Prevalence of metabolic syndrome in an adult rural population of venezuelan andes: exploring different diagnostic criteria and its level of agreement

Prevalencia del síndrome metabólico en una población adulta rural de los Andes venezolanos: Explorando diferentes criterios de diagnóstico y su grado de acuerdo

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RESUMEN

Introducción: El Síndrome Metabólico (SM) comprende una constelación de factores de riesgo interrelacionados que aumenta el riesgo de enfermedad cardiovascular. Desde 1999 han surgido numerosos criterios diagnósticos para SM. Además, la literatura actual carece de información sobre la prevalencia de SM en poblaciones rurales venezolanas.

Objetivo: Determinar la prevalencia de SM utilizando diferentes criterios diagnósticos en una población rural adulta de la parroquia Capital del Municipio Uribante (Pregonero) Estado Táchira y comparar su prevalencia según las diferentes clasificaciones.

Materiales y Métodos: Estudio descriptivo, transversal, aleatorio, en una muestra de 311 individuos mayores a 18 años de edad, de ambos géneros, habitantes de Pregonero, Táchira. Previo consentimiento informado se le realizó a cada paciente una historia clínica completa incluyendo medición de circunferencia abdominal y toma de presión arterial, determinación de niveles séricos de glucosa, colesterol total, HDL-c y triacilglicéridos. El diagnóstico de SM se realizó utilizando criterios de la Federación Internacional de Diabetes (IDF-2006), el Adult Treatment Panel III, ATP-III (2001 y 2004) y la Asociación Latinoamericana de Diabetes, ALAD y la armonización IDF/NHLBI/AHA/WHF/IAS/IASO-2009. Se compararon prevalencias con la prueba de McNemar, y la concordancia con kappa de Cohen.

Resultados: La prevalencia de SM según las definiciones fueron ATP-III 2001, 27%; ATP-III 2004, 35%; IDF-2006, 41,6% e IDF-2009, 43,1%. Se observaron diferencias estadísticamente significativas entre las definiciones utilizadas (McNemar $p<0.001$), excepto entre IDF-2006 y -2009 (McNemar $p=0.125$), donde además se encontró el mayor grado de concordancia ($\kappa=0,973$, IC95% 0,948 - 0,998).

Conclusiones: En Pregonero existe una prevalencia de SM similar a otras poblaciones venezolanas. Resulta indiferente emplear los criterios de la IDF-2006 o -2009 para realizar el diagnóstico de SM, no así cuando se utilizan los propuestos por el ATP-III.

Palabras clave: síndrome metabólico, prevalencia, diagnóstico, población rural.

ABSTRACT

Introduction: metabolic syndrome (MS) comprises a constellation of cardiovascular risk factors that together increase de risk of acute coronary events and stroke. Since 1999 several diagnostic criteria have been proposed for MS. Venezuela lacks of epidemiological data regarding MS's prevalence in rural populations.

Aim: to determine the prevalence of MS according to International Diabetes Federation (IDF) and Treatment Panel III (ATP-III) among an adult population of Pregonero, a small and relatively isolated rural population in Venezuelan Andes.

Methods: we carried out a descriptive, cross sectional and ramdomized study in a sample of 322 adult participants of both gender inhabitants of Pregonero municipality in Táchira State, Venezuela. We collected the informed consent of each participant then a complete clinical history was carried out including waist circumference, blood pressure, glycaemia, cholesterol HDL, VLDL, LDL and triacylglycerides. MS diagnosis was performed using IDF-2006 criteria, ATP-III (2001-2004) and IDF/NHLBI/AHA/WHF/IAS/IASO-2009 harmonizing criteria. Then we compared prevalences applying McNemar test and Kappa of Cohen concordance index.

Results: MS prevalence according to ATP-III 2001 was 27%; ATP-III 2004 was 35% and IDF-2006 and -2009 were 41,6% and 43,1% respectively. We observed significant differences among every definition (McNemar $p<0.001$), excepting IDF-2006 and -2009 (McNemar $p=0.125$), were also we found the best concordance level ($k=0,973$, IC95% 0,948 - 0,998).

Conclusions: in Pregonero we found similar prevalence rates of those in other Venezuelan populations. It results indifferent to apply IDF-2006 or the harmonizing criteria-2009 for MS diagnosis in this population. High prevalence of MS will require large scale efforts to increase the level consciousness among these populations and interventional strategies to decrease morbid conditions due to MS.

