes más prevalentes fueron obesidad abdominal con 75,1% (IDF-2005 e IDF-2009) y 48,9% (ATPIII-2005), HDL-C bajas (57,8%) e HTA (38.8%). En el análisis multivariante se observó que la edad, insulinorresistencia, IMC y PCR-us son factores de riesgo para padecer SM en las tres clasificaciones. HOMA b-cell y actividad física en tiempo de ocio son factores protectores.

Conclusión: La prevalencia de SM en nuestra población constituye una de las más elevadas a nivel mundial. Las clasificaciones utilizadas exhiben un nivel casi perfecto de concordancia debido a que 4 de los 5 componentes son iguales, por lo que las diferencias observadas radican en los puntos de corte de circunferencia abdominal.

Palabras clave: síndrome metabólico, criterios diagnósticos, inflamación crónica subaguda, insulinorresistencia, obesidad.

Objective: the purpose of this investigation was to determine the prevalence of Metabolic Syndrome (MS) and associated factors in the adult population of Maracaibo.

Materials and Methods: This is a descriptive, crosssectional study, with a randomized multietapic sampling method, which recruited 2,230 individuals from both genders, 18 years and older. To diagnose MS, 3 definitions were used: the IDF-2009, IDF-2005 and ATPIII-2005; level of agreement was calculated using the k Cohen function and the Landis and Koch assessment scale. Finally, three logistic regression models were constructed to evaluate risk factors associated with each MS definition.

Results: MS prevalence was 42.4%, 41.6% and 35.5% using IDF-2009, IDF-2005 and ATPIII-2005 respectively. Agreement level between IDF-2009 and ATPIII-2005 was k=0.86 (p<0,00001); between IDF-2005 and ATPIII-2005 was k=0.84 (p<0,0001); and between IDF-2005 and IDF-2009 was k=0.98 (p<0,000001). The most prevalent metabolic component was abdominal obesity with 75.1% using IDF-2005/IDF-2009 and 48.9% with ATPIII-2005, Low HDL-C with 57.8% and high blood pressure with 38.38%. Multivariate analysis showed that age, insulin resistance, BMI, and CRP-us are risk factors for MS; HOMA b-cell function and leisure time physical activity resulted to be a protective factors for MS.

Conclusions: MS in our population is one of the highest in the world. All 3 criteria showed a near-perfect agreement levels, probably due to the fact that 4 out of 5 components are identical; therefore the observed differences are due to differences in waist circumference cut-off points.

Key words: metabolic syndrome, diagnostic criteria, low grade inflammation, insulin resistance, obesity.

he clustering of dysglycemia, abdominal obesity, hypertriacylglyceridemia, Low HDL-C and high blood pressure has been recognized as Meta-

bolic Syndrome (MS)¹, a well-known risk factor for cardiovascular diseases (CVD)² and Type 2 Diabetes Mellitus (T2DM)³. Several diagnostic criteria have been proposed to identify subjects with MS, having evolved through the years in accordance to pathophysiological factors and epidemiological evidence⁴.

There are, however, three MS classifications that have endured the test of time and are still applied to investigate this clinical entity's prevalence and epidemiological behavior worldwide⁵. In chronological order, the International Diabetes Federation statement was published in September 2005 (IDF-2005)⁶, in order to easy the confusion that was observed between comparability studies using several SM criteria, especially concerning the difficult task to properly assess Insulin Resistance (IR) in large cross-sectional studies and the real influence of this phenomenon in cardiovascular risk. They proposed that abdominal obesity should be a prerequisite for the diagnosis of MS, and suggested the application of ethnic-specific cut-off points for waist circumference (WC); albeit, several regions in the world remain without proper reference values, such as Latin America. This lack of information is important, given the essential role of obesity on cardiovascular risk and clustering of other metabolic variables as agreed during the panel.

The Third Report of the National Education Program-Adult Treatment Panel (NCEP-ATPIII) was first published in 2002⁷ and its update in October 2005 (ATPIII-2005) by the American Heart Association (AHA) and the National Heart, Lung and Blood Institute (NHLBI)⁸. This expert panel didn't use any direct measure of IR, placed great interest in abdominal obesity, and reduced the threshold for impaired fasting glycemia (IFG) from 110 mg/dL to 100 mg/ dL. Moreover, it reinforced the notion that other satellite diseases may also predispose to IR and MS itself, such as polycystic ovary syndrome, non-alcoholic fatty liver, elevation of C-Reactive Protein (CRP) and microalbuminuria⁸.

Finally, the Harmonizing criteria were published in October 2009 by the International Diabetes Federation, NHLBI, AHA, World Heart Federation, International Atherosclerosis Society and International Association for the Study of Obesity (IDF-2009)⁹, in order to resolve the differences between IDF-2005 and ATPIII-2005, deciding denying to consider obesity as an obligatory prerequisite for MS diagnosis, but however, the issue of appropriate ethnic-specific WC cutoffs was reinforced, suggesting the necessity of more investigation in order to obtain regional cut-off values for WC. Regrettably, this matter is still a problem in many areas so that regions without local WC cutpoints were recommended to those from other continents. This statement also highlighted the importance of mixed ethnicity, its genetic influence over metabolic traits and cardiovascular risk, and that changes will have to be done in future diagnostic criteria in order to fill the need in such populations¹⁰.

The diagnostic efficacy of each set of criteria depends on the characteristics of the population applied to, and factors such as age, gender, ethnicity and end-point of prevention and intervention¹¹⁻¹⁹ can influence the veracity of the results. The city of Maracaibo is known for its high prevalence of obesity²⁰, physical inactivity²¹, and presence of biochemical markers of low grade inflammation^{22,23}, all metabolic variables which would be influential during MS diagnosis. Therefore, the purpose of this investigation was to evaluate prevalence of MS using the ATPIII-2005, IDF-2005 and IDF-2009 criteria, their agreement and factors associated with this diagnosis.

Subject Selection

<u>Materiales y métodos</u>

The cross-sectional research, The Maracaibo Metabolic Syndrome Prevalence Study (MMSPS)²⁴, was planned and executed in the city of Maracaibo, the second largest city of Venezuela with 2,500,000 inhabitants. The sampling method has been previously published, but the main aspects will be detailed²⁴. Using population estimations for the population of Maracaibo (1,428,043 for 2007 according to the National Institute of Statistics) the sample size estimate was calculated to be 1,986 individuals' ≥18 years of age. Considering that in a previous pilot study approximately 10% of the subjects didn't accomplish all the steps of the study (unpublished data), an oversampling number of 200 individuals was calculated. Between July 2008 and July 2011, a total of 2,230 subjects were recruited, with 244 added for oversampling purposes. The inclusion criterion was to be \geq 18 years of age; meanwhile, the exclusion criteria were pregnancy and any current acute illness that may alter biochemical parameters: recent surgery, viral hepatitis, acute pancreatitis and other acute infections.

The city of Maracaibo is divided into parishes 18: Antonio Borjas Romero, Bolívar, Cacique Mara, Caracciolo Parra Pérez, Cecilio Acosta, Cristo de Aranza, Coquivacoa, Chiquinquirá, Francisco Eugenio Bustamante, Idelfonso Vásquez, Juana de Ávila, Luis Hurtado Higuera, Manuel Dagnino, Olegario Villalobos, Raúl Leoni, Santa Lucía, San Isidro, and Venancio Pulgar. The sampling method was done using a 2-stage method²⁴. In the first phase, the sorting was random and stratified —where each stratus was represented by sectors from each of the 18 parishes— choosing 4 from each parish. The second sampling was stratified to represent a city block, selected using a random number generation tool. Once the houses were selected, every adult in the family unit from the selected city blocks was invited to participate in the study. Each individual signed a written consent prior to any interrogation, physical examination or laboratory workup. This study was approved by the Ethic Committee from the Endocrine and Metabolic Diseases Research Center at University of Zulia, Venezuela.

Anamnesis

A complete medical history was obtained with trained personnel. Important history details were gathered such as personal history of chronic diseases such as hypertension, T2DM, and ischemic heart disease. Ethnicity was divided in Hispanic Whites, Amerindians, Afro-Venezuelans, Mixed Race (any individuals with 2 or more genetic lineages²⁵) or Others (Arabic and/or Asian). The Graffar Scale modified by Mendez-Castellano²⁶ was applied to assess socioeconomic class. Academic status was evaluated in the following manner: a) Illiterate, those who do not posses any skills in reading and writing; b) Primary Education, those who only achieved primary school education; c) Secondary Education, those who had obtained a high school degree; and d) Higher Education, those who had attained technical or university/college degrees. Occupational Status was classified into 'Currently Employed' and 'Unemployed'. Alcohol intake was evaluated by estimating the amount of milliliters (mL) of ingested alcohol based on the type of drink (beer, spirit drinks and wine)27. Then, daily grams of alcohol consumed were calculated using the formula [daily consumed mL x Degree of Alcohol x 0.8/100]²⁸. Alcohol consumption ('Drinker') was defined as an ingestion of more than 1gr per day of any type of alcoholic drink²⁹. Smoking pattern was defined as follows³⁰: a) 'Non-Smokers', those who have never smoked, or have consumed less than 100 cigarettes in their life; b) 'Current Smokers', those who have smoked ≥100 cigarettes in their life or whom have stopped the habit less than 1 year of this interrogation; and c) 'Former Smokers', those who have smoked ≥100 cigarettes in their life yet stooped the habit over a year ago.

Physical activity

Physical activity (PA) was evaluated using the International Physical Activity Questionnaire³¹, which categorized it in four domains, Transportation, Occupation, Household and Leisure Time; being the latter the domain used in this data analysis. Once the data was obtained in the leisure sphere, it was divided in two groups: individuals with MET's=0 (Inactive) and those with METs >0. Afterwards, this last group was divided into quintiles, obtaining the following classification: a) Q1 or very low PA, with Male: <296,999 METs and Female <230,999 METs; b) Q2 or Low PA, with Male 297,000-791,999 METs and Female 231,000-445,499 METs; c) Q3 or Moderate PA, with Male 792,000-1532,399 METs and Female 445,500-742,499 METs; d) Q4 or High PA, with Male 1532,400-2879,999

METs and Female 742,500-1798,499 METs; and e) Q5 or Very High PA, with Male >2879,000 METs and Female 1798,500 METs.

