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ORIGINAL ARTICLE

Metabolic syndrome and psychiatric disorders: a population-based study

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Objective: To identify the association of metabolic syndrome (MetS) and psychiatric disorders in young adults in southern Brazil.
Methods: This population based cross-sectional study involved a total of 1,023 young adults between the ages of 21 and 32 years. Current episodes of psychiatric disorders were assessed using the Mini International Neuropsychiatric Interview – Plus version. MetS was evaluated using the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATP III).
Results: Of the 1,023 participants, 24.3% were identified with MetS, 13.5% were diagnosed with anxiety disorders, 7.5% with current depression, 3.9% with bipolar disorders and 10.1% were at risk of suicide. MetS was associated with ethnicity ($p = 0.022$), excess weight ($p < 0.001$), current anxiety disorders ($p < 0.001$), current mood disorders (bipolar disorder in mood episode and current depression) ($p < 0.001$), and suicide risk ($p < 0.001$).
Conclusions: MetS was associated with psychiatric disorders. Awareness of factors associated with MetS can help identify high-risk individuals and stimulate disease prevention and control programs, as well as lifestyle changes.

Keywords: Metabolic syndrome; psychiatric disorders; mood disorders; anxiety disorders; suicide

Introduction

Metabolic syndrome (MetS) is defined as a cluster of conditions – abdominal obesity, dyslipidemia, high blood pressure, and hyperglycemia – that occur together and can increase the risk of developing heart disease, stroke and diabetes. The pathophysiology of MetS, although currently unknown, is considered multifactorial, with a complex interaction between genetic predisposition and significant changes in lifestyle behavior, including physical inactivity, high carbohydrate diets, and alcohol and tobacco consumption.[1,2]

The worldwide prevalence of MetS has increased in recent years, in parallel with the increasing prevalence of diabetes and obesity, and has become a major public health problem.[3] Studies conducted in developed countries, such as the United States, have shown prevalence rates reaching nearly 35% in adults,[4] while a mean prevalence of approximately 25% has been found in Latin-America.[5-7] A recent systematic review found rates ranging from 14.9 to 65.3% among Brazilian adults. However, this review included rural, urban and indigenous populations, and few studies have described the prevalence and predictors of MetS in Brazil.[8] Moreover, the included studies had a broad age range.

A review and meta-analysis investigating the link between depression and MetS reported a positive and bidirectional association.[9] Lifetime history of major depression was also found to predict the development of MetS in middle-aged women.[10] Moreover, disruption to biological rhythms (sleep, social, activities, and eating pattern) has been associated with key components of MetS in community adults with major depressive disorder[11] and bipolar disorder (BD), while a recent meta-analysis demonstrated a higher risk of MetS in subjects with BD than the general population, with a prevalence of approximately 30%.[12] In a subsequent study, it was found that MetS and its components were associated with increased suicide risk, indicating that public mental health interventions targeting suicide reduction may need to focus on individuals with MetS and its individual components.[13] Taken together, these studies have shown that patients with psychiatric disorders have a high mortality risk, mainly for cardiovascular events, which could be

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up to three times higher than that of the general population.[14,15]

Despite MetS' importance in metabolic, cardiovascular and psychiatric disorders, few studies have reported on the prevalence of this syndrome and mental health in southern Brazil. Thus, the objective of this study was to identify the association of MetS and psychiatric disorders in a population-based study of young adults in a mid-sized city in the southernmost state of Brazil (Pelotas, RS).

Methods

Sample

This cross-sectional study is the second phase of a population-based cohort study of young adults conducted between 2007 and 2009. The sample selection was by clusters, considering a population of 39,667 in the targeted age range[16-22] according to current census data for the 448 sectors of the city of Pelotas (Instituto Brasileiro de Geografia e Estatística [IBGE]). To assure the necessary sample size, 89 census-based sectors were randomly selected. Home selection in these sectors was performed using systematic sampling. The first home considered was that at the corner pre-established by the IBGE as the beginning of a sector. The selection interval was every third house. Upon finding prospective participants, trained interviewers explained the objectives of the study. The second phase took place from 2012 to 2014, approximately five years after the first phase. All young adults who participated in the first phase were invited to participate in the second phase. Complete details of this large cohort study are available elsewhere.[23] All participants provided free and informed consent before inclusion in the study.

The present study included individuals who had participated in the first phase (having completed five years since the first interview) and who allowed the collection of new biological material and anthropometric data. Individuals with physical or cognitive impairment, which made it impossible for them to participate in the second phase of the study, were excluded. This study was approved by the research ethics committee of the Universidade Católica de Pelotas (protocol 2008/118).

Instruments

The socioeconomic status of the participants was assessed using Brazilian Association of Research Companies guidelines. This classification is based on a series of household consumer product indicators and education level: class A and D are the highest and lowest socioeconomic levels, respectively.