Keywords: metabolic syndrome, Pregonero, Prevalence, cardiovascular disease.

INTRODUCTION

In 2012 World Health Statistics, it's reported that almost 48% of deaths due to non-communicable diseases were explained by underlying cardiovascular diseases, an array of illnesses which remain in the first place as leading causes of death in middle and high income countries[1]. The most important cardiovascular risk factors are modifiable such as sedentary lifestyles, smoking habit, unhealthy diet/obesity and the harmful use of alcohol[1]. Diabetes mellitus, hypertension, smoking, obesity and dyslipidemia are the main risk factors associated to increased mortality due to ischemic heart disease and stroke[2-7]. The understanding of these medical conditions from its natural history and epidemiology to the underlying molecular mechanisms is target of intensive investigation worldwide.

Several definitions for Metabolic Syndrome (MS) have been proposed since its first description by Gerald Reaven during his 1988 Banting Lecture[8]. The Syndrome X as he named it, was defined as the association of central obesity, dyslipidemia, diabetes and hypertension significantly increasing the risk of acute coronary syndromes and stroke. Peripheral resistance to insulin effects appears to be the converging link between the MS components and it occupies a prominent place in the issues of scientific journals of endocrinology, internal medicine and diabetology with a broad and rich discussion in terms of definition and clinical significance[9].

Recent efforts to harmonize MS definition has lead to the unifying criteria of the Joint Interim Statement for the harmonization of the MS carried out by the International Diabetes Federation (IDF), National Heart, Lung, and Blood Institute (NHLBI), American Heart Association (AHA), World Heart Federation (WHF), International Atherosclerosis Society (IAS) and International Association for the Study of Obesity[9]. They proposed that the coexistence of any 3 of the following 5 conditions is diagnostic for MS: elevated waist circumference defined by ethnic specific thresholds, hypertriacylglyceridemia (≥150 mg/dL), reduced HDL-c (men with <40 mg/dL and women with <50 mg/dL), hypertension (≥130/85 mmHg) and fasting hyperglycaemia (≥100 mg/dL); Table 1.

Most of epidemiological studies in Latin America[10] and Venezuela[11] aimed to describe the behaviour of metabolic variables or cardiovascular risks factors have not been homogenized and most of them have been carried out in relatively small populations. The applicability of North American MS criteria in our territories has been independently explored and discussed by several groups, and to respond to this question the Latin-American Society of Diabetes[12] (ALAD), has proposed a diagnostic criteria for South-American countries and the Caribbean. (table 1)[9,12,13,14,15]

The purpose of this study was to determine the prevalence of MS using five different definitions in an adult ru-

ral population from the Venezuelan Andes, evaluate the concordance between different definitions and compare of our results with other rural populations.

MATERIAL AND METHODS

Ethical considerations

The study protocol was designed in compliance with the Helsinki declaration and approved by the Research Ethics Board from the Endocrine and Metabolic Diseases Research Center "Dr. Felix Gomez" (CIEM). Written consent was obtained from all participants participating in the study.

Study Design, Size of the sample and Metabolic Syndrome Diagnosis

This is a cross-sectional study designed to provide realistic estimations of MS prevalence in Pregonero using a sample size of 311 clinically healthy adults of both gender. To calculate the sample size to we used the equation suggested by Camacho-Sandoval et al[16] for the estimation of prevalence, with an expected prevalence of 26% were 'z' represents a level of confidence of 95% (1.96) and 'e' an error of 5%:

Pregonero was divided geographically into 4 separated Zones as follows: Zone 1 has 1.697 inhabitants and includes 4th avenue, 11th street, Colinas de Uribante and Potreritos borough, Zone 2 has 1.377 inhabitants and includes 2th avenue, La Pupita, 1st, 2nd, 3rd, 9th and 10th streets, Coromoto borough, lower Los Rastrojos and El Tropico, Zone 3 has 1.379 inhabitants and includes 3th avenue, Santa Lucia, San Miguel, El Carmen, 4th, 5th, 6th, 7th and 8th streets and Escondido and Zone 4 has 1.490 inhabitants and includes 1st avenue, La Montana Urbanism, Bella Vista, Parcelas, La Pamplonesa, 12th and 13th streets, Vereda Los Mangos, La Esperanza and Santa Eduviges. Summarizing, Pregonero has a total of 5.043 inhabitants according to 2011 statistics and 3.795 of them were older than 18 years old including both gender subjects.

