ORIGINAL RESEARCH

Beyond the Definition of Metabolic Syndrome: Uric Acid, High Sensitivity C Reactive Protein and Global Cardiovascular Risk

Más allá de la definición de síndrome metabólico: ácido úrico, proteína c reactiva de alta sensibilidad y riesgo cardiovascular global

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ABSTRACT

Introduction: the metabolic syndrome is becoming one of the main problems in public health.
Objective: to evaluate the relation between metabolic syndrome and uric acid, high sensitivity c reactive protein, total cardiovascular risk and cardiovascular events.
Methods: a study of cases controls nested in a dynamic cohort was carried out in Velasco Teaching Polyclinic from 2010 to 2015, the cases were 67 patients that developed metabolic syndrome during the period and the control group were 67 patients matched by sex and age ± 5 years. The participants underwent a physical examination, anthropometry, laboratory test; all the study participants were under continuous surveillance during 4.5 years for development of cardiovascular events.

Results: the waist circumference (p = 0.000), systolic (p= 0.0042) and diastolic blood pressure (p= 0.0298), high sensitivity c reactive protein (p= 0.0039) and uric acid (p= 0.0283)   were significantly associate in both groups. The body mass index was higher than 30 kg/m^2 (OR 7.54; CI95%:3.35-16.9), LDL cholesterol greater than 4.16 mmol/l (OR 3.49; CI 95%:1.58-7.70) and hs CRP higher than 1 mg/dl (OR 3.59; CI 95%:1.51-8.51) showed statistically significant differences according to groups of studies. Global cardiovascular risk greater 20%, it was 3.84 times higher in the group with metabolic syndrome (CI 95%:1.67-8.82), 13.4% of the patients with metabolic syndrome developed a cardiovascular event during the period in comparison with the 2.9% in the group without metabolic syndrome (OR= 5.04; CI 95%: 1.04-24.3).

Conclusions: metabolic syndrome was significantly associated with mean level of uric acid, high sensitivity c reactive protein, total cardiovascular risk and cardiovascular events.

Keywords: metabolic syndrome, high sensitivity c reactive protein, uric acid, total cardiovascular risk, primary health care

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RESUMEN

Introducción: el síndrome metabólico se está convirtiendo en uno de los principales problemas de salud pública

Objetivo: evaluar la relación entre el síndrome metabólico y el ácido úrico, la proteína c reactiva de alta sensibilidad, el riesgo cardiovascular global y la incidencia de eventos cardiovasculares.

Métodos: se realizó un estudio de casos controles anidados en una cohorte dinámica en el Policlínico Docente de Velasco desde 2010 a 2015, los casos fueron 67 pacientes que desarrollaron síndrome metabólico en el periodo y 67 controles que fueron apareados por sexo y edad de ± 5 años en relación con los casos, los participantes fueron sometidos a un examen físico, determinaciones antropométricas y de laboratorio, fueron sometidos a seguimiento durante 4,5 años para la aparición de eventos cardiovasculares.

Resultados: mostraron que la circunferencia abdominal (p 0,000), la presión arterial sistólica (p 0,0042) y diastólica (p 0,0298), la proteína c reactiva de alta sensibilidad (p 0,0039) y el ácido úrico (p 0,0283) mostraron asociación estadísticamente significativa en ambos grupos. El índice de masa corporal mayor de 30 kg/m^2 (OR 7,54; IC 95%: 3,35-16,9), LDL colesterol mayor de 4,16 mmol/l (OR 3,49; IC 95%:1,58-7,70) y proteína c reactiva de alta sensibilidad mayor de 1 mg/dl (OR=3,59; IC 95%:1,51-8,51) mostraron asociación estadísticamente significativa de acuerdo con los grupos de estudio. El riesgo cardiovascular global mayor de 20% fue 3,84 veces mayor en el grupo con síndrome metabólico (IC 95 %: 1,67-8,82), el 13,4% de los pacientes con   síndrome   metabólico   desarrollaron   un   evento   cardiovascular   durante   el   periodo   de

seguimiento en comparación con el 2,9% en el grupo sin síndrome metabólico (OR= 5,04; IC 95%: 1,04-24,3).

Conclusiones: el síndrome metabólico se asoció significativamente con la concentración media de ácido úrico, con la proteína c reactiva de alta sensibilidad, el riesgo cardiovascular global y el desarrollo de eventos cardiovasculares.

Palabras clave: síndrome metabólico, proteína c reactiva de alta sensibilidad, ácido úrico, riesgo cardiovascular total, atención primaria de salud.

