Metabolic Syndrome in Patients with High Blood Pressure in Cuiabá - Mato Grosso State: Prevalence and Associated Factors

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Summary

Background: **Metabolic Syndrome (MS) is a cluster of predisposing factors for cardiovascular diseases and diabetes mellitus, whose epidemiological characteristics are poorly known at regional and national levels.**

Objective: **To estimate the prevalence of MS and its associated factors in a sample of patients with high blood pressure in the urban area of Cuiabá, Mato Grosso State.**

Metods: **This was a cross-sectional study (May to November 2007) in a sample of 120 patients with high blood pressure (aged ≥ 20 years), paired by gender and selected by the systematic sampling of a source population of 567 patients with high blood pressure in Cuiabá. All patients answered to home inquiries to provide sociodemographic and life habits data. The following measurements were taken: blood pressure; body mass index (BMI); waist and hip circumferences; plasma glucose, insulin, and lipid levels; homeostasis model assessment-estimated insulin resistance (HOMA); C-reactive protein, uric acid and fibrinogen levels. High blood pressure criterion: average systolic blood pressure ≥ 140mmHg and/or diastolic blood pressure ≥ 90mmHg; and Metabolic Syndrome diagnosis according to the I Brazilian Directive for Metabolic Syndrome and the NCEP-ATP III criteria.**

Results: **120 patients (60 women), with high blood pressure and an average age of 58.3 ± 12.6 years, were analyzed. We found a MS prevalence of 70.8% (95%CI 61.8 to 78.8), predominantly among women (81.7% vs. 60.0%; p=0.009), with no difference between adults (71.4%) and elderly patients (70.2%). The multiple regression analysis showed a positive association between MS and BMI ≥ 25 kg/m², insulin resistance and family history of high blood pressure.**

Conclusion: **A high prevalence of MS was observed among patients with high blood pressure living in Cuiabá, with a significant association with BMI > 25 kg/m², insulin resistance (HOMA index) and, especially, a family history of high blood pressure. These results suggest the need for deeper studies on this subject. (Arq Bras Cardiol 2009; 92(6) : 437-442)**

Key Words: **Metabolic syndrome; hypertension; risk factors; Cuiaba (MT); Brazil.**

Introduction

Metabolic Syndrome (MS) is a clinical condition in which some cardiovascular risk factors coexist in a higher prevalence than that found in the general population. From the initial description and studies by Reaven (1988), MS has been defined as the combination of several metabolic and hemodynamic abnormalities in the same individual, and which share the same pathophysiological basis: resistance to insulin[1]. These factors are: blood pressure (BP) ≥ 130 x 85mmHg; insulin resistance; changes in the metabolism of glucose (fasting plasma glucose > 100 mg/dl, or type 2 diabetes); central obesity (waist circumference ≥ 102 cm in men and 88 ≥ cm in women);l abnormal lipid levels (HDL < 40 mg/dl in men or < 50 mg/dl in women; triglycerides > 150 mg/dl); blood clotting disorders; pro-inflammatory state; and microalbuminuria[2-4]. The term Metabolic Syndrome, proposed by the World Health Organization (WHO) in 1998, helped reformulate the understanding that multiple cardiovascular risk factors, not related by chance, concurrently affect the development of atherosclerosis. The term MS, which is the most widely accepted today, was preceded by others: insulin resistance syndrome; plurimetabolic syndrome; Syndrome X; and deadly quartet. MS can increase overall mortality by about 1.5 times and cardiovascular mortality by approximately 2.5 times[3]. High blood pressure (HBP), an important component of MS that occurs with the highest prevalence in obese and type 2 diabetes populations, is the main cause of early cardiovascular mortality in the world, especially from cerebral vascular accident (CVA)[5,6]. The prevalence of MS is high and variable (13.7% to 39%), and according to some studies, it is predominant in women[7-10]. Epidemiological studies have confirmed its occurrence in different ethnic groups: Europeans, African-Americans, Mexican-Americans, Asians, Chinese, Aboriginal Australians, Polynesians and Micronesians[11]. The existence of a molecular link (gene or genes) unifying the pathophysiology of MS, suggested by several studies, lacks more consistent evidence[11]. In Brazil, there is a growing interest in finding out the epidemiological features of this syndrome[4]. The objective

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of this study is to estimate the prevalence of MS, and its association with certain risk factors, in hypertensive patients from Cuiabá, Midwest Brazil.