Blood Pressure

After 15 minutes rest, with the subject in a sitting position with both feet touching the floor and arm resting at heart level, blood pressure was taken using a calibrated mercury sphygmomanometer with a proper sized cuff. Systolic blood pressure was determined when the first Korotkoff sound is heard, while diastolic blood pressure was determined at the fifth Korotkoff sound. Pressure measurement was taken 3 times, with at least 15 minutes in between takes.

Anthropometry

Waist circumference was measured using calibrated nonelastic measuring tape in accordance to the anatomical landmarks proposed by the USA National Institutes of Health protocol³²: with subjects standing in their undergarments, an imaginary mark was delimited midpoint between the lower border of the rib cage and the iliac crest, taking the length at the end of expiration. Weight was assessed using a digital scale (Tanita, TBF-310 GS Body Composition Analyzer, Tokyo – Japan), while Height was obtained with a calibrated rod in millimeters and centimeters; the patients were shoeless and wearing light clothing at all times. Body Mass Index was calculated using the formula [Weight/Height², expressed in kg/m²]³³.

Laboratory Analysis

After 8-12 hours of fasting, serum levels of total cholesterol, triacylglycerides (TAG), HDL-C and basal glycemia were determined using computerized equipment (Human Gesellschoft Biochemica and Diagnostica MBH, Magdeburg, Germany). Fasting insulin was quantified using a commercial ultrasensitive ELISA-based kit (DRG international. Inc. USA. New Jersey), with a detention limit of <1mU/L. HOMA2-IR and HOMA2-bcell models were calculated using the HOMA Calculator available at http://www. dtu.ox.ac.uk/homacalculator/; HOMA2-IR cut-off point was set at ≥ 2 as previously evaluated in our population (unpublished data). HOMA b-cell was distributed in tertiles as follows: Tertil 1: <117.90; Tertil 2: 117.90-162.06; and Tercil 3: \geq 162.07). Likewise, Lipoprotein(a) [Lp(a)] concentration was determined using the turbidimetric latex method (Human Gesellschoft Biochemica and Diagnostica MBH, Magdeburg, Germany); the threshold for Lp(a) was ≥30 mg/dL³⁴. High sensivity C-Reactive Protein (hs-CRP) was determined employing turbidmetric immune essays (Human Gesellschoft Biochemica and Diagnostica MBH, Magdeburg, Germany); elevated serum levels was set at 75th percentile in our population (0.765 mg/L)²². Finally, the plasma concentration of TSH, FT, and FT, was determined using the DRG International Inc. USA kit; Subclinical Hypothyroidism diagnosis was made according to NHANES criteria³⁵: normal levels of FT₄ (0.9-1.9 ng/

dL) with elevated TSH (\geq 4.12 mUI/L) and absence of prior personal history of thyroid disease.

Metabolic Syndrome Definitions

The MS criteria used in this study were:

- IDF-2009 definition required 3 of the following 5 variables⁹: a) Elevated WC (Men ≥90 cm and Women ≥80 cm); b) Hypertriacylglyceridemia ≥150 mg/dL or specific treatment for this abnormality; c) Low HDL-C, Men <40 mg/dL, Women <50 mg/dL or specific treatment for this abnormality; d) Elevated Blood Pressure, Systolic ≥130 mmHg, Diastolic ≥85 mmHg, or previous diagnosis of hypertension; e) Elevated Fasting Glucose, Glycemia ≥100 mg/dL or drug treatment for hyperglycemia.
- The IDF-2005 stated the following⁶: mandatory Elevated WC (Men ≥90 cm and Women ≥80 cm) plus any two of the following: a) Hypertriacylglyceridemia ≥150 mg/dL or specific treatment for this abnormality; b) Low HDL-C, Men <40 mg/dL and Women <50 mg/dL or specific treatment for this abnormality; c) Elevated Blood Pressure, Systolic ≥130 mmHg, Diastolic ≥85 mmHg, or previous diagnosis of hypertension; d) Elevated Fasting Glucose, with Impaired Fasting Glycemia ≥100 mg/dL or previous diagnosis of T2DM.
- 3. The ATPIII-2005 definition required 3 of the following 5 components⁸: a) Elevated WC (Men ≥102 cm and Women ≥88 cm); b) Hypertriacylglyceridemia ≥150 mg/dL or specific treatment for this abnormality; c) Low HDL-C, Men <40 mg/dL, Women <50 mg/dL or specific treatment for this abnormality; d) Elevated Blood Pressure, Systolic ≥130 mmHg, Diastolic ≥85 mmHg, or previous diagnosis of hypertension; e) Elevated Fasting Glucose: Glycemia ≥100 mg/dL or drug treatment for hyperglycemia.</p>

Statistical Analysis

Initially, the quantitative variables distribution was evaluated using the Geary test and those with not normal distribution were submitted to logarithmic transformation. The quantitative variables were expressed as arithmetic means ± standard deviation (SD), except CRP-us which was expressed as median and p25-p75. t-Student test and one way ANOVA with Tukey's post-hoc analysis were employed in order to assess differences between arithmetic means. For medians comparisons the Mann-Whitney's U test was employed. Qualitative variables were expressed in absolute and relative frequencies and their association was evaluated with the ² (Chi square) test and difference of proportions with the Z Test. The degree of concordance between SM classifications was determined employing both, the Cohen's Kappa coefficient and the Landis-Koch's assessment scale^{36,37}. This scale covey a classification for kappa agreement results: a) <0,00: no agreement; >0,00-0,20: insignificant; 0,21-0,40: discreet; >0,41-0,60: moderate; 0,61-0,80: substantial; 0,81-1,00: near perfect. Two logistic regression models were made in order to estimate the Odds Ratio (IC95%) for MS according to each diagnostic classification. The first SM model (MS according to the IDF-2009) was adjusted for: sex, age group, ethnic groups, educational status, socioeconomic status, family history of diabetes mellitus, alcohol consumption, smoking habit, physical activity in the leisure sphere according to IPAQ, presence of IR, BMI categories and HOMA β -cell tertiles; a second adjustment was made including the previous variables (model 1) plus the presence of elevated CRP. In the second and third model (SM according to IDF-2005 and SM according to ATPIII-2005 respectively); the variable adjustment was similar to the first one. The data were analyzed employing the Statistical Package for Social Sciences (SPSS) for Windows (SPSS IBM Chicago, IL). The results were considered statistically significant if p<0,05.

Resultados

General characteristics of the population

Overall, there were 2,230 individuals, 47.4% (n=1,058) were men and 52.6% (n=1,172) were women, with an arithmetic mean age of 39.3 ± 15.4 years. The metabolic and anthropometric characteristics of the population are depicted in Table 1.

Prevalence of Metabolic Syndrome

The overall prevalence of MS was 42.4% (n=946) according to the IDF-2009, 41.6% (n=927) using the IDF-2005 and finally, 35.5% (n=791) when applying the ATPIII-2005 criteria (Figure 1). When distributing the individuals according to gender and IDF-2009 consensus, there was a higher prevalence of MS in men, with 44.6% of the men and 40.4% of women (c2=3,956, p=0,047; Z Test <0,05). Such pattern was observed when using the IDF-2005 but with no significant difference between genders ($\chi^2 = 3,02$ p=0,082; Z Test >0,05). Contrary, there were more women diagnosed with MS when applying the ATPIII-2005 criteria, albeit no differences were observed ($\chi^2 = 0.85$ p=0,358; Z Test >0,05). Likewise, there was an increase in MS diagnosis as age progressed (Figure 2), observing that the majority of the patients were seen at 40 years and beyond. Finally, Figure 3 shows the distribution of the subjects according to the MS consensus used and the level of agreement between them. When considering the ATPIII-2005 and IDF-2009 consensus, the level of agreement is k=0.86 (p<0,00001). Meanwhile, when evaluating ATPIII-2005 and IDF-2005, the level of agreement was k=0.84 (p<0,0001). Lastly, the level of agreement between IDF-2005 and IDF-2009 was k=0.98 (p<0,000001).

Metabolic Syndrome components

When evaluating each component of the syndrome individually, it was observed that abdominal obesity was the most prevalent with 75.1% (n=1,675) according to IDF-2009/IDF-2009, while it was 48.9% (n=1,091) when using the ATPIII-2005 WC cutpoints. When stratified by gen-

der, women were mostly found to have obesity compared to men, during application of IDF-2005/IDF-2009 (79,0% vs. 70,8% respectively; $c^2=20,080$, p<0,001) as well as ATPIII-2005 (57,8% vs. 39,0% respectively; $c^2=78,764$ p<0,001) cutoff points. The second most prevalence component was Low HDL-C levels, with 57.8% (n=1,288), and as elevated WC, it was more prevalent in women than in men (64,2% vs. 50,7%; $c^2=41,549$ p<0,001).

Metabolic Syndrome and Sociodemographic variables

For this investigation, the Sociodemographic variables analyzed were ethnicity, socioeconomic status, educational status and working condition according to each MS consensus (Table 2). The only variable with a significant association was Educational status, with χ^2 =86,465; p<0.001 for the IDF-2009, χ^2 =82.583; p<0.001 for IDF-2005, and χ^2 = 93,334; p<0.001 for ATPIII-2005.

Metabolic Syndrome and Psychobiological variables The psychobiological variables, alcohol, smoking and leisure time physical activity and their association with MS criteria are depicted in Table 3. Former and current smokers had higher prevalence of MS, and this habit was found to be associated with all three MS definitions, with χ^2 =35,804; p<0.001 for the IDF-2009, χ^2 =36,066; p<0.001 for IDF-2005, and χ^2 =34,663; p<0.001 for AT-PIII-2005. This pattern was also observed in inactivity or low leisure time physical activity individuals, where lack of this type of physical activity was associated with all the MS criteria, where IDF-2009 rendered χ^2 =51,754; p<0.001, IDF-2005 χ^2 =91,065; p<0.001, and ATPIII-2005 χ^2 =58,947; p<0.001. Alcohol doesn't seem to be associated with any MS definition.