From those 4 separated zones we randomly selected numbered city blocks using the random number generation tool of SPSS ver. 17 for Windows and finally, all the adult subjects from each selected family who fulfilled the inclusion criteria (older than 18 years, without any acute disease or pregnancy) were invited to participate in the study. They were interviewed on prior written consent, and subjected to a routine medical examination using the clinical chart provided by the Health and Social Development Ministry of Venezuela as a data collecting tool. We also collected physical activity data through the International Physical Activity Questionnaire.[17]

MS Diagnosis was performed using the diagnostic criteria of the Latin-American Diabetes Association (ALAD),[12] International Diabetes Federation (IDF) 2006,[13] National Cholesterol Education Programme-Adult Treatment Panel III definition (ATPIII) 2002,[14] modified National Cholesterol Education Programme-Adult Treatment Panel III definition (modified ATPIII) 2004,[15] and the 2009 Joint Interim Statement for the harmonization of the Metabolic Syndrome[9] from the IDF, AHA, NHLBI (**Table 1**).

Data Collection

Blood Pressure was measured using the traditional auscultatory method with a calibrated sphygmomanometer and stethoscope with the patients seated still with their feet on the ground for more than 15 minutes before the determination. During the procedure, the arm will be at the same level of the heart, being the systolic pressure the first sound that is heard (phase 1) and diastolic pressure the point where the sound fades (phase 5). The procedure was done 3 times, 15 minutes apart from each other during the interview, and at least, in 2 different days (the day of blood sampling and the day for results dispatch). The Joint National Committee VII on prevention, detection and evaluation of high blood pressure was used to diagnose hypertension.[18]

Waist circumference measurements were done using a plastic tape, graded in centimetres, in a medium point between the lower rib border and the anterior–superior iliac spine.[19] Height was measured using a metal height measurer graded in centimetres. The results were converted to meters dividing the result into 10. Body mass index[20] will be calculated applying the formula: weight over squared height (kg/mt^2).

Laboratory Determinations

Blood samples were obtained from antecubital vein puncture after a 8 to 12 hours fasting, levels of cholesterol, triacylglycerides, high density lipoproteins (HDL-c), and glucose were determined using computerized equipment (Human Gesellschoft Biochemica and Diagnostica MBH, Magdeburg, Germany). The time between sample taken and its processing never exceeded one month. Low density lipoprotein (LDL-c) levels were calculated using the Fridewald formula[21] if triacylglycerides levels were bellow 400 mg/dL, and if they are above, they were determined by electrophoresis of lipoproteins in agarose gel and ulterior band densimetry (GS-800 densitometer, Bio-Rad, Hercules, CA).

Statistical Analysis

Clinical history, International Physical Activity Questionnaire and laboratory variables were reviewed and typed into a digital database using SPSS 17.0 (SPSS Inc., Chicago, IL) for Windows. The normal distribution of quantitative variables was studied by the kolmogorov-Smirnov test, the homogeneity of variances was tested by Levene test and randomization was confirmed by the Wald-Wolfowitz runs test. Although we observed randomization in our sample we found a no normal distribution and heterogedasticity in most of quantitative variables by which we show our results as median and percentile 05 and 95 and used non parametric testing. Contrasts between two in-

dependent groups were made though Mann-Whitney test and between three or more groups though Kruskal-Wallis test. Statistical analyses for dichotomous variables were performed by chi-square test. Proportions comparisons were made through the McNemar test when two proportions of paired samples were contrasted and through the Cochran's Q test when three or more proportions were compared we also explored the level of agreement between different classifications through Kappa (k) of Cohen statistic. All P values are 2 tailed, and a p=0.05 value will be considered statistically significant. All data was analyzed using SPSS ver. 17.0.

RESULTADOS

Characteristics of the population

A total of 311 participants of 18 year or older had complete information for the study variables and were included in the analyses. Clinical and laboratory variables of these 311 participants are resumed in **Table 2**. In terms of ethnicity we distributed the sample in mixed Venezuelans (76%), Hispanic whites (9.9%), Afro-Americans (1.3%), Arabs (0.6%) and Caucasians (1.9%). Median age among women was 43 years and among men was 49 years, 59.5% of the participants were women. Significant differences were observed between men and women in terms of anthropometric and biological variables, women had higher levels of fasting insulin (10.40 vs. 8.50 µIU/ml, p=0.079) and HDL-c (55.00 vs. 52.00 mg/dl, p=0.001) than men and conversely men showed higher waist circumference (96.50 vs. 91.00cm, p=0.000) and triacylglycerides (146.00 vs. 134.00 mg/dl, p=0,046).