INTRODUCTION

Metabolic syndrome (MetS) is a combination of medical disorders that, including obesity, insulin resistance, impaired glucose metabolism, dyslipidemia of high triglycerides, low level of high density lipoprotein cholesterol (HDLc) and elevated blood pressure, when occurring together, increase the risk of developing cardiovascular disease and diabetes. It has become a major public health challenge worldwide[1, 2].

Since the first official definition of the MetS by a World Health Organization Working Group in 1999, a number of alternative definitions have been proposed. The most widely accepted of these have been produced by the European Group for the Study of Insulin Resistance (EGIR), International Diabetes Federation (IDF) and the National Cholesterol Education Program Adult Treatment Panel III (ATP III) [3].

Although a consensus criterion has not been reached for diagnosing MetS, it is recommended that screening should consider central obesity, insulin resistance; dyslipidemia (elevated triglycerides and low density lipoprotein cholesterol (LDLc)) and decreased high density lipoprotein cholesterol (HDLc), and high blood pressure. Other factors such as proinflammatory and prothrombotic states have also been associated with MetS [4].

These various definitions differed not only in the proposed components but also in the cut-off points used for each component, leading to considerable confusion, the confusion relates not only to the usefulness in the clinical setting but also was apparent in attempts to compare the burden of the MetS in different populations[3,5].

There is an abundance of widely varying data comparing prevalence using different criteria and this only served to reinforce the need for a standardized definition internationally. There is an urgent need to rationalize the variety of definitions that had been developed for the MetS. This need should be extended from clinical practice through to research[5].

The construct of the MetS diagnostic criteria has inherent limitations which impact on its clinical usefulness, it does not include other important risk factors for predicting diabetes or cardiovascular disease (CVD), such as age, sex, family history socioeconomic status, ethnicity, current treatment, previous CVD events and LDLc, C reactive protein, uric acid or important behavioral variables such as smoking and physical activity[5, 6].

The MetS has proposed as a means to identify people with increased risk of cardiovascular disease and type 2 diabetes mellitus (T2DM) and to guide the clinical decisions and it has shown its utility to predict the morbidity and mortality for cardiovascular diseases and diabetes.

Cardiovascular disease often occurs in people with considered acceptable or average risk factors values, this suggests that there are other risk factors that must be the cause of this disease. If these factors were considered to the present set of CVD risk factors, it would improve risk estimation. A number of risk factors, some of them new and often called novel risk factors, have been proposed: inflammatory markers such as C-reactive protein, coronary calcium, lipoprotein (a), interleukin-6, fibrinogen, homocysteine, insulin resistance, MetS, platelet function, and genetic scores[7].

The aim of this study was to evaluate the relation between MetS and uric acid, high sensitivity c reactive protein, global cardiovascular risk and cardiovascular events.

METHODS

A nested case control study in a dynamic cohort of 309 patients was carried out, the sample were 134 patients, with age between 35 to 74 years, without cardiovascular disease at baseline, of the Jose Avila Serrano Teaching Polyclinic, from Velasco, Holguin, during January 2010 to December 2015.

The cases were 67 patients that developed MetS during the period, according to definition of the ATP III proposed in 2005 by American Heart Association y and the National Heart, Lung, and Blood Institute[3] and the controls were 67 patients matched by sex and age ± 5 years, MetS was considered if the patients have three of the five criteria: abdominal obesity (waist circumference

≥ 102 cm in male and ≥ 88 cm in female), elevated triglycerides ≥ 1.70 mmol/l, decreased high-density lipoprotein cholesterol < 0.9 mmol/l in male y   < 1.1 mmol/l in female, elevated blood pressure ≥ 130 mmHg for systolic or ≥ 85 mmHg for diastolic blood pressure or blood pressure treatment, and fasting glucose level ≥ 5.55 mmol/l (100 mg/dl) or T2DM previously diagnosed[3].

The participants underwent a physical examination, anthropometry, blood pressure determination, blood pressure measurements were made on the right arm of the seated participants with a aneroid sphygmomanometer and an appropriately sized cuff; the average of two physician-obtained measures constituted the examination blood pressure; waist circumference was measured (cm) at level of the navel; cigarette smoking status was ascertained if the patients smokes or had smokes in the last six months, past history of diabetes and hypertension was ascertained by the physician; serum total cholesterol and HDLc, LDLc, calculated according to Friedewald formula. Uric acid, glycaemia, high sensitivity c reactive protein (hs CRP) levels were determined with standardized enzymatic methods; hs CRP were determined in two times with an interval of 15 days, being used the value average of both measurements.