Metabolic Syndrome and other metabolic disturbances

When analyzing MS and markers of Low grade inflammation such as CRP-us and Lp(a), both particles were associated with all three MS consensuses, where Lp(a) obtained IDF-2009 χ^2 =26,766; p<0.001, IDF-2005 χ^2 =26,968; p<0.001, and ATPIII-2005 χ^2 =20,594; p<0.001; while CRP-us rendered IDF-2009 x²=78,313; p<0.001, IDF-2005 x²=70,597; p<0.001, and ATPIII-2005 x²=84,541; p<0.001. Moreover, insulin resistance was highly associated with MS diagnosis with every definition used, with IDF-2009 χ^2 =160,97; p<0.001, IDF-2005 χ^2 =198,339; p<0.001, and ATPIII-2005 χ^2 =198,339; p<0.001. Likewise, HOMA b-cell function was also associated with MS, with IDF-2009 χ^2 =26,63; p<0.001, IDF-2005 χ^2 =21,90; p<0.001, and ATPIII-2005 χ^2 =24,14; p<0.001. Interestingly, Subclinical Hypothyroidism was found to be associated with the 3 definitions, where the following results were obtained: IDF-2009 x²=4,485; p=0.028, IDF-2005 χ^2 =5,536; p=0.019, and ATPIII-2005 χ^2 =7,416; p=0.006. Just as expected, T2DM and obesity measured by BMI were also associated with the 3 MS criteria; see Table 3.

Risk factors for each Metabolic Syndrome classification

When analyzing MS definitions and associated risk factors, the models were analyzed according to each classification. Table 4 shows IDF-2009 and associated factors, where male gender (OR: 1.67; IC95% 1.24-2.35, p<0.01), 60-69 year age group (OR: 21.15; IC95% 8.09-55.27, p<0.01), obesity (according to WHO) (OR: 7.65; IC95% 4.87-12.01, p<0.01) and insulin resistance (OR: 3.29; IC95% 2.25-4.83, p<0.01) were associated with higher risk for MS with this criteria; whereas, the highest HOMA b-cell tertile was assocviated with lower risk for MS (OR: 0.47; IC95% 0.29-0.76, p<0.01). When using the IDF-2005 criteria, the same variables retained a similar pattern (Table 5), with higher risk offered by 60-69 year age group and elevated BMI with OR: 8.71; IC95% 5.53-13.73, p<0.01. Lastly, when evaluating ATPIII-2005 (Table 6), 3 important findings can be highlighted: a) First, male gender no longer conferred risk for MS; b) Very high physical activity in leisure time is a protective factor (OR: 0.46; IC95% 0.25-0.86, p<0.02); and c) BMI resulted in a higher risk for MS with OR: 17.05; IC95% 9.99-29.08, p<0.01.

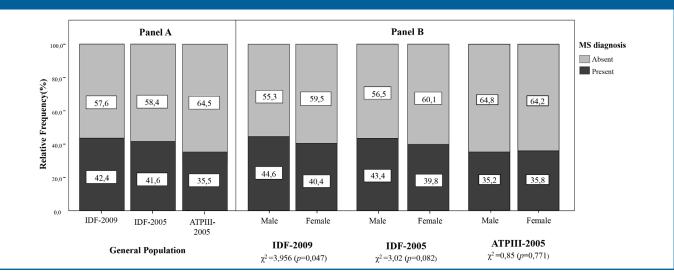


Figure 1. Prevalence of Metabolic Syndrome in the general population according to gender and 3 Metabolic Syndrome Diagnostic criteria. Maracaibo, 2012

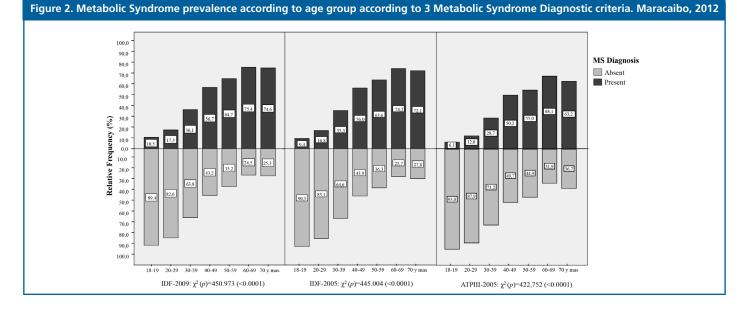
	IDF-:	2009		IDF	-2005		A	TPIII-2005	
	MS Absent (n=1284, 57,6%)	MS Present (n=946, 42,2%)		MS Absent (n=1303, 58,4%)	MS Present (n=927, 41,6%)		MS Absent (n=1439,64,5%)	MS Present (n=791,35,5%)	p*
	Mean±SD	Mean±SD	p *	Mean±SD	Mean±SD	p *	Mean±SD	Mean±SD	
Age (years)	33,4±13,6	47,3±13,9	9,63x10 ⁻¹²	33,5±13,7	47,4±13,8	6,98x10 ⁻¹²	34,45±14,23	48,19±13,28	1,53x10 ⁻¹
BMI (kg/m²)	26,1±5,3	31,2±6,13	2,93x10 ⁻⁸³	26,1±5,3	31,4±6,0	1,19x10 ⁻⁵⁸	26,19±5,18	32,21±6,15	3,17x10 ⁻¹
Waist circumference (cm)	88,4±13,0	102,9±14,1	7,05x10 ⁻¹³	88,3±13,0	103,3±13,9	2,04x10 ⁻¹⁴	88,71±12,57	105,24±14,09	7,48x10 ⁻
Fasting glycemia (mg/dL)	89,7±16,0	110,7±42,2	3,74x10 ⁻⁶⁴	90,4±19,1	110,1±41,1	3,63x10 ⁻³⁵	90,17±15,97	113,98±45,05	1,00x10-
Fasting insulin (µU/mI)	12,6±7,8	17,4±10,8	7,52x10 ⁻³⁴	12,6±7,9	17,5±10,8	2,33x10 ⁻³	12,77±8,10	18,15±10,96	2,15x10-
HOMA 2-IR	1,84±1,10	2,70±1,63	1,86x10 ⁻⁴⁵	1,85±1,11	2,70±1,64	5,89x10 ⁻⁴⁶	1,86±1,12	2,82±1,67	2,26x10-
HOMA β-cell	146,7±59,2	140,0±72,2	1,51x10 ⁻⁶	145,9±59,4	141,0±72,3	8,16x10⁻⁵	146,91±62,32	138,53±69,79	5,08x10 ⁻⁰
Total Cholesterol (mg/dL)	179,8±40,3	205,4±48,8	7,10x10 ⁻⁴¹	180,5±40,9	204,9±48,6	3,32x10 ⁻³⁷	181,94±41,62	206,67±49,00	7,51x10 ⁻⁰
Non-HDL-C cholesterol (mg/dL)	131,6±39,1	166,9±47,7	1,30x10 ⁻⁷⁰	132,5±39,9	166,4±47,5	8,69x10 ⁻⁶⁵	134,78±40,95	168,19±47,86	1,53x10 ⁻⁰
Triacylglycerides (mg/dL)	88,2±46,9	186,9±126,5	1,28x10 ⁻¹⁸	89,8±49,2	186,7±127,3	2,64x10 ⁻¹⁷	94,86±54,56	194,16±132,92	7,45x10
HDL-C Male (mg/dL)	45,1±11,8	35,7±8,3	1,81x10 ⁻⁵¹	44,9±11,8	35,7±8,3	1,14x10 ⁻⁴⁹	43,91±11,80	35,50±8,26	6,87x10-
HDL-C Female (mg/dL)	50,7±12,1	41,2±8,7	8,28x10 ⁻⁴⁶	50,66±12,19	41,20±8,75	1,8x10 ⁻⁴⁶	50,11±12,12	41,09±8,89	8,44x10 ⁻⁰
LDL-C (mg/dL)	113,8±36,0	130,6±39,4	4,77x10 ⁻²⁰	114,4±36,5	130,1±39,1	5,96x10 ⁻¹⁸	115,42±36,82	131,02±39,29	3,35x10-
VLDL (mg/dL)	17,6±9,4	37,3±25,1	4,88x10 ⁻⁹⁵	17,9±9,8	37,7±25,3	3,50x10 ⁻⁸⁹	18,92±10,90	38,85±26,42	6,95x10-
Lp(a) (mg/dL)	27,0±13,6	29,8±14,0	<0.0001	27,0±13,6	29,8±13,9	<0.0001	27,27±13,76	29,97±13,84	<0.0001
SBP (mmHg)	113,5±13,7	127,9±17,0	5,06x10 ⁻⁹⁶	113,7±13,8	127,9±17,1	3,86x10 ⁻⁹²	114,33±14,09	129,36±17,01	1,47x10-
DBP (mmHg)	73,3±9,5	82,5±11,2	7,84x10 ⁻⁸⁸	73,4±9,6	82,5±11,2	1,04s10 ⁻⁸⁵	73,86±9,74	83,43±11,18	1,37x10-
hs-CRP-us total (mg/L) [¶]	0,3(0,08-0,5)	0,4 (0,1-1,0)	3,84x10 ⁻¹⁶	0,3(0,08-0,6)	0,4(0,1-1,0)	4,75x10 ⁻¹⁵	0,3(0,08-0,61)	0,5(0,21-1,16)	6,36x10-
CRP-us Male (mg/L [¶]	0,3(0,08-0,575)	0,4(0,18-0,95)	6,67x10⁻ଃ	0,3(0,08-0,576)	0,4(0,18-0,94)	4,72x10 ⁻⁷	0,3(0,08-0,57)	0,5(0,28-1,01)	3,71x10 ^{-₀}

IDF-2009: IDF/AHA/NHLBI/WHF/IAS/IASO-2009; IDF-2005: International Diabetes Federation-2005; ATPIII-2005: Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults.

BMI: Body Mass Index; hs.-CRP: high sensivity C-Reactive Protein; DBP: Diastolic blood pressure; SBP, Systolic blood pressure.

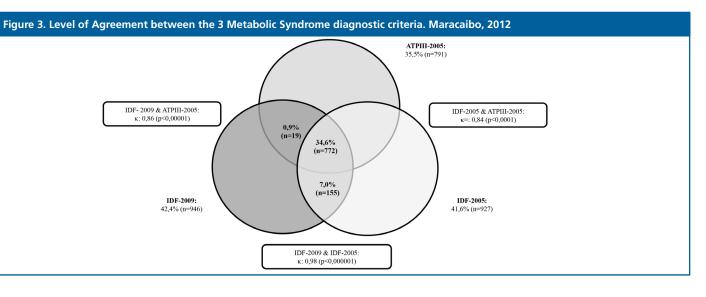
* t Student Test

[¶]Expressed in Median (p25-p75), comparison calculated with U Mann-Whitney test.