Methods

This was a cross-sectional study that used the database of the study on "Prevalence and Awareness of High Blood Pressure and some Risk Factors in a Region of Brazil", conducted by the Institute of Collective Health and the School of Medical Sciences (Federal University of Mato Grosso - UFMT), in cooperation with the Federal University of Goiás - UFG (Hypertension League and School of Medicine). The source population was entirely composed of subjects (N = 567) who had been classified as having high blood pressure in a previous study on prevalence of high blood pressure in Cuiabá, Mato Grosso State, conducted from February 2003 to August 2004[12]. The estimated prevalence of high blood pressure in this study was of 33.4%. Through systematic sampling, which estimated the population density of the areas, a population sample of 120 individuals, matched by gender, aged 20 years or over, was calculated. We excluded bedridden and disabled individuals, pregnant women, nursing mothers and housemaids. The 120 participants answered a pre-tested questionnaire on socio-demographic data, living habits (consumption of salt and fat, physical activity, smoking, and alcohol drinking habit), awareness, treatment and control of high blood pressure, and family history of high blood pressure, coronary artery disease (CAD) and stroke. Three measurements of blood pressure (BP) were taken, with an interval of 10 minutes between each one , and the average of the last two measurements, classified according to the V Brazilian Guidelines on High Blood Pressure (2006), were taken into account[13], with the use of an electronic, automatic, oscillometric sphygmomanometer (OMRON HEM-705 PC), which had been endorsed and recommended by relevant international institutions for epidemiological studies[14]. The measurements were taken with the subjects in a sitting position, with their feet on the floor, their left arm relaxed and supported on the table, at heart level, palm upwards, bladder empty, without having practiced moderate or heavy exercise, smoked or drunk alcohol in the 30 minutes before the measurements. A cuff that was compatible with the arm circumference was used. Height and weight were measured with a SECA BODY METTER 208 stadiometer and a PLENNA LITTHIUM DIGITAL MEA 08128 scale to calculate the Body Mass Index (BMI) and classify the nutritional state[15]. The waist circumference (WC) was measured with an inextensible CARDIOMED metallic measuring tape, wrapped around the bare abdomen, taking as parameter the narrowest part of the trunk between the chest and the hips. The waist-hip ratio (WHR) was calculated. The WC was classified as severely increased or increased, by the WHO criteria (1998), and the waist-hip ratio (WHR) was classified as increased (> 1 for men, and > 0.85 for women)[15].

A venous blood sample was collected (after 12 hours of fasting), by a puncture in the antecubital fossa, for determination of: fasting glucose; serum lipids; serum uric acid (enzymatic method); insulin (chemiluminescence); C-reactive protein (CRP); and fibrinogen (turbidimetry). The homeostasis model assessment-insulin resistance index (HOMA) was calculated with the formula: glucose (mg / dL) x 0.0555 x insulin / 22.4. We adopted the cutoff point of 2.71 for the definition of insulin resistance[16], and the IV Brazilian Guidelines on Dyslipidemia and Prevention of Atherosclerosis criteria for serum lipids[17].

Abnormalities and definitions criteria

Dependent Variables - Metabolic Syndrome, criterion of the "I Brazilian Guidelines on Diagnosis and Treatment of Metabolic Syndrome" (IDBSM)[3], that used the National Cholesterol Evaluation Program for Adult Treatment Panel III (NCEP-ATP III) criteria[18].