The global cardiovascular risk to the ten years was stratified using Framingham - D´Agostino (2008)[8] risk table, that it use for the calculation of the risk: age, sex, smoking, diabetes mellitus, treated or untreated systolic blood pressure, total cholesterol and HDLc, classifying the patients as low risk (< 10%), among 10-20% as intermediate risk and > 20% as high risk.

All the study participants were under continuous surveillance during 4.5 years; for development of cardiovascular events or death. Study defines hard cardiovascular events if the patients developed a myocardial infarction, ischemic stroke, hemorrhagic stroke mortal or no, and coronary death, and it was considered all cardiovascular events if the patient developed hard events plus coronary angina, transitory ischemic attack and peripheral arterial disease.

The means, standard deviation and percentages were calculated. Student t test was used to compare mean of the independent samples with significant value of $p < 0.05$ and Odd Ratio (OR) with 95% confidence intervals, the data was coded and processed using the Statistical Package for Social Sciences (SPSS, version 15) and Med Calc software (version 4.16g).

All participants provided written informed consent, and the study protocol was approved by the Institutional Review Ethics Committee at the Jose Avila Serrano Teaching Polyclinic.

RESULTS

In the cases and controls groups there were 49 women (73.1%) and 18 men (26.9%). The results showed that in the studied population the waist circumference, systolic and diastolic blood pressure, level of high sensitivity c reactive protein and mean uric acid levels were significantly associated in both groups (table I)

Table I. Characteristic of the study population.

Variable	Metabolic Syndrome	n	Means	Standart Deviation	Difference Between means	95% Confidence Interval	P value
Age (years)	Yes	67	56.2	± 11.8	1,8	-2.15-5.75	0.3688
	No	67	54.4	±11.3			
Waist Circumference (cm)	Yes	67	104.3	±11.7	15.1	11.44-18.76	0.0000
	No	67	89.2	±9.6			
Systolic Blood Pressure (mmHg)	Yes	67	142	±23.2	10.8	3.48-18.12	0.0042
	No	67	131.2	±19.5			
Diastolic Blood Pressure (mmHg)	Yes	67	86.9	±12.3	4.5	0.45-8.55	0.0298
	No	67	82.4	11.4			
Total Cholesterol (mmol/l)	Yes	67	5.54	±1.31	0.38	-0.06-0,82	0.0968
	No	67	5.16	±1.32			
LDL cholesterol (mmol/l)	Yes	67	3.22	±1.39	0.23	-0.23-0.69	0.3261
	No	67	2.99	±1.31			
Uric Acid (µmol/l)	Yes	67	348.6	±166.3	59.7	6.47-112.9	0.0283
	No	67	288.9	±144.5			
Hs CRP (mg/dl)	Yes	67	3.8	±2.8	1.3	0.42-2.18	0.0039
	No	67	2.5	±2.3			

LDLc: Low density lipoprotein cholesterol

Hs CRP: High sensitivity c reactive protein

The proposed components   of MetS according to the ATPIII definition (table II) showed statistically significant differences between both groups.

Table II. Factors considered as identifying abnormalities of metabolic syndrome according to ATP III definition.

Factors	Metabolic Syndrome* n=67 n (%)	No Metabolic Syndrome n=67 n (%)	OR	95 % CI
Waist Circumference	48(71.6)	15(22.4)	7.54	3.35-16.9
Increase BP or Past history HBP	50(74.6)	27(40.3)	4.35	2.08-9.09
Increase fasting glucose or Diabetes Mellitus	26(38.8)	4(5.9)	9.98	3.24-30.7
Triglycerides	54(70.1)	28(41.8)	5.78	2.66-12.57
HDL cholesterol	37(55.2)	14(20.9)	4.67	2.18-9.99

Met S: Metabolic Syndrome

HBP: High Blood Pressure

HDLc: High- density lipoprotein cholesterol

* Diagnosis of metabolic syndrome according to ATP III, 2005 (Adult Treatment Panel III)[3]

- Elevated waist circumference: ≥ 102 cm in men and ≥ 88 cm in women

- Elevated blood pressure: 130 mm Hg systolic BP or 85 mm Hg diastolic BP or, drug treatment for hypertension.