		IDF	-2009				IDF-2	2005				ATPIII	-2005		
	Ab	sent	Pre	sent		Absent Pres		sent		Abs	ent	Preser			
	n	%	n	%	χ² (<i>p</i>)ຶ	n	%	n	%	χ² (p) ຶ	n	%	n	%	χ2 (p) [≈]
Ethnic grpup					2.006 (0,735)					2.720 (0,606)					3,319 (0,506)
Mixed Race	985	58,2	707	41,8		1000	59,1	692	40,9		1103	65,2	589	34,8	
Hispanic White	192	54,5	160	45,5		193	54,8	159	45,2		217	61,6	135	38,4	
Afro-Venezolan	36	54,5	30	45,5		37	56,1	29	43,9		39	59,1	27	40,9	
Amerindian	63	59,4	43	40,6		65	61,3	41	38,7		72	67,9	34	32,1	
Others	8	57,1	6	42,9		8	57,1	6	42,9		8	57,1	6	42,9	
Socioeconomic Status					5,662(0,226)					4,383(0,357)					4,074 (0,396)
Strata I: Upper Class	24	66,7	12	33,3		24	66,7	12	33,3		25	69,4	11	30,6	
Strata II: Upper-Middle Class	238	57,6	175	42,4		239	57,9	174	42,1		273	66,1	140	33,9	
Strata III: Middle Class	524	59,7	354	40,3		529	60,3	349	39,7		580	66,1	298	33,9	
Strata IV: Working Class	444	55,6	354	44,4		456	57,1	342	42,9		497	62,3	301	37,7	
Strata V: Extreme Poverty	54	51,4	51	48,6		55	52,4	50	47,6		64	61,0	41	39,0	
Educational Status					86,465(<0.001)					82.583(<0.001)					93,334 (<0.001)
Illiterate	22	42,3	30	57,7		23	44,2	29	55,8		29	55,8	23	44,2	
Primary Education	138	39,1	215	60,9		144	40,8	209	59,2		159	45,0	194	55,0	
Secondary Education	688	66,1	353	33,9		697	67,0	344	33,0		759	72,9	282	27,1	
Higher Education	436	55,6	348	44,4		439	56,0	345	44,0		492	62,8	292	37,2	
Working Status					0,458(0,496)					0,355(0,551)					0,70 (0,792)
Employed	739	57,0	558	43,0		751	57,9	546	42,1		834	64,3	463	35,7	
Unemployed	545	58,4	388	41,6		552	59,2	381	40,8		605	64,8	328	35,2	

[®]Chi-square Test.



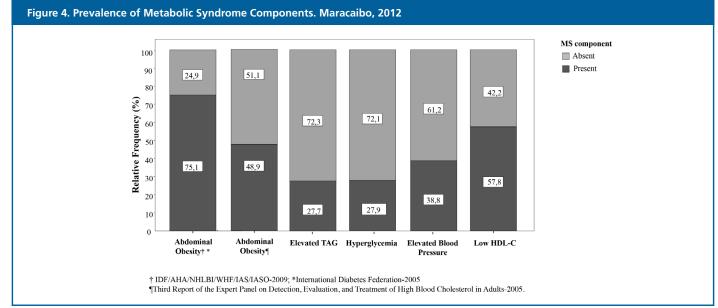


Table 3. Metabolic Syndro		- Tranc	ande u			l									
	С	Consenso 2009		09			IDF-	2005				ATPII	1-2005		
	Abs	sent	Pre	sent		Abs	sent	Pre	sent		Abs	sent	Pre	sent	
	n	%	n	%	χ2(p) [≈]	n	%	n	%	χ2 (p) [≈]	n	%	n	%	χ2 (p) [≈]
Alcohol consumptionΦ					0,418 (0,518)					0,131 (0,717)					0,105 (0,746)
Non-Drinker	904	58,0	654	42,0		913	58,6	645	41,4		1002	64,3	556	35,7	
Drinker	380	56,5	292	43,5		390	58,0	282	42,0		437	65,0	235	35,0	
Smoking					35,804 (<0,001)					36,066 (<0.001)					34,663 (<0,001
Non-smoker	953	61,7	591	38,3		965	62,5	579	37,5		1055	68,3	489	31,7	
Current smoker	169	51,5	159	48,5		175	53,4	153	46,6		197	60,1	131	39,9	
Former smoker	155	45,6	185	54,4		156	45,9	184	54,1		178	52,4	162	47,6	
Leisure time physical activity					51,754 (<0,001)					91,065 (<0.001)					58,947(<0.001
Inactive	721	53,2	634	46,8		735	54,2	620	45,8		812	59,9	543	40,1	
Very low	100	59,9	67	40,1		102	61,1	65	38,9		110	65,9	57	34,1	
Low	106	58,9	74	41,1		108	60,0	72	40,0		121	67,2	59	32,8	
Moderate	107	61,5	67	38,5		107	61,5	67	38,5		118	67,8	56	32,2	
High	100	59,9	67	40,1		100	59,9	67	40,1		114	68,3	53	31,7	
Very high	150	80,2	37	19,8		151	80,7	36	19,3		164	87,7	23	12,3	
Lipoprotein(a)					26,766 (<0.001)					26,962 (<0.001)					20,594 (<0.001
Normal	706	61,7	439	38,3		716	62,5	429	37,5		777	67,9	368	32,1	
High	344	49,4	353	50,6		350	50,2	347	49,8		400	57,4	297	42,6	
hs-CRP					78,313(<0.001)					70,597(<0.001)					84,541(<0.001
Normal	681	63,9	385	36,1		684	64,2	382	35,8		70,8	311	29,2	70,8	
High	132	37,1	224	62,9		138	38,8	218	61,2		43,8	200	56,2	43,8	
Insulin resistence [§]					160,97 (<0.001)					198,339(<0.001)					198,339 (<0.00 ⁻
Absent	761	70,3	322	29,7		848	78,3	235	21,7		848	78,3	235	21,7	
Present	399	42,3	544	57,7		455	48,3	488	51,7		455	48,3	488	51,7	
HOMA β-cell Tertiles					26,63 (<0.001)					21,90 (<0.001)					24,14 (<0.001)
<117.90	377	32,5	358	41,3		390	33,1	345	40,6		430	33,0	305	42,2	
117.90-162.06	427	36,8	231	26,7		429	36,4	229	27,0		468	35,9	190	26,3	
≥162.07	356	30,7	277	32,0		358	30,4	275	32,4		405	31,1	228	31,5	
BMI (kg/m²) [¶]					370,713(<0.001)					396,625 (<0.001)					482,977 (<0.007
≤ 24.9	583	83,9	112	16,1		594	85,5	101	14,5		631	90,8	64	9,2	
25 – 29.9	448	57,0	338	43,0		456	58,0	330	42,0		539	68,6	247	31,4	
≥ 30	253	33,8	496	66,2		253	33,8	496	66,2		269	35,9	480	64,1	
T2DM					179,51 (<0.001)					170,63 (<0.001)					225,748 (<0.00
Absent	1263	61,8	780	38,2		1278	62,6	765	37,4		1412	69,1	630	30,9	
Present	21	11,2	166	88,8		25	13,4	162	86,6		27	14,4	161	85,6	
Subclinical Hypothyroidism					4,485 (0,028)					5,536 (0,019)					7,416 (0,006)
Euthyroid state	216	61,7	134	38,3		220	62,9	130	37,1		237	67,7	113	32,3	
Hypothyroid state	18	43,9	23	56,1		18	43,9	23	56,1		19	46,3	22	53,7	

^eDrinker > 1gr/day; [§]HOMA2-IR >2.00; [¶]According to WHO. [#]Chi-square test

Table 4. Risk factors asso	ciated with Metabolic Syndro	ome accord	ling to IDF/AHA/NHLBI/WHF/	'IAS/IASO-	2009. Maracaibo 2012.					
		Model 1*								
	Crude Odds Ratio (IC 95%ª)	p^{b}	Adjusted Odds Ratio (IC 95%³)	p	Adjusted Odds Ratio (IC 95%ª)	p				
Gender										
Female	1.00	-	1.00	-	1.00	-				
Male	1.19 (1.00 - 1.40)	0.05	1.62 (1.24 - 2.12)	< 0.01	1.67 (1.18 - 2.35)	< 0.01				
Age Groups (years)										
< 20	1.00	-	1.00	-	1.00	-				
20-29	1.78 (1.06 - 3.00)	0.03	1.57 (0.82 - 3.00)	0.18	1.21 (0.54 - 2.70)	0.65				
30-39	4.79 (2.85 - 8.04)	< 0.01	2.77 (1.42- 5.43)	< 0.01	2.64 (1.15 - 6.03)	0.02				
40-49	11.10 (6.67- 18.48)	< 0.01	7.00 (3.59 - 13.63)	< 0.01	6.52 (2.84 - 14.97)	< 0.01				
50-59	15.58 (9.25 - 26.24)	< 0.01	9.35 (4.74 - 18.45)	< 0.01	10.11 (4.34 -23.55)	< 0.01				
60-69	26.06 (14.38 - 47.21)	< 0.01	17.04 (7.99 - 36.34)	< 0.01	21.15 (8.09 - 55.27)	< 0.01				
≥ 70	24.99 (12.47 - 50.10)	< 0.01	15.23 (6.43 - 36.06)	< 0.01	15.46 (5.13 - 46.59)	< 0.01				
Leisure time Physical Activ	vity					-1				
Inactive	1.00	-	1.00	-	1.00	-				
Very low	0.76 (0.55 - 1.06)	0.10	0.95 (0.62 - 1.48)	0.83	1.05 (0.58 - 1.94)	0.86				
Low	0.79 (0.58 - 1.09)	0.15	0.76 (0.49 - 1.17)	0.21	0.96 (0.54 - 1.72)	0.89				
Moderate	0.71 (0.52 - 0.98)	0.04	0.95 (0.61 - 1.47)	0.80	1.26 (0.71 - 2.23)	0.43				
High	0.76 (0.55 - 1.06)	0.10	1.15 (0.73 - 1.81)	0.55	1.09 (0.60 - 1.99)	0.76				
Very high	0.28 (0.19 - 0.41)	< 0.01	0.62 (0.38 - 1.03)	0.07	0.81 (0.44 - 1.51)	0.51				
BMI (kg/m ²)										
≤ 24.9	1.00	-	1.00	-	1.00	-				
25 – 29.9	3.93 (3.07 - 5.03)	< 0.01	3.20 (2.32 - 4.40)	< 0.01	3.85 (2.51 - 5.90)	< 0.01				
≥ 30	10.21 (7.93 - 13.14)	< 0.01	6.17 (4.40 - 8.64)	< 0.01	7.65 (4.87 - 12.01)	< 0.01				
HOMA β-cell	·									
<117.90	1.00	-	1.00	-	-	-				
117.90-162.06	0.57 (0.46 - 0.71)	< 0.01	0.50 (0.37 - 0.69)	< 0.01	0.57 (0.38 - 0.87)	< 0.01				
≥162.07	0.82 (0.66 - 1.01)	0.07	0.43 (0.29 - 0.63)	< 0.01	0.47 (0.29 - 0.76)	< 0.01				
Insulinorresistence ^c										
Absent	1.00	-	1.00	-	1.00	-				
Present	3.22 (2.68 - 3.87)	< 0.01	3.71 (2.74 - 5.02)	< 0.01	3.29 (2.25 - 4.83)	< 0.01				
hs-CRP ^d										
Normal	1.00	-	-	-	1.00	-				
High	3.00 (2.34 - 3.85)	< 0.01	-	-	2.74 (1.92 - 3.91)	< 0.01				