Independent Variables - High blood pressure, criterion of the "V Brazilian Guidelines on Hypertension"[13], systolic blood pressure (SBP) ≥ 140 mmHg and / or diastolic blood pressure (DBP) ≥ 90 mmHg. Overweight - defined by the BMI (weight/height^2) (> 25 kg/m^2 and <30kg/m^2) and obesity (body surface area > 30kg/m^2; central obesity defined by the WC cut-off points of 102 cm for men and 88 cm for women). Serum lipids (12-hour fasting) defined by the criterion of the IV Brazilian Guidelines on Prevention of Dyslipidemia and Ateroesclerose[17]. Total cholesterol, triglycerides and glucose levels were determined by enzymatic colorimetric test, and LDL levels were calculated with the Friedwald formula[18,19] (for triglycerides <400 mg/dl). Total cholesterol: fine (≤ 200%), borderline (200 to 239mg%), high (≥ 240 mg%). LDL cholesterol: fine (<100 mg%), borderline (130 to 159mg %), high (160 to 189 mg%), very high (≥ 190mg%). Low HDL cholesterol: < 40mg%, high HDL cholesterol: > 60 mg%. Glucose (12-hour fasting): disglycemia or high (between 100 and 125mg%); diabetes mellitus (≥ 126 mg%)[17]. Insulin (12-hour fasting): by chemiluminescence, expressed in μU / ml. Determination of C-reactive protein (12-hour fasting): by turbidimetric method, expressed in mg/l, with a cutoff point for high CRP of 3mg/dl[20]. Serum uric acid (12-hour fasting): high (> 7mg/dl for men and 6mg/dl for women)[21]. Fibrinogen (12-hour fasting): high (> 4mg/l)[22].

Independent socio-demographic variables - Age ≥ 20 years; gender: male or female; marital status: with or without a partner; education, income, number of household members; eating habits: use of salt, consumption of fats, caloric intake; physical activity: inactivity - defined as self-reported occupational, commuting and leisure-time physical inactivity; smoking habit: smoker - at least one cigarette per day; former smoker - an individual who regularly smoked in the past and completely abandoned the smoking habit; alcohol: use of alcohol - frequency, type and amount ingested. Family history - parents or first-degree relatives, aged < 60 years, with a history of hypertension, myocardial infarction or stroke.

For data management and analysis, a database was organized with the programs Microsoft Office Access 2003, Epi Info 2000 (version 11.0, for exploratory, bivariate and stratified analysis), and SPSS (version 3.3.4, for multiple analysis). For the whole group, stratified by gender, and for independent variables, MS prevalence rates, 95% confidence intervals (CI), and measures of association were calculated. The association between independent variables and MS was tested with the chi-square Pearson test. For continuous

variables, the hypothesis of normality was tested with the Kolmogorov-Smirnov test. The means of the variables with normal distribution were compared with the Student t-test, and the non-parametric Mann-Whitney test was used for the variables which did not present a normal distribution. The critical level of significance adopted for the rejection of the null hypothesis was up to 5% ($p < 0.05$). The forward stepwise method was used for multiple logistic regression analysis.

This study was approved by the Research Ethics Committee of the University Hospital Julio Muller (HUJM). A term of free and informed consent was used, according to the Resolution 196/96 of the National Health Council of October 10th,1996.

Results

Of the 120 study participants, 60 were women. The average age of the study population was 58.3 ± 12.6 years, with no difference regarding gender, age (adult and elderly), and family history of hypertension. The overall prevalence of MS among hypertensive patients was 70.8%, significantly higher among women (81.7% vs 60%, PR = 1.36, 95% CI 1.07 to 1.73). Fifteen percent of the hypertensive patients had five criteria of MS, and 21.7% had four criteria of MS (Figure 1). The bivariate analysis showed significant association between MS and gender, family history of hypertension, BMI greater than 25 kg/m², severely increased WC and increased WHR. There was no association with other socio-demographic variables, sedentary lifestyle, smoking, alcohol or food habits (Table 1).

Regarding the laboratory variables, there was an association between MS and low HDL-cholesterol, high VLDL-cholesterol, high uric acid, and the presence of insulin resistance (Table 1).

The multiple regression analysis showed a statistically significant ORadj for associations between MS and BMI ≥ 25kg/m², insulin resistance and the presence of first-degree relatives with hypertension (Table 2).