- Elevated fasting glucose 100 mg/dl or drug treatment for elevated glucose

- Elevated triglycerides:> 1.70 mmol/l

- Reduced   HDL cholesterol: <0.9 mmol/l in men and <1.1 mmol/l in women

Other factors that increased the probability of MetS were body mass index more than 30 kg/m², LDL cholesterol level more than 4.16 mmol/l   and level of hs CRP higher than 1 mg/dl showed statistically significant differences according to groups of study (table III).

Table III. Factors that increased probability of the metabolic syndrome.

Factors		Metabolic Syndrome n=67 n (%)	No Metabolic Syndrome n=67 n (%)	OR	95 % CI
Smoking	Yes	19(28.4)	20(29.8)	0.93	0.44-1.96
	No	48(71.6)	47(70.1)	1.07	0.51-2.26
Body Mass Index (kg/m^2)	< 24.9	9(13.4)	32(47.8)	0.16	0.07-0.39
	25-29.9	20(29.8)	24(35.8)	0.76	0.36-1.57
	> 30	40(59.7)	11(16.4)	7.54	3.35-16.9
Total Cholesterol (mmol/l)	< 6	44(65.7)	52(77.6)	0.55	0.65-1.18
	6-7.2	14(20.9)	9(13.4)	1.70	0.68-4.25
	> 7.2	9(13.4)	6(8.9)	1.57	0.52-4.70
LDL Cholesterol (mmol/l)	< 3.37	25(37.3)	40(59.7)	0.40	0.20-0.80
	3.38-4.13	13(19.4)	15(22.4)	0.83	0.36-1.92
	> 4.16	29(43.3)	12(17.9)	3.49	1.58-7.70
Uric acid (μmol/l)	> 440(Male) >350(Female)	27(40.3)	20(29.8)	1.58	0.77-3.24
Hs CRP (mg/dl)	< 1	9(13.4)	24(35.8)	0.27	0.12-0.66
	> 1	58(86.6)	43(64.2)	3.59	1.51-8.51

LDLc: Low-density lipoprotein cholesterol

Hs CRP: High sensitivity c reactive protein

Total cardiovascular risk greater 20% was 3.84 times higher in the group with MetS (95 % CI: 1.67-8.82) and 13.4% of the patients with MetS developed a cardiovascular event during the period in comparison with 2.9% of patients in the group without MetS (OR= 5.4; 95% CI: 1.04-24.3) (table IV)

Table IV. Global cardiovascular risk and cardiovascular events according to study groups.

Variable		Metabolic Syndrome n (%)	No Metabolic Syndrome n (%)	OR	95 % CI
Global Cardiovascular Risk	< 10 %	19(28.4)	29(43.3)	0.51	0.25-1.06
	10-20 %	21(31.3)	28(41.8)	0.63	0.31-1.29
	> 20 %	27(40.3)	10(14.9)	3.84	1.67-8.82
Cardiovascular Events*	Hard	5(7.5)	1(1.5)	5.32	0.60-46.8
	All	9(13.4)	2(2.9)	5.04	1.04-24.3

* Followed by 4.5 years

DISCUSSION

Among the contributing major cardiovascular risk factors, an increased waistline, elevated triglycerides, impaired fasting plasma glucose, high systolic blood pressure and low levels of HDL cholesterol are referred to as MetS[3,9]. Obesity is a growing burden worldwide; hence, forecasts predict an increase in prevalence from 35%, to 51% by 2030 in US Americans[9].

In this research the waist circumference (p 0.0000) was significantly associated in both groups (table I) and the BMI > 30 kg/m^2 showed significantly statistical differences (OR 7.54; 95 % CI: 3.35-16.9) (table III).

In spite of the fact that high BMI values are associated with adverse risk profiles for morbidity and mortality, particularly in relation to T2DM and atherothrombotic cardiovascular disease, various sub-types of obesity have been described which complement the apparent dose-response relationship between BMI and its impact on health. The most classic sub-types are android obesity (abdominal) and gynoid obesity (gluteal obesity) [10].

Less well-known sub-types are, however, also of interest. For example, a phenotype corresponding to metabolically obese normal-weight (MONW) individuals has been reported, these individuals have a normal BMI together with some of the characteristics of obese individuals such as insulin resistance, central adiposity, low levels of HDL and high levels of triglycerides, and high blood pressure. At the same time, metabolically healthy obese (MHO) individuals have also been identified. These individuals have BMI>30, but none of the metabolic alterations which are typical of obese individuals[10].