Prevalence of Metabolic Syndrome

Prevalence of MS ranged from 27% (95% CI: 22-31%) according to 2002 ATP III to 43,1% (95% CI: 37-48%) using IDF/AHA/NHLBI-2009 definition (**Figure 1**). MS prevalence according to 2004 NHLBI/AHA definition was 35% (95% CI: 29-40%), for 2006 IDF was 41,6% (95% CI: 35-46%) and for ALAD definition was 28.5% (95% CI: 23-32%). We observed a difference of 1,5% between IDF 2006 and IDF/AHA/NHLBI definitions by not considering central obesity a mandatory criteria. Similarly, we observed an 8% difference between 2002 ATPIII and the 2004 ATPIII-modified by NHLBI/AHA definitions by reducing fasting glycaemia threshold from 110 mg/dL to 100 mg/dL. Prevalence of MS using ALAD definition showed an increase with age observing the highest prevalence in those between 51 and 60 years and then a decrease in the 61 to 70 group and among those with 71 years or more (**Figure 2**).

Distribution of Diagnostic Criteria

Central obesity according to IDF and ALAD (Men≥ 90 cm Women ≥ 80 cm and Men ≥ 94 cm Women ≥ 88 cm, respectively) were the most prevalent positive criteria in general population with 76.3% and 48.1% followed by high triacylglycerides with 45.2% and hypertension with 38.8%. The positive criteria among those with MS diagnosis are shown in Table 2.

Differences between the definitions and level of agreement

We contrasted the proportion participants with MS diagnosis according to the five classifications observing significant differences (Cochran's Q test=125.175, p<0.001). Nonetheless, we did not observe statistical difference between 2006 IDF and IDF/AHA/NHLBI 2009 definitions (p=0.123) in which the only change in the definition is not considering central obesity as a mandatory criteria. MS diagnosis using these two definitions showed a very good agreement coefficient (k=0.973, p<0.001) meaning that 97% of those participants classified as having MS according to the 2006 IDF criteria might also be classified as MS patients by the IDF/AHA/NHLBI definition, thus, might result indifferent to apply 2006 IDF or the harmonizing 2009 IDF/AHA/NHLBI criteria for MS diagnosis in this population. Significant differences were observed when contrasting ALAD and IDF/AHA/NHLBI definitions (p<0.001) in which ALAD differs from IDF/AHA/NHLBI considering central obesity as mandatory criteria and also using different waist circumference threshold. MS diagnosis using these two definitions showed a good agreement coefficient (k=0.692, p<0.001) meaning that 69% of those classified as having MS for the ALAD criteria might also be classified as MS patients by the IDF/AHA/NHLBI definition. Additionally, 2002 ATP III and 2004 modified ATPIII 2004 also showed significant differences by decreasing fasting glycaemia threshold from 110mg/dl to 100md/dl (p<0.001). The level of agreement between these two definitions was (k=0.816, p<0.001). Changes in waist circumference and fasting glycaemia thresholds in the different definitions (Table 1) are responsible for the important variations of MS prevalence in our study.

Table 1.- Diagnostic Criteria for Metabolic Syndrome according to the ATP III, NHLBI/AHA, IDF, the Joint Interim Statement for the MS harmonization of IDF/AHA/NHLBI and ALAD