Discussion

This work is part of a larger project that aims at describing some epidemiological characteristics associated with hypertension in the Midwest of Brazil, in several cities of the States of Goiás (Goiânia and Firminópolis) and Mato Grosso (Cuiabá and Nobres). The objective of this cross-sectional study was to present the analysis of some of the characteristics of metabolic syndrome among hypertensive individuals from Cuiabá, Mato Grosso. The sample selection took into account the population proportionality of each urban macrozone. Data were collected by household survey, which was standardized and previously implemented through a pilot study. Despite the well defined criteria for the diagnosis of MS, a variety of factors makes it difficult to compare prevalence rates among different populations. In specific populations, it may occur with different individual components[23]. Differences in the distribution by sex, age, diet, and level of physical activity, as well as genetic and ethnic characteristics, may affect the proportions of the various components of MS. Therefore, the prevalence rates found in this study are representative of an urban, heterogeneous, ethnically mixed population of adults, aged over 20 years, in the Midwest region of the country.

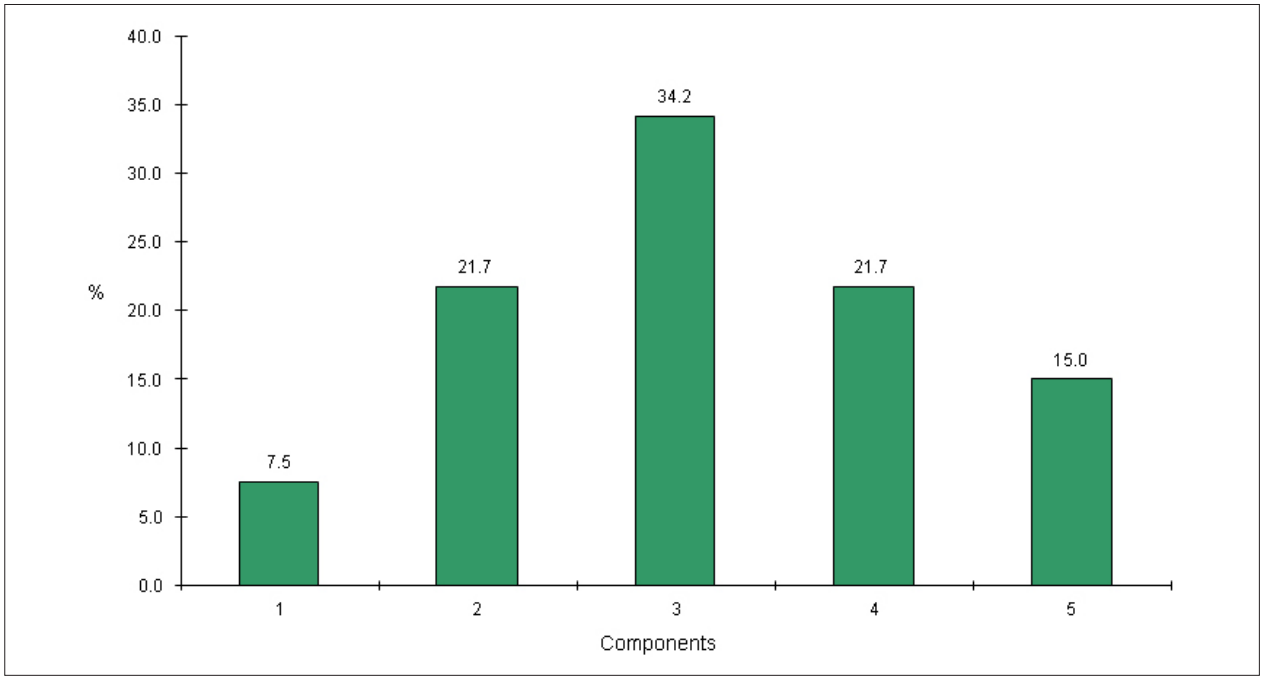

Figure 1 - Distribution of the number of Metabolic Syndrome components; Cuiabá, Mato Grosso State, 2007.

Table 1 - Prevalence of Metabolic Syndrome according to sociodemographic, anthropometric and laboratory variables; Cuiabá, Mato Grosso State, 2007