The existence of these 2 "paradoxical" sub-types led to several studies over the last 2 decades which contributed to metabolically characterization and quantify visceral adipose tissue as opposed to subcutaneous adipose tissue. These studies showed that the quantity of visceral adipose tissue is directly correlated in both men and women with a seriously altered metabolic risk profile which leads the development of T2DM and cardiovascular disease. Therefore, although it is true that obesity increases the risk of chronic disease, it seems clear that patients with visceral obesity constitute a sub-group of individuals with the most serious metabolic alterations[10].

Indeed, adipose tissue is no longer regarded as a simple long-term storage organ for fatty acids but rather appreciated as an important role in the metabolism of lipids and glucose, since numerous hormones and proinflammatory cytokines are released from adipocytes themselves, macrophages, fibroblasts and endothelial cells, early, primary inflammatory changes in adipose

tissue have consequently been identified to play a key role in systemic inflammation, atherosclerosis and cardiovascular death[9,11].

It has been demonstrated that excess body fat, abdominal visceral fat, and larger waist circumference have been associated with accelerated arterial stiffening. Abdominal obesity has been associated with an adverse effect on blood vessels, independently of age, sex, blood pressure, fasting glucose and BMI. Combination of diabetes mellitus and abdominal obesity, but not overall obesity, has been associated with significant deterioration in terms of arterial stiffness parameters. Body fat distribution is one of the major determinants of metabolic health, and visceral adiposity has a stronger correlation with metabolic abnormalities and cardiovascular disease than subcutaneous adipose tissue[11].

The mean level of uric acid was significantly associated in both groups (table I) but the level more than 440 and 350 µmol/l in male and female respectively were not significantly associated in the groups with and without MetS (table III).

Serum uric acid (UA) is a strong predictor of stroke, coronary artery disease, and MetS, however, the definite role of uric acid in these diseases is still the subject of much discussion and debate because it is always accompanied with other risk factors such as diet, obesity, and dyslipidemia. Specifically, disputation exists about whether serum uric acid is a causative risk factor or only a coexisting marker of those pathologic processes[12].

However, few studies have investigated the predictive role of UA levels, and studies that investigate the relation between UA and MetS criteria in patients previously detected with cardiovascular risk are still scarce[13]. Abreu da Silva, et al found higher UA levels in subjects showing MetS when compared to those who did not[13] , previous epidemiologic studies have also shown increased serum UA levels in adults with MetS, as well as an association between increased UA levels and oxidative stress, endothelial dysfunction, inflammation, atherosclerosis, and increased risk of cardiovascular events[13-15].

BMI and total body fat, indicators of total adiposity; and waist circumference, indicator of central adiposity, showed an association with UA levels[13], therefore, the independence of the associations of hyperuricaemia with atherosclerosis and CVD has remained controversial[15], given that low-grade inflammation and insulin resistance are two important risks factors for MetS, uric acid may play a key role in the pathogenesis of MetS that is partially mediated by an inflammatory pathway, additionally, uric acid might play a causal pathogenic role in the cause of MetS that could possibly be mediated by the inhibition of endothelial function[14,15] .

Evidence from prospective and interventional studies of various populations suggests that gout and hyperuricaemia are independent risk factors for cardiovascular diseases, the mechanisms linking hyperuricaemia and gout with cardiovascular events are unclear but may include oxidative stress generated by xanthine oxidase (XO), the enzyme that catalyses the formation of urate, other explanations are a direct contribution to endothelial dysfunction and low-grade inflammation associated with increased urate levels and tophi[16].

During the recent years, an increasing number of publications have supported that allopurinol might have a benefit effect in a variety of cardiovascular diseases, and may provide a survival benefit among patients with hyperuricaemia. Indeed, allopurinol, a free radical scavenger, was found to improve both endothelial dysfunction and levels of some markers of oxidative stress[16].

The precise mechanism by which allopurinol exerts a beneficial effect on the cardiovascular system is poorly known, the drug is thought to act mainly through an increase in the bioavailability of endothelium derived nitric oxide, presumably by blocking the production of reactive oxygen species generated by the XO activity[16].

Recent data have also suggested that the cardiovascular benefit of allopurinol in patients with heart failure might be due to its urate lowering property, although this point is a matter of debate. Indeed, post hoc analyses of clinical trials have suggested that the reduced vascular risk afforded by therapeutics, such as atorvastatin and losartan which are not XOs, was due to their urate lowering property[16].