a Confidence Interval (95%); b Significance level; c HOMA2-IR: ≥2; d High hs-CRP ≥0.765mg/L * Model 1: Adjusted by gender, age group, ethnicity, education status, working status, socioeconomic statis, antecedente familiar de diabetes mellitus, alchol consumption, smoking, leisure time physical activity, BMI insulin resistance, and HOMA β-cell tertiles. ** Model 2: Model 1 adding High hs-CRP.

		Model 2**				
	Crude Odds Ratio (IC 95%ª)	p	Adjusted Odds Ratio (IC 95%ª)	/ ^b	Adjusted Odds Ratio (IC 95%ª)	р ь
Gender						
Female	1.00	-	1.00	-	1.00	-
Male	1.19 (1.00 - 1.40)	0.05	1.57 (1.20 - 2.05)	< 0.01	1.62 (1.15 - 2.28)	< 0.01
Age Groups (years)						
< 20	1.00	-	1.00	-	1.00	-
20-29	1.78 (1.06 - 3.00)	0.03	1.64 (0.84 - 3.21)	0.15	1.20 (0.54 - 2.68)	0.65
30-39	4.79 (2.85 - 8.04)	< 0.01	2.89 (1.45- 5.77)	< 0.01	2.54 (1.11 - 5.81)	0.03
40-49	11.10 (6.67- 18.48)	< 0.01	7.52 (3.79 - 14.93)	< 0.01	6.34 (2.77 - 14.53)	< 0.01
50-59	15.58 (9.25 - 26.24)	< 0.01	9.76 (4.86 - 19.62)	< 0.01	9.53 (4.09 -22.15)	< 0.01
60-69	26.06 (14.38 - 47.21)	< 0.01	17.09 (7.91 - 36.93)	< 0.01	19.69 (7.58 - 51.3)	< 0.01
≥70	24.99 (12.47 - 50.10)	< 0.01	14.38 (6.04 - 34.26)	< 0.01	11.92 (4.06 - 34.99)	< 0.01
Leisure time Physical Activity						
Inactive	1.00	-	1.00	-	1.00	-
Very low	0.76 (0.55 - 1.06)	0.10	0.94 (0.61 - 1.47)	0.80	1.13 (0.89 - 2.06)	0.69
Low	0.79 (0.58 - 1.09)	0.15	0.75 (0.48 - 1.15)	0.19	0.89 (1.32 - 1.59)	0.70
Moderate	0.71 (0.52 - 0.98)	0.04	0.99 (0.64 - 1.55)	0.99	1.32 (1.13 - 2.33)	0.35
High	0.76 (0.55 - 1.06)	0.10	1.22 (0.77 - 1.92)	0.39	1.13 (0.85 - 2.05)	0.68
Very high	0.28 (0.19 - 0.41)	< 0.01	0.63 (0.38 - 1.05)	0.08	0.85 (0.91 - 1.56)	0.59
BMI (kg/m ²)						
≤ 24.9	1.00	-	1.00	-	1.00	-
25 – 29.9	3.93 (3.07 - 5.03)	< 0.01	3.49 (2.51 - 4.83)	< 0.01	4.11 (2.67 - 6.33)	< 0.01
≥ 30	10.21 (7.93 - 13.14)	< 0.01	7.01 (4.97 - 9.87)	< 0.01	8.71 (5.53 - 13.73)	< 0.01
HOMA β-cell						
<117.90	1.00	-	1.00	-	-	-
117.90-162.06	0.60 (0.49 - 0.75)	< 0.01	0.55 (0.40 - 0.76)	< 0.01	0.64 (0.42 - 0.97)	0.03
≥162.07	0.87 (0.70 - 1.08)	0.20	0.48 (0.33 - 0.69)	< 0.01	0.55 (0.34 - 0.88)	0.01
Insulinorresistence						
Absent	1.00	-	1.00	-	1.00	-
Present	3.22 (2.68 - 3.87)	< 0.01	3.53 (2.61 - 4.78)	< 0.01	3.01 (2.07 - 4.39)	< 0.01
hs-CRP⁴						
Normal	1.00	-	-	-	1.00	-
High	3.00 (2.34 - 3.85)	< 0.01	_	-	2.46 (1.73 - 3.49)	< 0.01

a Confidence Interval (95%); b Significance level; c HOMA2-IR: ≥2; d High CRP-us: ≥0.765mg/L * Model 1: Adjusted by gender, age group, ethnicity, education status, working status, socioeconomic statis, antecedente familiar de diabetes mellitus, alchol consumption, smoking, leisure time physical activity, BMI insulin resistance, and HOMA β-cell tertiles.

** Model 2: Model 1 adding High hs-CRP.

		Model 1*							
	Crude Odds Ratio (IC 95%ª)	P	Adjusted Odds Ratio (IC 95%ª)	p ^b	Adjusted Odds Ratio (IC 95%ª)	p ^b			
Gender									
Female	1.00	-	1.00	-	1.00	-			
Male	0.98 (0.82 - 1.16)	0.77	1.13 (0.85 - 1.51)	0.39	0.98 (0.68 - 1.41)	0.92			
Age Groups (years)	·								
< 20	1.00	-	1.00	-	1.00	-			
20-29	2.11 (1.09 - 4.07)	0.03	1.83 (0.77 - 4.32)	0.17	1.24 (0.46 - 3.34)	0.6			
30-39	6.21 (3.25 - 11.87)	< 0.01	3.01 (1.26 - 7.19)	0.01	2.01 (0.74 - 5.50)	0.1			
40-49	15.50 (8.20- 29.29)	< 0.01	8.39 (3.55 - 19.85)	< 0.01	4.78 (1.77 - 12.90)	< 0.0			
50-59	18.79 (9.87 - 35.75)	< 0.01	9.66 (4.04 - 23.06)	< 0.01	7.05 (2.58 - 19.29)	< 0.0			
60-69	32.80 (16.40 - 65.59)	< 0.01	18.69 (7.41 - 47.12)	< 0.01	16.23 (5.45 - 48.34)	< 0.0			
≥ 70	26.49 (12.36 - 56.78)	< 0.01	16.59 (6.07 - 45.35)	< 0.01	12.91 (3.83 - 43.49)	< 0.0			
Leisure time Physical Activity				^					
Inactive	1.00	-	1.00	-	1.00	-			
Very low	0.78 (0.55 - 1.09)	0.14	1.08 (0.68 - 1.72)	0.75	0.97 (0.51 - 1.86)	0.9			
Low	0.73 (0.52 - 1.01)	0.06	0.72 (0.45 - 1.14)	0.16	0.87 (0.46 - 1.63)	0.6			
Moderate	0.71 (0.51 - 0.99)	0.05	0.97 (0.60 - 1.56)	0.89	1.29 (0.69 - 2.39)	0.43			
High	0.70 (0.49 - 0.98)	0.04	0.89 (0.54 - 1.48)	0.67	0.78 (0.40 - 1.55)	0.4			
Very high	0.21 (0.13 - 0.33)	< 0.01	0.46 (0.25 - 0.86)	0.02	0.56 (0.26 - 1.21)	0.1			
BMI (kg/m²)				^					
≤ 24.9	1.00	-	1.00	-	1.00	-			
25 – 29.9	4.52 (3.35 - 6.09)	< 0.01	3.57 (2.44 - 5.22)	< 0.01	4.68 (2.80 - 7.83)	< 0.0			
≥ 30	17.59 (13.07 - 23.68)	< 0.01	11.93 (8.06 - 17.66)	< 0.01	17.05 (9.99 - 29.08)	< 0.0			
HOMA β-cell	÷								
<117.90	1.00	-	1.00	-	-	-			
117.90-162.06	0.57 (0.46 - 0.72)	< 0.01	0.41 (0.29 - 0.58)	< 0.01	0.36 (0.22 - 0.58)	< 0.0			
≥162.07	0.79 (0.64 - 0.99)	0.04	0.29 (0.19 - 0.43)	< 0.01	0.21 (0.12 - 0.36)	< 0.0			
Insulinorresistence°									
Absent	1.00	-	1.00	-	1.00	-			
Present	3.87 (3.19 - 4.69)	< 0.01	4.97 (3.55 - 6.95)	< 0.01	5.28 (3.41 - 8.19)	< 0.0			
hs-CRP⁴									
Normal	1.00	-	-	-	1.00	-			
High	3.11 (2.43 - 3.99)	< 0.01	-	-	2.77 (1.91 - 4.02)	< 0.0			

a Confidence Interval (95%); b Significance level; c HOMA2-IR: ≥2; d High CRP-us: ≥0.765mg/L * Model 1: Adjusted by gender, age group, ethnicity, education status, working status, socioeconomic statis, antecedente familiar de diabetes mellitus, alchol consumption, smoking, leisure time physical activity, BMI insulin resistance, and HOMA β-cell tertiles. ** Model 2: Model 1 adding High hs-CRP.