Variables (yes/no)	Sample (%)	SM + (%)	SM – (%)	p
Gender (Male/Fem)	50.0 / 50.0	60.0 / 81.7	40.0 / 18.3	0.009
Age group < 60 / ≥ 60 years	52.4 / 47.6	71.4 / 70.2	28.6 / 29.8	0.880
Education > 8 / ≤ 8 years	63.3 / 36.7	72.1 / 71.0	28.9 / 29	0.902
Physical inactivity	28.3 / 71.7	79.4 / 67.4	20.6 / 32.6	0.194
Alcohol habit	33.3 / 66.7	72.5 / 70.0	27.5 / 30.0	0.776
Smoking habit	47.5 / 52.5	64.9 / 76.2	35.1 / 23.8	0.204
Relative with high blood pressure	67.5 / 32.5	80.2 / 51.3	19.8 / 48.7	0.001
BMI (kg/m^2) (< 25 / ≥ 25)	30.8 / 69.2	43.2 / 83.1	56.8 / 16.9	< 0.001
Very high WC	64.0 / 36.0	92.2 / 46.4	7.8 / 53.6	< 0.001
High WHR	55.8 / 44.2	80.6 / 58.5	29.4 / 41.5	0.008
High total cholesterol	22.5 / 77.5	81.5 / 67.7	18.5 / 32.3	0.167
Low HDL	63.3 / 36.7	78.9 / 56.8	21.1 / 43.2	0.010
High LDL	24.2 / 75.8	69.0 / 71.4	31.0 / 28.6	0.799
High VLDL	29.2 / 70.8	97.1 / 60.0	2.9 / 40.0	< 0.001
High Uric Acid	14.2 / 85.8	94.1 / 67.0	5.9 / 33	0.016
High CRP	5.8 / 94.2	71.4 / 70.8	28.6 / 29.2	0.971
High Fibrinogen	1.7 / 98.3	100.0 / 70.3	0.0 / 29.7	0.840
HOMA > 2.71	60.8 / 39.2	86.3 / 46.8	13.7 / 53.2	< 0.001

Table 2 – Results of the multiple regression analyses for the characteristics associated with metabolic syndrome in hypertensive patients; Cuiabá, Mato Grosso State, 2007

Variables	*Odds Ratio*	IC95%	p
BMI ≥ 25 kg/m^2	5.61	1.92 – 16.42	0.014
HOMA > 2.71	9.85	3.23 – 30.05	0.001
Relative with high blood pressure	4.15	1.33 – 13.03	0.002

In a specific group of hypertensive individuals, the diagnosis of MS by the traditional criteria was associated with a 2.64 times increase (95% CI = 1.52 to 4.58) in the relative risk of a first cardiovascular event[24]. In this study, in hypertensive individuals living in Cuiabá, there was an overall MS prevalence of 70.8%, according to the NCEP-ATP III criteria, with significant prevalence among women. Studies of prevalence of MS among hypertensive patients are still scarce in Brazil. In Salvador, Bahia, Bulhões and Araújo[25], studied 102 hypertensive patients, aged > 18 years, treated in a university hospital, and they recorded a prevalence of MS of 71.6% (by the NCEP-ATP III criteria), which was similar to the results obtained in this study. Despite the different proportions between the genders, and the fact that the study conducted in Salvador have assessed the spontaneous demand of a university hospital, there was similarity in age and BMI and in the average frequency of five criteria (NCEP-ATP III) in both studies (17.9% in Salvador, and 15% in Cuiabá).

The prevalence of MS among women (81.7% vs 60.0%, p = 0009), with no difference between adults and the elderly, agrees with the study conducted among the rural population of the Jequitinhonha Valley, State of Minas Gerais (33.6% vs 7.7%), which recorded an overall prevalence of 21.6%[26], and also with another study conducted in the semi-arid region of Bahia[27], among a population aged ≥ 45 years. The prevalence of MS in this age group, possibly due to the influence of menopause, may justify the speed of progression of cardiovascular events in women with MS after menopause[28]. Unlike what was observed among adult Americans (overall prevalence of 23.7% - NCEP-ATP III), there was an increase of MS with age, with no difference between genders[29], in agreement with the population-based study conducted among adults in Vitória, State of Espírito Santo (overall prevalence of 29.8%), in which also no difference was observed between genders[23]. On the contrary, the SESI study, which was conducted among industrial workers of five Brazilian states, showed an overall prevalence of MS of 10.5%, significantly higher among men (11.5% vs. 8.1%)[30].