Parameters	ATP III (2002)	NHLBI/AHA (2004)	IDF (2006)	IDF/AHA/NHLBI (2009)	ALAD (2010)
Interpretation of Criteria	The presence of three of the following five criteria	The presence of three of the following five criteria are diagnostic	Central Obesity plus two more of the following criteria are diagnostic	The presence of three of the following five criteria are diagnostic	Central Obesity plus two more of the following criteria are diagnostic
Waist Circumference	Men ≥ 102cm Women ≥ 88cm	Men ≥102cm Women ≥88cm	Men ≥90cm Women ≥80cm	Men ≥ 90cm Women ≥ 80cm	Men ≥94cm Women ≥88cm
Triacylglycerides	≥ 150mg/dL	≥ 150mg/dL	TAG ≥150mg/dL or receiving treatment	TAG ≥ 150mg/dL or receiving treatment	TAG ≥ 150mg/dL or receiving treatment
HDL-c	Men <40mg/dL Women <50mg/dL	Men <40mg/dL Women <50mg/dL	Men <40mg/dL Women <50mg/dL	Men <40mg/dL Women <50mg/dL	Men <40mg/dL Women <50mg/dL
Blood Pressure	≥130/85 mmHg	≥130/85 mmHg	≥130/85 mmHg or receiving treatment	≥130/85 mmHg or receiving treatment	≥130/85 mmHg or receiving treatment
Fasting Glycaemia	≥ 110 mg/dL	≥ 100 mg/dL	≥100 mg/dL or receiving treatment	≥100 mg/dL or receiving treatment	≥100 mg/dL, impaired glucose tolerance or diabetes.

Table 2. Anthropometric and laboratory variables in the studied population

	Women			**Men**			p
	Median	P05	P95	Median	P05	P95	
Weight (kg.)	63.00	47.00	88.00	76.50	55.50	102.00	0.000*
Height (mt.)	1.59	1.47	1.69	1.71	1.56	1.81	0.000*
Body Mass Index	25.10	19.20	35.06	26.57	19.61	34.72	0.091*
Waist Circumference (cm)	91.00	71.00	112.00	96.50	75.50	118.00	0.000*
Systolic Blood Pressure (mmHg)	120	95	162	120	100	160	0.014*
Diastolic Blood Pressure (mmHg)	80	60	100	80	60	99	0.116
Fasting Glucose (mg/dL)	94.00	79.00	133.00	95.00	81.00	134.00	0.317
Triacylglycerides (mg/dL)	134.00	55.00	345.00	146.00	61.00	531.00	0.042*
Total Cholesterol (mg/dL)	201.00	139.00	284.00	197.50	135.00	291.00	0.826
HDL-c (mg/dL)	55.00	37.00	78.00	52.00	33.00	71.00	0.001*
VLDL-c (mg/dL)	26.80	11.00	69.00	29.20	12.20	106.20	0.042*
LDL-c (mg/dL)	116.00	58.40	183.20	114.20	43.60	173.20	0.552
Uric Acid (mg/dL)	4.45	2.81	6.69	5.79	3.70	8.13	0.000*
Fasting Insulin (µIU/ml)	10.40	2.90	26.59	8.50	3.10	41.20	0.079

Figure 1.- Prevalence of Metabolic Syndrome according to five different classifications