Continent	City (Country)	Total	Male (%)	Female (%)	n	Author, Year (Reference)	MS Criteria
	San Juan (Puerto Rico)	43,3	45,3	42,2	859	Pérez, 2008 (34)	ATPIII*
	Maracaibo (Venezuela)	42,4	44,6	40,4	2.230	Bermúdez, 2012	IDF/AHA/NHLBI§
	Santic spiritus (Cuba)	39,8	40,0	39,8	1.019	Bustillo, 2011 (36)	ALAD‡
	United States of America	38,5	41,9	35,0	3461	Ford E, 2010 (35)	IDF/AHA/NHLBI
	Brasil FD (Brasil)	32,0	30,9	33,0	2.130	Dutra, 2012 (33)	IDF/AHA/NHLBI
	Mexico City (Mexico)	27,0	22,4	22,2	1.720	Escobedo, 2009 (40)	ATPIII
America	Barquisimeto (Venezuela)	26,0	23,0	22,7	1.836	Escobedo, 2009 (40)	ATPIII
	Santiago (Chile)		15,3	19,0	1.648	Escobedo, 2009 (40)	ATPIII
Bogotá (Colombia) Canadá	20,0	14,7	18,2	1.550	Escobedo, 2009 (40)	ATPIII	
	19,1	17,8	20,5	1800	Riediger, 2011 (41)	IDF/AHA/NHLB	
	Lima (Perú)	18,0	13,2	17,7	1.645	Escobedo, 2009 (40)	ATPIII
	Buenos Aires (Argentina)	17,0	17,3	9,7	1.476	Escobedo, 2009 (40)	ATPIII
	Quito (Ecuador)	14,0	5,5	16,4	1.627	Escobedo, 2009 (40)	ATPIII
	Tehrán (Iran)	30,1	24,0	42,0	10.368	Azizi, 2003 (37)	ATPIII
	Northern India	31,6	22,9	39,9	1.091	Gupta ,2004 (42)	ATPIII
Asia	Beijing (China)	23,2	24,5	22,7	16.442	Li, 2010 (43)	IDF¶
	Hong Kong	17,1%	15,3	18,8	2.843	Thomas, 2005 (44)	ATPIII
	Taiwan	а	11,2	18,6	8.320	Chuang, 2002 (45)	ATPIII
	Turkey	33,9	28,0	39,6	4.259	Kozan, 2007 (38)	ATPIII
Furana	Greece	а	24,2	22,8	4.753	Athyros, 2005 (16)	ATPIII
Europe	Yecla (Murcia, Spain)	20,2	23,8	16,8	317	Martínez, 2006 (46)	ATPIII
	Italy	а	15,0	18,0	2.100	Miccoli, 2005 (47)	ATPIII
	Australia	30,7	34,0	27,2	11.247	Cameron, 2007 (39)	IDF
rica y Oceanía	Seychelles	25,1	25,0	35,0	1255	Kelliny, 2008 (48)	IDF

^aData not shown

*Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults

§IDF/AHA/NHLBI/WHF/IAS/IASO-2009

+Latinamerican Diabetes Association

¶International Diabetes Federation-2005

Discusión

he Metabolic Syndrome is one of the most controversial definitions in the medical field due to the number of criteria that have been proposed and the notorious issue concerning the anthropometric variable, waist circumference. Nevertheless, the purpose of these definitions throughout time is the identification of high risk individuals for CVD² and T2DM³. The definitions used in this investigation are in chronological order, the International Diabetes Definition published in 2005⁶, the Adult Treatment Panel III whose actualization came out in 2005⁸, and finally the Harmonizing consensus which was released in 2009⁹.

Each definition criteria has a crucial characteristic. For example, IDF-2005 established that abdominal obesity was mandatory to diagnose MS and WC was defined according to ethnic group. The ATPIII-2005⁸ was an update from the ATPIII-2002⁷, which maintained the previous cutpoints for WC, TAG, HDL-C and blood pressure, but adjusted

glycemia to 100 mg/dL. These two criteria had major differences concerning WC cut-off points where the first was established to be ethnic specific, whereas the second maintained a simpler worldwide cutpoint of WC, ≥ 102 cm in men and ≥88 cm in women. Both ATPIII kept such cutpoint because it was observed that subjects tended to have 2 metabolic components presents and to be insulin resistance when having WC was between 94-101 cm^{7,8}. However, these arbitrary cutpoints cannot be considered population-specific and this lack of sensitivity would under diagnose obesity in certain populations, such as in Latin America. This argument was revised in IDF-2009⁹ and it was concluded that each ethnic group should research and develop appropriate WC in order to accurately evaluate abdominal obesity, and therefore improve diagnostic precision of MS diagnosis. Given all these modifications, prevalence of MS around the world depend on the criteria used (Table 6³⁸⁻⁵³), and this offers limitation in regards to comparison and prediction of CVD risk.

Worldwide prevalence of MS varies according to age, gender, ethnic group, prevention goal and MS definition applied. The Chinese Multi-provincial Cohort Study⁵⁴ evaluated prevalence of MS in over 26 thousand adults from the Chinese population using ATPIII-2005 and IDF-2005, reporting a level of agreement between both criteria of k=0.786 in men and k=0.0887 in women; also ATPIII-2005 was able to diagnose 4% more people with MS because it doesn't reduce the spectrum of diagnosis to just obese individuals, because those with 3 metabolic variables other than elevated WC are considered to have MS. These conclusions are also observed in other investigations such as Forero et al.¹¹ in Colombia with scarce agreement of k=0.3997 apparently due to differences in detecting obese subjects.

When comparing agreement on 3 or more criteria, varying results are observed especially when age and gender is concerned. Paula et al.¹² evaluated the adequacy of 4 MS diagnosis in a Brazilian sample of elderly women (AT-PIII-2002, ATPIII-2005, IDF-2005 and IDF-2009), reporting that the ATPIII-2005 consensus was more adequate to diagnose MS in elderly women, with an agreement of k=0.79 between ATPIII-2002 and IDF-2009; such findings are supported by recent results from Saad et al.¹³ in another Brazilian sample of women beyond 60 years of age.

In another Latin American country, Mora García et al.¹⁷ evaluated the level of agreement of 4 MS definitions in the population of Cartagena, reporting that IDF-2009 rendered the highest prevalence of MS with 36.3%, with an agreement between IDF-2005 of k=0.893, while a lower Cohen function of k=0.711 with ATPIII-2005, apparently due to differences between WC cut-off points. The recommended application of IDF-2009 in an adult population is not only observed in South American studies^{13,17}, it has also been suggested in the Greeks¹⁹, in Iranians¹⁸ and Malaysians¹⁴. However, the recommendation seems to change when CVD prevention is the main objective, where ATPIII-2005 seems to be more predictive than other definitions (ANOVA p<0.001¹⁹), and it's associated with higher risk for coronary disease (OR=2.48; 95%CI 1.80-3.82¹⁶), cerebrovascular disease (OR=2.14; 95%CI 1.19-3.86¹⁶), and peripheral artery disease (OR=1.55; 95%CI 1.04-2.32 ¹⁶).

Our results show that there is a very good level agreement between these 3 MS consensuses, probable due to high prevalence not only of overweightness and obesity²⁰, but of other metabolic components in the city such as hypertension⁵⁵ and dyslipidemia⁵⁶, and amplifying factors such as low grade inflammation^{22,23} and sedentary life style²¹. In fact, 2 previous studies evaluated the prevalence of MS in Venezuela using ATPIII-2005 criteria: the CARMELA study⁴⁵ and the investigation from Florez et al.⁵⁷. The city of Barquisimeto was the place of analysis in the CARMELA reporting a prevalence of 26%. Whereas, Florez et al.⁵⁷ published a prevalence of MS in the city of Maracaibo of 31.2%, very similar results to ours when using the same criteria, with 35.5%. However, higher results are observed using the IDF-2009 consensus, demonstrating that the only anthropometric variable might be the key to define an appropriate MS consensus.

As was confirmed within these results, abdominal obesity was the most prevalent component with all the definitions used here, followed closely by low HDL-C levels and high blood pressure. Moreover, the only Sociodemographic variable associated with MS diagnosis was education status, specifically in those with lowest educational achievements. These results differ from those published by Moebus et al.¹⁵, where IDF-2005 dependent MS diagnosis was higher in those with the highest educational status, measured as more than 10 years of schooling. Other factors associated with MS were former smoking probably due to rebound obesity observed in these individuals⁵⁸, and low physical activity during leisure time which associated with higher tendency for obesity^{21,59}, high blood pressure⁶⁰, hyperglycemia⁶¹ and MS⁶². Indeed, this type of physical activity resulted to be a protective variable in all the MS consensuses, especially when applying ATPIII-2005, a criteria that selects heavier subjects during the MS diagnosis, which by definition would show sedentary lifestyles⁶³.

Insulin resistance and decreased insulin secretion are features observed previous to the actual installment and diagnosis of metabolic syndrome or dysglycemia⁶⁴, as early as 3 years prior to the diagnosis of diabetes⁶⁵. These two features tend to worsen as other MS components cluster, being abdominal obesity the most important aggregating variable^{64,65}. In this regard, Chen et al.⁶⁶ reported that insulin resistance and HOMA b-cell function associated with BMI in men, while WC was associated with such variables in women. Finally, it has been reported that a 20% decrease in HOMA b-cell function is associated with cardiovascular events (OR: 1.09; 95%CI 1.05-1.14) and cardiovascular-related death (OR: 1.10; 95%CI 1.07-1.14)⁶⁷. Therefore, early detection and management of pancreatic beta cell function appears to be important⁶⁸, especially when presence of lower insulin secretion is associated with MS, as shown in our results (Table 3), where higher HOMA b-cell function serves as a protection factor in all three MS definitions.

Low grade inflammation seems to play an important role in MS, as both markers used here are positively associated with this diagnosis. Lipoprotein(a) is a modified LDL-C particle which has an additional apoprotein, apoprotein (a), and has been widely related to higher risk of coronary and cerebrovascular events^{69,70}, being recognized as a determinant for residual risk (HR:1.27; 95%CI 1.01-1.59, p=0.04) (71). We have previously demonstrated that MS diagnosis is associated with higher levels of Lp(a) (c^2 =28,33; p<0.0001)²³. Therefore, it is not surprising to find it associated with diagnosis of MS in all 3 criteria. In regards to CRP-us, higher levels of this particle have been related to lower physical activity, higher BMI and insulin resistance in our population²², and consequently with higher risk of MS in those with CRP ≥0.765 mg/L, independent of which MS consensus.