There was no association between low educational level and MS, in agreement with the results of the SESI study[28], conducted among industrial workers, and the study conducted among hypertensive individuals of Goiânia, State of Goiás[31], and this may be associated with the spread of obesity in almost all ages and social levels, especially among individuals with low-income and low-educational level. No association was established between per capita income and MS, in contrast to what was observed in Vitória, State of Espírito Santo, where upper-class women had lower prevalence of MS (17.9% vs

38.7%) than working-class and lower-class women, who had lower income[23].

On multiple regression analysis other variables related to lifestyle, such as: inactivity; hours of television watching; smoking, alcohol and eating habits (removing fat from meat, removing chicken skin, or table salt use), showed no association with MS in this study. Velasquez-Melendez et al[26] found no association between smoking habit and MS. In this study, the lack of a quantitative assessment of ethanol and salt intake among participants may have influenced these results.

Regarding the association between MS and insulin resistance, Bulhões and Araújo[25] observed significantly higher values of fasting insulin among individuals with MS ($p = 0.006$). In this study, according to the criteria used[16], we found that over 80% of hypertensive patients with MS showed a HOMA index greater than 2.71, in agreement with other relevant studies on the role of insulin resistance in the pathogenesis of MS[32]. The fact that the HOMA index remained associated with MS on multivariate analysis suggests the possibility of using this index as an indicator of insulin resistance in patients with MS, with obvious consequences in the therapy and prognosis, especially for non-diabetics[33,34]. In this study, a significant and substantial prevalence of increased and much increased WC was observed in patients with MS, especially among women. The mean BMI was significantly higher in patients with MS, and values over 25 kg/m^2 exerted important influence on the outcome variable ($p = 0.014$), in agreement with Oliveira et al[20], and contrary to Bulhões and Araújo[25]. This result reinforces the existence of a pathophysiological link between central adiposity and insulin resistance[34]. As for the relationship between inflammatory state and MS, no significant association was found between CRP levels and MS, or insulin resistance. This can be attributed to the fact that MS and hypertension are both vascular inflammatory syndromes[35], or the technique used (turbidimetry). The determination of ultra-sensitive CRP by another method (hypersensitive immunonephelometry) could have provided more accurate results. The LDL-cholesterol fraction, especially the small dense fraction, though not included in the diagnostic criteria of MS, has an important association with insulin resistance and MS.[3] As to the lipid fractions, in this study a significant and positive association was observed between high VLDL and MS, and a negative association with high levels of total cholesterol (> 240 mg%) and LDL-cholesterol (> 160mg%), in agreement with Oliveira et al[27].

Regarding family history, we observed in this study a positive association between MS and the presence of first-degree relatives with hypertension, revealed by multiple regression analysis ($p = 0.002$). This original finding draws attention to the results of some studies that addressed the importance of a genetic factor and a unifying molecular link in the pathophysiology of MS[32]. Wu et al[36] demonstrated that the region near the lipoprotein lipase gene (LPL gene) on the short arm of chromosome 8 influenced SBP variation in non-diabetic members of families who had substantially higher risk for developing insulin resistance and type 2 diabetes mellitus (MS)[36]. Cheng et al[37], studying 390 members of Hispanic hypertensive families, observed a coincidental connection between fasting insulin and BP, on the long arm of chromosome 7, showing an important genetic determinism for MS components located in this chromossome[37]. The search for SA gene polymorphisms, conducted by Iwai et al[38], in a group of 4 thousand individuals representative of the general population of Japan, showed an association between the SA gene and hypertriglyceridemia, hypercholesterolemia, obesity and hypertension, reinforcing the hypothesis of a common genetic basis for MS[38]. Love-Gregory et al[39] found a specific association between the CD36 gene of chromosome 7 and MS and HDL-cholesterol metabolism. This study population showed that hypertensive individuals from Cuiabá, with a family history of stroke, had a 1.7 times greater risk of hypertension than those who had no such antecedents[40]. These investigations, conducted in different populations, and in different regions of the world, demonstrate the great difficulty in understanding the genetic basis of MS.

This study showed a high prevalence of MS among hypertensive individuals living in Cuiabá, and a significant association with BMI > 25 kg/m^2, insulin resistance (assessed by the HOMA index), and, especially, a family history of hypertension. These results suggest the need for further epidemiological studies, so as to obtain greater understanding of this issue, preferably population-based studies, and assessment of the involved gene or genes.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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