The pathophysiological mechanism by which the MetS increases cardiovascular risk remains under debate; earlier definitions by the World Health Organization and the EGIR emphasize the independent role of insulin resistance as the underlying component of the MetS. Insulin resistance progresses toward hyperinsulinemia and hyperglycemia, thus triggering peripheral vasoconstriction and sodium retention. Hepatic production of very low-density lipoprotein also increases, leading to hypertriglyceridemia, low HDL cholesterol, elevated apolipoprotein B, elevated small LDL cholesterol, and consequently, atherosclerosis, as a result of these lipid imbalances, individuals with the MetS typically exhibit a prothrombotic and proinflammatory state[17, 18].

Adipocytes secrete mediators including Tumor Necrotic Factor (TNF), leptin, adiponectin, and resistin, which lead to insulin resistance, it is postulated that central obesity causes systemic hypertension and dyslipidemia independently and through the induction of insulin resistance[18].

At least half of the attributable risk in patients who end up with a thrombus or atherosclerosis is caused by this inflammatory response, major meta-analyses have shown that if you measure inflammation using the high-sensitivity C-reactive protein (hs-CRP) test, the magnitude of risk associated with hs-CRP is larger than the magnitude of risk of high blood pressure or high cholesterol[19, 20].

However, all of these parameters are associated with elevated levels of hs-CRP, an easily measured inflammatory biomarker that has proven to be a strong, independent predictor of both incident diabetes and incident cardiovascular disease, CRP levels also correlate with several other components such as fasting insulin, microalbuminuria, and impaired fibrinolysis that are not easily evaluated in usual clinical practice[19- 21].

Rapidly evolving work now demonstrates that in addition to being a marker of innate immunity, CRP also has several direct effects at the level of the vessel wall, these observations, along with basic research into the inflammatory mechanisms of both diabetes and vascular dysfunction, provide strong evidence that insulin resistance and atherosclerosis share a common inflammatory basis, CRP, however, is also associated with several aspects of the MetS not easily ascertained in usual clinical practice, including fasting insulin, hypofibrinolysis, and microalbuminuria[19]

MetS is associated with increased oxidative stress, furthermore, it appears that some component pathologies of the MetS contribute to a higher percentage of total oxidative stress than others; however, additional studies are needed to determine the exact contribution of individual components to total oxidative stress[4].

In this study no differences in the smoker in the groups were found, this can be explained by the prevalence of women in both groups, smoking and air pollution interact with the MetS which are not insufficiently assumed, but they clearly combined to deliver a cardiovascular risk factor which is greater than the sum of each of them.

Smokers and ex-smokers are more likely to have MetS than nonsmokers, both cigarette smoking and the MetS are strong independent risk factors for cardiovascular disease; however, smoking also potentiates the negative cardiovascular effects of the MetS. For example, MetS is associated with higher rates of cardiac events after acute myocardial infarction and smoking has an additive effect. These effects are largely mediated via Reactive Oxygen Species (ROS) generation[4].

There is an increasing interest in the development of novel biomarkers and imaging methods to refine CV risk prediction, The Emerging Risk Factors Collaboration has explored the benefit of

including lipid-related markers [i.e. apolipoprotein B, apo-lipoprotein A-I, lipoprotein (a), or lipoprotein-associated phospholipase A2] in prognostic models for CV disease risk prediction[22-25].

MetS was commonly defined by the presence of obesity, diabetes, hypertension, and dyslipidemia, and these factors were involved in the mechanisms of insulin resistance, inflammation, and atherosclerosis, but does not include other novel risk factor, the tools for prediction of cardiovascular risk include other different risk factors and both (MetS and scores for cardiovascular risk prediction) do not include other risk factors, with the improving of knowledge on metabolic syndrome and the prediction of cardiovascular risk the investigators have opportunities for the certain identification of novel biomarkers or risk factors that could be considered for cardiovascular disease and the prevention of the cardiovascular diseases is based in the opportune identification in the primary health care with the biggest precision possible of the people with risk of developed cardiovascular disease[26-28].

Specific strengths of the present study were the use of nested case control study in a dynamic cohort design tended to results in estimated with lower bias and greater precision, controls matched to cases on classical matching factors (eg, age, sex); a limitation of this study was its small sample due to lack of laboratory reagents and suitable technology that did not allow to investigate more people.

CONCLUSIONS

In conclusion, this research showed relation statistically significant between the MetS and the mean level of uric acid, the level of hs CRP higher than 1 mgl/dl, level of LDLc greater than 4.16 mmol/l, the global cardiovascular risk higher than 20% and the incidence of all cardiovascular events.

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