It has been previously demonstrated that Lp(a) and CRP are observed in insulin resistance states⁷² and have been correlated as CVD risk markers^{73,74}. A very complicated cycle is observed between insulin resistance, CVD, low grade inflammation and metabolic components of MS⁷⁵, and it seems to require the development of adiposopathy⁷⁶. Our results demonstrate that not only is insulin resistance related to MS diagnosis, but it also confers risk for the syndrome reminiscing earlier MS definitions which would require the presence of insulin resistance^{77,78}. However, not all patients with MS have insulin resistance and vice versa, limiting the use of this metabolic variable as component of the MS criteria, but it doesn't belittles the importance of insulin resistance as a predictive variable in our population, especially when low grade inflammation is present.

We can conclude that IDF-2009 results in higher detection of MS, which could be explained by the characteristics of the anthropometric variable – the WC. All three definitions obtained high levels of agreement probable because 4 out of the 5 components of the definition are identical; the only differences rely on the WC cut-offs. Finally, insulin resistance and low grade inflammation are important risk factors for MS, independent of MS consensus applied.

FUNDING

This work was supported by research grant N° CC-0437-10-21-09-10 from CONDES - University of Zulia, and research grant N° FZ-0058-2007 from Fundacite-Zulia.

DISCLOSURE

The authors have are no conflicts of interest to disclose.

Referencias

- Brietzke SA. Controversy in diagnosis and management of the metabolic syndrome. Med Clin North Am 2007;91:1041-1061.
- Wilson P, D'Agostino R, Parise H. Metabolic Syndrome as a Precursor of Cardiovascular Disease and Type 2 Diabetes Mellitus. Circulation. 2005; 112: 3066-3072.
- Grundy SM. Pre-diabetes, metabolic syndrome, and cardiovascular risk. J Am Coll Cardiol 2012;59:635-43.
- Sarafidis PA, Nilsson PM. The metabolic syndrome: a glance at its history. J Hypertens 2006;24:621-6.
- Oda E. Metabolic syndrome: its history, mechanisms, and limitations. Acta Diabetol 2012;49:89-95.
- Alberti KG, Zimmet P, Shaw J; IDF Epidemiology Task Force Consensus Group. The metabolic syndrome--a new worldwide definition. Lancet 2005;366:1059-1062.
- National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol. Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106: 3143–3421
- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA, Gordon DJ, Krauss RM, Savage PJ, Smith SC Jr, Spertus JA, Costa F; American Heart Association; National Heart, Lung, and Blood Institute. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation 2005;112:2735-2752.
- Robert A, Eckel R, Grundy S, et al. Harmonizing the Metabolic Syndrome: A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention: National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; Interna-

tional Association for the Study of Obesity. Circulation 2009; 20:1640-1645.

- Hari P, Nerusu K, Veeranna V, Sudhakar R, Zalawadiya S, Ramesh K, Afonso L. A gender-stratified comparative analysis of various definitions of metabolic syndrome and cardiovascular risk in a multiethnic U.S. population. Metab Syndr Relat Disord 2012;10:47-55.
- 11. Forero Y, Gina E, Morales EB. Comparison of two methodologies used for determining metabolic syndrome in adult population. Biomedica 2013;33:233-240.
- 12. Paula HA, Ribeiro Rde C, Rosado LE, Pereira RS, Franceschini Sdo C. Comparison of the different definition criteria for the diagnosis of the metabolic syndrome in elderly women. Arq Bras Cardiol 2010;95:346-353.
- Saad MA, Cardoso GP, Martins WD, Velarde LG, Cruz Filho RA. Prevalence of Metabolic Syndrome in Elderly and Agreement among Four Diagnostic Criteria. Arq Bras Cardiol 2014; DOI: <u>http://dx.doi.org/10.5935/abc.20140013</u>
- 14. Ramli AS, Daher AM, Nor-Ashikin MN, Mat-Nasir N, Ng KK, Miskan M, Ambigga KS, Ariffin F, Mazapuspavina MY, Abdul-Razak S, Abdul-Hamid H, Abd-Majid F, Abu-Bakar N, Nawawi H, Yusoff K. JIS definition identified more Malaysian adults with metabolic syndrome compared to the NCEP-ATP III and IDF criteria. Biomed Res Int 2013;2013;760963.
- 15. Moebus S, Hanisch JU, Aidelsburger P, Bramlage P, Wasem J, Jöckel KH. Impact of 4 different definitions used for the assessment of the prevalence of the Metabolic Syndrome in primary healthcare: The German Metabolic and Cardiovascular Risk Project (GEMCAS). Cardiovasc Diabetol 2007;6:22.
- Ivezić-Lalić D, Bergman Marković B, Kranjčević K, Kern J, Vrdoljak D, Vu ak J. Diversity of metabolic syndrome criteria in association with cardiovascular diseases--a family medicine-based investigation. Med Sci Monit 2013;19:571-578.
- 17. Mora García G, Salguedo Madrid G, Ruíz Díaz M, Ramos Clason E, Alario Bello A, Fortich A, Mazenett E, Gómez Camargo D, Gómez Alegría C. Agreement between Five Definitions of Metabolic Syndrome: Cartagena, Colombia. Rev Esp Salud Pub 2012;6:301-311.
- Esmailzadehha N, Ziaee A, Kazemifar AM, Ghorbani A, Oveisi S. Prevalence of metabolic syndrome in Qazvin Metabolic Diseases Study (QMDS), Iran: a comparative analysis of six definitions. Endocr Regul 2013;47:111-120.
- Athyros VG, Ganotakis ES, Tziomalos K, Papageorgiou AA, Anagnostis P, Griva T, Kargiotis K, Mitsiou EK, Karagiannis A, Mikhailidis DP. Comparison of four definitions of the metabolic syndrome in a Greek (Mediterranean) population. Curr Med Res Opin 2010;26:713-719.
- Bermúdez V, Pacheco M, Rojas J, Córdova E, Velázquez R, Carrillo D, Parra MG, Toledo A, Añez R, Fonseca E, Marcano RP, Cano C, Miranda JL. Epidemiologic behavior of obesity in the Maracaibo City metabolic syndrome prevalence study. PLoS One 2012;7:e35392.
- Bermúdez VJ, Rojas JJ, Córdova EB, Añez R, Toledo A, Aguirre MA, Cano C, Arraiz N, Velasco M, López-Miranda J. International physical activity questionnaire overestimation is ameliorated by individual analysis of the scores. Am J Ther 2013;20:448-458.
- 22. Bermúdez V, Cbrera M, Mendoza L, Chávez ME, Martínez MS, Rojas J, Nava A, Fuenmayor D, Apruzzese V, Salazar J, Torres Y, Rincón T, Bello L, Añez R, Toledo A, Chacín M, Villalobos M, Pachano F, Montiel M, Aguirre MA, París Marcano R, Velasco M. Epidemiological behavior of high-sensitivity C-Reactive Protein (hs-CRP) in adult individuals in the Maracaibo city, Venezuela. Rev Latinoamericana Hipertension 2013;8(4) in press.
- 23. Bermúdez V, Rojas J, Salazar J, Bello L, Añez R, Toledo A, Chacín M, Aguirre M, Villalobos M, Chávez M, Martínez MS, Torres W, Torres Y, Mejías J, Mengual E, Rojas L, Sánchez de Rosales M, Quevedo A, Cano R, Cabrera M, París R, Lubo A, Montiel M, Cano C. Variations of lipoprotein(a) levels in the metabolic syndrome: a report from the Maracaibo City Metabolic Syndrome Prevalence Study. J Diabetes Res 2013;2013:416451.
- 24. Bermúdez V, Marcano RP, Cano C, Arráiz N, Amell A, Cabrera M, Reyna N, Mengual E, Vega L, Finol F, Luti Y, Sánchez D, Sánchez W, González J, Montes J, Rojas E, Cano J, Cano R, Velasco M, Miranda JL. The Maracaibo City Metabolic Syndrome Prevalence Study: Design and Scope. Am J Therapeutics 2010;17:288-294.
- Salzano FM. Interthnic variability and admixture in Latin America social implications. Rev Biol Trop 2004;52:405–15.
- 26. Méndez-Castellano H, De Méndez MC. Estratificación social y biología humana: método de Graffar modificado. Arch Ven Pueric Pediatr 1986;49:93–104.
- Baglietto L, English DR, Hopper JL, Powles J, Giles GG. Average volume of alcohol consumed, type of beverage, drinking pattern and the risk of death from all causes. Alcohol 2006;41:664–671.
- Ministerio de Sanidad, Servicios Sociales e Igualdad. Gobierno de España. Campaña 2007. Disponible en:

http://www.msssi.gob.es/en/campannas/campanas07/alcoholmenores9.htm

29. National Health and Medical Research Council's 2009 Australian Guidelines to Reduce Health Risks from Drinking Alcohol.