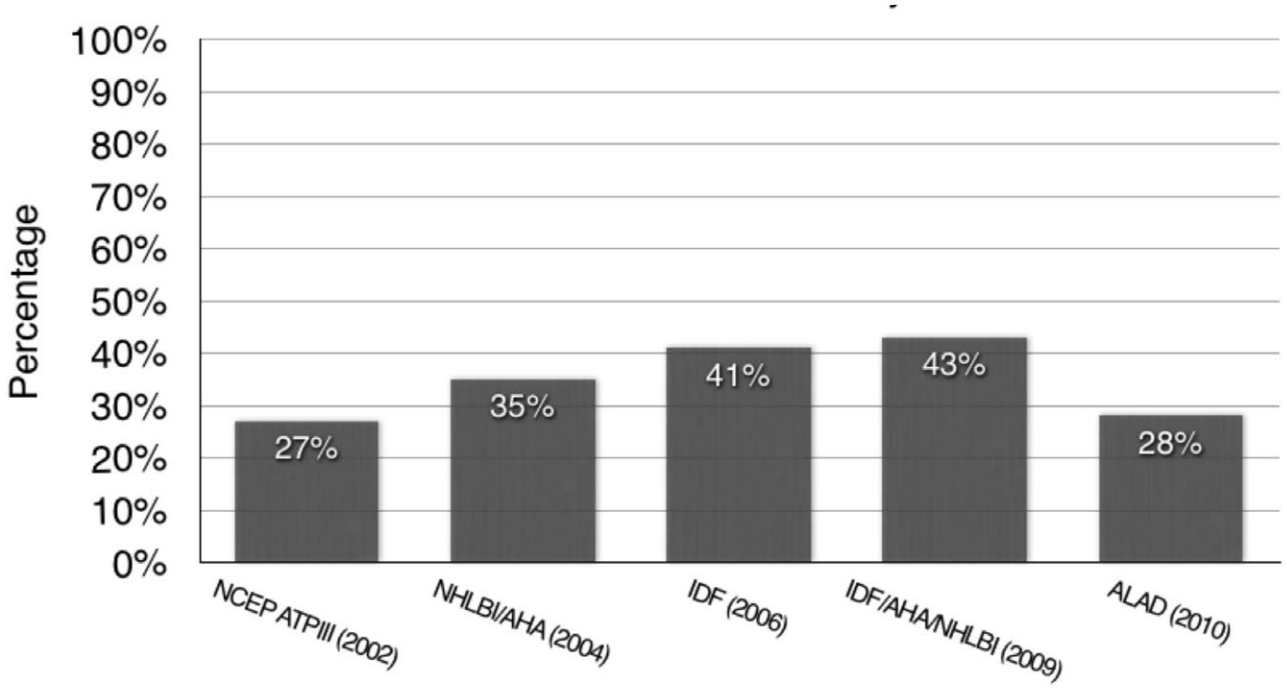

Figure 2.- Prevalence of Metabolic Syndrome according to age groups

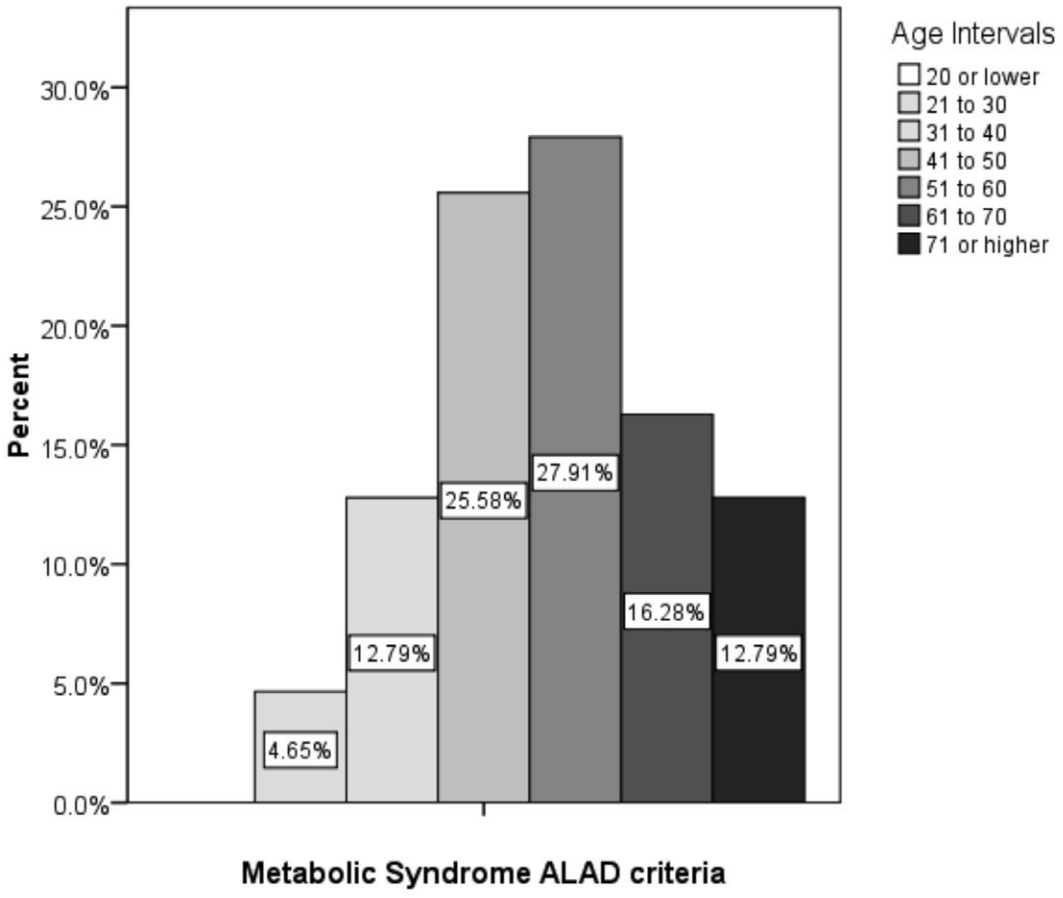

Table 3.- Positive Diagnostic Criteria among the population with Metabolic Syndrome					
Criteria*	**Central Obesity**	**Hypertriacylglyceridaemia**	**Hypertension**	**Hyperglycemia**	**Low HDL-c**
Yes	96.9%	72.7%	71.2%	62.1%	36.4%
No	3.1%	27.3%	28.8%	37.9%	63.6%

*The most prevalent criteria among the population with Metabolic Syndrome were central obesity, hypertriacylglyceridaemia and hypertension.