- Berlin I, Lin S, Lima J, Bertoni A. Smoking Status and Metabolic Syndrome in the Multi-Ethnic Study of Atherosclerosis. A cross-sectional study. Tobacco Induced Diseases 2012;10:9
- 31. Guidelines for Data Processing and Analysis of the International Physical Activity Questionnaire (IPAQ) – Short and Long Forms. IPAQ core group 2005. Available at: <u>http://www.ipaq.ki.se/ipaq.htm</u>
- 32. Health Statistics. NHANES III reference manuals and reports (CDROM). Hyattsville, MD: Centers for Disease Control and Prevention, 1996. Available at: http://www. cdc.gov/nchs/data/nhanes/nhanes3/cdrom/NHCS/MANUALS/ ANTHRO.pdf
- 33. World Health Organization. The World Health Report 2003. Available at: <u>http://</u> www.who.int/whr/2003/en/
- Leino A, Impivaara O, Kaitsaari M, Järvisalo J. Serum concentrations of apolipoprotein A-I, apolipoprotein B, and lipoprotein(a) in a population sample. Clin Chem 1995;41:1633-6.
- 35. National Health and Nutrition Examination Survey (NHANES III). The Journal of Clinical Endocrin & Metabolism. 2002; 87: 2489-499.
- 36. Cohen J. A coefficient of agreement for nominal scales. Educ Psychol Meas 1960;20:37-46.
- Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics 1977;33:159-174.
- Dutra E, Baiocchi K, Miyazaki É, Merchán-Hamman E, Kiyomi M. Metabolic syndrome in central Brazil: Prevalence and correlates in the adult population. Diabetology & Metabolic Syndrome. 2012;4:20.
- Pérez CM, Guzmán M, Ortiz AP, Estrella M, Valle Y, Pérez N et al. Prevalence of the metabolic syndrome in San Juan, Puerto Rico. Ethn Dis. 2008;18(4):434-441.
- Ford E., Li C., Zhap G. Prevalence and correlates of metabolic syndrome based on a harmonious definition among adults in the US. Journal of Diabetes. 2010; 2:180-193.
- Bustillo E, Pérez Y, Brito A, González A, Castañeda D, Santos M, et al. Síndrome metabólico, un problema de salud no Diagnosticado. Rev Cubana Endocrinol. 2011; 22(3): 167-181.
- 42. Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. Diabetes Res Clin Pract. 2003; 61(1):29-37.
- Kozan O, Oguz A, Abaci A, Erol C, Ongen Z, Temizhan A, et al. Prevalence of the metabolic syndrome among Turkish adults. Eur J Clin Nutr. 2007;61(4):548-53.
- 44. Cameron AJ, Magliano DJ, Zimmet PZ, Welborn T, Shaw JE. The metabolic syndrome in Australia: prevalence using four definitions. Diabetes Res Clin Pract. 2007;77(3):471-8.
- 45. Escobedo J, Schargrodsky H, Champagne B, Silva H, Boissonnet C, Vinueza R, et al. Prevalence of the Metabolic Syndrome in Latin America and its association with sub-clinicalcarotid atherosclerosis: the CARMELA cross sectional study. Cardiovascular Diabetology 2009;8:52.
- Riediger N, Clara I. Prevalence of metabolic syndrome in the Canadian adult population. CMAJ 2011;183(15):1-8.
- Gupta R, Deedwania PC, Gupta A, Rastogi S, Panwar RB, Kothari K. Prevalence of metabolic syndrome in an Indian urban population. Int J Cardiol. 2004; 97(2):257-61.
- Li G, de Courten M, Jiao S, Wang Y. Prevalence and characteristics of the metabolic syndrome among adults in Beijing, China. Asia Pac J Clin Nutr. 2010;19(1):98-102.
- 49. Thomas GN, Ho SY, Janus ED, Lam KS, Hedley AJ, Lam TH, et al. The US National Cholesterol Education Programme Adult Treatment Panel III (NCEP ATP III) prevalence of the metabolic syndrome in a Chinese population. Diabetes Res Clinical. 2005;67:251–257.
- 50. Chuang SY, Chen CH, Chou P. Prevalence of Metabolic Syndrome in a Large Health Check-up Population in Taiwan. J Chin Med Assoc. 2004;67(12):611-620.
- Martínez J, Franch J, Romero J, Cánovas C, Gallardo A, Páez M. Prevalence of metabolic syndrome in the adult population of Yecla (Murcia). Degree of agreement between three definitions of it. Aten Primaria. 2006 38(2):72-79.
- Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F, Giovannitti MG, et al. Prevalence of the metabolic syndrome among Italian adults according to ATP II definition. Nutr Metab Cardiovasc Dis. 2005;15(4):250-4.
- Kelliny C, William J, Riesen W, Paccaud F, Bovet P. Metabolic Syndrome according to different definitions in a rapidly developing country of the African region. Cardiovasc Diabetol. 2008; 7: 27.
- Liu J1, Grundy SM, Wang W, Smith SC Jr, Vega GL, Wu Z, Zeng Z, Wang W, Zhao D. Ethnic-specific criteria for the metabolic syndrome: evidence from China. Diabetes Care 2006;29:1414-6.
- 55. Sulbarán T, Silva E, Calmón G, Vegas A. Epidemiologic aspects of arterial hypertension in Maracaibo, Venezuela. J Hum Hypertens. 2000; 1: 6-9.
- Bermúdez V, Bello LM, Naguib A, Añez R, Fortul Y, Toledo A, Salazar JJ, Torres Y, Angulo V, Silva Paredes C, Linares S, Arraiz N, Prieto C, Pacheco E, Chacín M, Rojas

J, Aguirre M, Villalobos M, Cano Ponde C, París Marcano R. Lipid profile reference intervals in individuals from Maracaibo, Venezuela: an insight from the Maracaibo City Metabolic Syndrome prevalence study. Rev Latinoamericana de Hipertensión 2012;7:24-34.

- 57. Florez H, Silva E, Fernández V, Ryder E, Sulbarán T, Campos G, et al. Prevalence and risk factors associated with the metabolic syndrome and dyslipidemia in White, Black, Amerindian and Mixed Hispanics in Zulia State, Venezuela. Diabetes Res Clin Pract. 2005;69(1):63-77.
- Chiolero A, Faeh D, Paccaud F, Cornuz J. Consequences of smoking for body weight, body fat distribution, and insulin resistance. Am J Clin Nutr. 2008;87(4): 801-809.
- Sugiyama T, Healy GN, Dunstan DW, Salmon J, Owen N. Joint associations of multiple leisure-time sedentary behaviours and physical activity with obesity in Australian adults. Int J Behav Nutr Phys Act 2008;5:35.
- 60. Shiroma EJ, Lee IM. Physical activity and cardiovascular health: lessons learned from epidemiological studies across age, gender, and race/ethnicity. Crculation 2010;122:743-52.
- 61. Ilanne-Parikka P, Laaksonen DE, Eriksson JG, Lakka TA, Lindstr J, Peltonen M, Aunola S, Keinánen-Kiukaanniemi S, Uusitupa M, Tuomilehto J; Finnish Diabetes Prevention Study Group. Leisure-time physical activity and the metabolic syndrome in the Finnish diabetes prevention study. Diabetes Care 2010;33:1610-17.
- Wennberg P, Gustafsson PE, Dunstan DW, Wennberg M, Hammarström A. Television viewing and low leisure-time physical activity in adolescence independently predict the metabolic syndrome in mid-adulthood. Diabetes Care 2013;36:2090-7.
- 63. Kaino W, Daimon M, Sasaki S, Karasawa S, Takase K, Tada K, Wada K, Kameda W, Susa S, Oizumi T, Fukao A, Kubota I, Kayama T, Kato T. Lower physical activity is a risk factor for a clustering of metabolic risk factors in non-obese and obese Japanese subjects: the Takahata study. Endocr J 2013;60:617-28.
- 64. Cubeddu LX, Hoffmann IS. Impact of traits of metabolic syndrome on β-cell function and insulin resistance in normal fasting, normal glucose tolerant subjects. Metab Syndr Relat Disord 2012;10:344-50.
- 65. Tabák AG, Jokela M, Akbaraly TN, Brunner EJ, Kivimäki M, Witte DR. Trajectories of glycaemia, insulin sensitivity, and insulin secretion before diagnosis of type 2 diabetes: an analysis from the Whitehall II study. Lancet 2009;373:2215-21.
- 66. Chen G, Liu C, Chen F, Yao J, Jiang Q, Chen N, Huang H, Liang J, Li L, Lin L. Body fat distribution and their associations with cardiovascular risk, insulin resistance and -cell function: are there differences between men and women? Int J Clin Pract 2011;65:592-601.
- 67. Curtis LH, Hammill BG, Bethel MA, Anstrom KJ, Liao L, Gottdiener JS, Schulman KA. Pancreatic beta-cell function as a predictor of cardiovascular outcomes and costs: findings from the Cardiovascular Health Study. Curr Med Res Opin 2008;24:41-50.
- Garg MK, Dutta MK, Mahalle N. Study of beta-cell function (by HOMA model) in metabolic syndrome. Indian J Endocrinol Metab 2011;15:S44-9.
- Luc G,Bard JM, Arveiler D, et al. Lipoprotein (a) as a predictor of coronary heart disease: the PRIME study. Atherosclerosis 2002;163:377-84.
- Souki-Rincón A, Urdaneta J, Mengual E, et al. Increased levels of lipoprotein (a) are related to family risk factors of cardiovascular disease in children and adolescents from Maracaibo, Venezuela. Am J Ther 2008;15:403-8.
- 71. Khera AV1, Everett BM, Caulfield MP, Hantash FM, Wohlgemuth J, Ridker PM, Mora S. Lipoprotein(a) concentrations, rosuvastatin therapy, and residual vascular risk: an analysis from the JUPITER Trial (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin). Circulation 2014;129:635-42.
- Güdücü N, Işçi H, Yiğiter AB, Dünder I. C-reactive protein and lipoprotein-a as markers of coronary heart disease in polycystic ovary syndrome. J Turk Ger Gynecol Assoc 2012;13:227-32.
- 73. El-Gendi SS, Bakeet MY, El-Hamed EA, Ibrahim FK, Ahmed R. The value of lipoprotein (a), homocysteine, and Doppler of carotid and femoral arteries in assessment of atherosclerosis in asymptomatic cardiovascular risk patients. J Cardiol 2008;52:202-11.
- 74. Torres JL, Ridker PM. Clinical use of high sensitivity C-reactive protein for the prediction of adverse cardiovascular events. Curr Opin Cardiol 2003;18:471-8.
- 75. Rojas J, Bermúdez V, Leal E, Cano R, Luti Y, Acosta L, Finol F, Aparicio D, Arraiz N, Linares S, Rojas E, Canelón R, Sánchez D. Insulinorresistencia e hiperinsulinemia como factores de riesgo para enfermedad cardiovascular. AVFT 2008;27:30-40.
- 76. Heilbronn LK, Campbell LV. Adipose tissue macrophages, low grade inflammation and insulin resistance in human obesity. Curr Pharm Des 2008;14:1225-30.
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus: provisional report of a WHO consultation. Diabet Med 1998;15:539–553.
- Balkau B, Charles MA. Comment on the provisional report from the WHO consultation. European Group for the Study of Insulin Resistance (EGIR). Diabet Med 1999;16:442-3.