DISCUSSION

Changes in waist circumference cut-off and fasting glycaemia threshold contributed significantly in the variety of the prevalence rates. Consequently, these two variables are the main determinants of the wide variation in MS prevalence in our study observed to range between 27% and 43.1% according to 2002 ATP III and harmonizing criteria of IDF/AHA/NHLBI 2009, respectively (Figure 1). An 8% increase in MS prevalence was observed by reducing fasting glycaemia threshold from 110 mg/dL to 100 mg/dL and 1.5% difference by not considering central obesity mandatory criteria. Reinehr et al.[22] observed even wider variations among children diagnosed with MS with a prevalence between 6% and 39% due to the lack of homogeneity between different classifications. On the other hand, another similar study carried out by Ford et al.[23] does not show important differences when comparing WHO criteria (25.1%) and ATPIII criteria (23.9%) with an agreement of 86.2%. Nonetheless, the differences between these two classifications are placed in a higher blood pressure threshold for WHO (≥160/90 mmHg), the use of waist-hip ratio and the presence of microalbuminuria and not changes in fasting glycaemia threshold.

Comparable to our results are those observed in studies of Chien et al.[24] Santos et al.[25] and Kelliny et al.[26] In the Chien et al. study[24] conducted in a Chinese population prevalence rates ranged from to 29.8% in men and 25.6% in women (AHA) to 8.8% in men and 8.0% in women (WHO) although the k values were all above 0.59 observing a substantial level of agreement. Similarly, in the Santos et al.[25] study in a Portuguese community the prevalence of MS was found to be 26.4% (WHO), 24.0% (NCEP-ATP III), 41.9% (IDF) and 37.2% (AHA/NHLBI) also with good agreement between definitions. Similar to our study Kelliny et al.[26] observed a 32% reduction in MS prevalence upon exclusion of diabetic patients and k values were 0.82 for ATP-IDF, 0.61 for IDF-WHO and 0.59 for WHO-ATP, respectively and later 0.81, 0.53 and 0.51, upon exclusion of people with diabetes. Can et al.[27] in its methodological study also observed very good agreement between IDF and NCEP ATPIII definitions (k: 0.77–0.84) but not between ATPIII or IDF and WHO or EGIR definitions (k: 0.32–0.37). It suggests that MS criteria should be adjusted to the population in which it shall be applied to and that a universal MS definition might not be as good in terms of specificity when applied to different ethnic groups.

Our study has some limitations in terms of the k statistic interpretation. Kappa of Cohen value is significantly affected by the level of prevalence of the studied character, consequently we must be cautious when making general interpretations or extrapolations especially in such variable prevalence of MS as we observed in our sample.[28] Another limitation might be the lack of homogeneity in terms of gender representation, women were more likely to participate in the study than men (59.5% of the participants were women).

Another studies carried out in rural populations have demonstrated very marked differences in SM prevalence according to gender. Velásquez-Meléndez et al.[29] observed a prevalence of MS of 7.7% among men and 33.6% among women in the rural community of Virgem das Graças in Sao Paulo, Brazil. They attribute this difference to high waist circumference and low HDL-c among women of this community. Similar behaviour was observed by Gyakobo et al.[30] in Ghana, Africa and they describe it as an alarming female preponderance in terms of MS prevalence.

CONCLUSIONS

Several classifications have become available for clinicians to accomplish the MS diagnosis. It might result confusing and the question of which classification is the most accurate is always rising up. Nonetheless and after decades of discussion, the clinical usefulness of the MS diagnosis has been questioned and recent approaches are aimed to effectively treat and control cardiovascular risk factors as independent entities.[31] Molecular and pathophysiological links between type 2 diabetes, hypertension, obesity and dyslipidaemia have been widely described in the literature although the only therapeutic strategy recognized to be able to improve all these conditions at the same time are lifestyle changes including low intake diet and physical activity. Efforts worldwide are made to reinforce this therapeutic approach that has demonstrated to be superior to other pharmaceutical interventions.

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