The Mini International Neuropsychiatric Interview – PLUS was administered to all participants by well-trained psychologists.[24] This instrument is a semi-structured clinical interview based on DSM-IV criteria. We evaluated current episodes of mood disorders (bipolar disorder and depression) and the following anxiety disorders: social phobia, post-traumatic stress disorder, obsessive-compulsive disorder, panic disorders and generalized anxiety disorder. We introduced the variable 'anxiety disorders' (AD), which is a sum of all anxiety disorders. All individuals who met the diagnosis criteria for at least one anxiety disorder were coded as 1 and those with no anxiety disorder were coded as 0. Suicidal ideation and behavior were gauged using the Mini International Neuropsychiatric Interview-Plus suicide module (module C), which consists of nine questions assessing the presence of lifetime suicide attempts, frequency of suicidal thoughts and intent to commit suicide. Individuals were considered at risk of suicide when they reported any suicidal ideations. Substance abuse or dependence was assessed using the Alcohol, Smoking, and Substance Involvement Screening Test, previously validated for Portuguese by Henrique et al.[16] As recommended, a cutoff of 4 points was used for substance abuse/dependence. Drugs such as cocaine, ecstasy and amphetamines were grouped and considered psychoactive drugs.[16] The participants were also asked about the use of psychotropic medications, such as antidepressants, antipsychotics and mood stabilizers. It should be pointed out that only five individuals reported using antipsychotics, and this was not included in our analysis.

Anthropometric measurements were taken as part of the MetS evaluation. Waist circumference (WC) was measured to the nearest 0.1 cm using an inelastic measuring tape at the midline between the lowest rib and the iliac crest in the horizontal plane. Height, measured barefoot, was to the nearest 0.1 cm. Weight was measured in kilograms to the nearest 0.1 kg. Body mass index (BMI) was defined as weight in kilograms divided by the square of the height in meters, i.e., BMI = kg/m^2. After sitting quietly for at least 5 minutes, the participants' systolic and diastolic blood pressure were measured using a sphygmomanometer. At least two blood pressure measurements were performed, spaced 1-2 min apart, and additional measurements were taken if the first two were quite different. The mean blood pressure was considered in the analysis.[17] In addition, 10 mL of blood were drawn from each subject by venipuncture into anticoagulant-free vacuum tubes. The tubes were immediately centrifuged at 3,500 g for 15 min, and the serum samples were stored at -80 ^{o}C until analysis. Serum levels of total cholesterol, HDL-cholesterol and triglycerides were measured according to manufacturer guidelines (Katal Biotecnologica,® MG, Brazil). LDL concentration was estimated indirectly from measurements of triglyceride, high density lipoprotein cholesterol, and total cholesterol using the Friedewald equation.[18] Serum levels of glucose, total cholesterol, HDL cholesterol, LDL cholesterol, and triglycerides were expressed in mg/dL.

MetS diagnosis was defined using modified criteria of the National Cholesterol Education Program Adult Treatment Panel III (NCEP/ATPIII).[19] When a participant had three of the five listed criteria, MetS was diagnosed. The criteria included: 1) glucose intolerance with fasting glucose $\geqslant$ 100 mg/dL; 2) abdominal obesity, determined by high WC ($\geqslant$ 102 cm for men and $\geqslant$ 88 cm for women); 3) elevated triglyceride levels $\geqslant$ 150 mg/dL; 4) low HDL-C $\leqslant$ 40 mg/dL for men and $\leqslant$ 50 mg/dL for women; and 5) elevated blood pressure (systolic blood pressure

>130 mmHg and/or diastolic blood pressure >85 mmHg). We also calculated the non-HDL cholesterol level (total cholesterol minus HDL cholesterol), since it is a predictor of CVD.[20]

Data analysis

The statistical analyses were performed in SPSS version 22.0 and Stata version 13.0. Descriptive data were expressed as mean and standard deviation or absolute and relative frequency. Demographic and clinical characteristics were analyzed using chi-square statistics or one-way analysis of variance. In the multivariate analysis, Poisson regression with robust error variance was used to analyze count data.[21] For the regression analysis, the following independent variables were considered: gender, age, ethnicity, education level and employment; smoking, alcohol use, psychoactive drugs, excess weight, and psychotropic medication use; any current anxiety disorders, mood disorders and suicide risk. The outcome was MetS. Confounders were defined as variables associated with alcohol use and/or dependence at a significance level of 20% or less. In all analyses, the significance level was 5%.

Results

Initially, 1,560 young adults were recruited for this study. The participation rate from the first cohort was 80.70%, totaling 1,244 young adults for this phase. However, 237 of these individuals did not allow blood collection, resulting in 1,023 eligible participants.

Of this total population; 59.1% were females, 60.7% were between 21 and 26 years of age, 39.3% were between 27 and 32 years of age, and 69.1% were Caucasian. The demographic characteristics, lifestyle habits and comorbidities of the sample are shown in Table 1. Regarding lifestyle, 24.9% reported smoking, 8.8% using psychoactive drugs and 22.6% using alcohol. In relation to comorbidities, 13.5% were diagnosed with anxiety disorder, 7.5% with current depression, 3.9% with bipolar disorder, and 10.1% were at risk of suicide (Table 1).

MetS was identified in 249 (24.3%) of the participants; 26.0% and 22% among females and males, respectively (Table 2). Regarding psychiatric disorders, MetS was present in 38.4% of individuals with any AD; in 46.3% of those diagnosed with bipolar disorder, in 40.0% of those with depression and in 40.8% of those at risk of suicide. Table 2 also shows the results of the crude and adjusted analysis for MetS and associated factors. Factors associated with MetS in the crude analysis were: excess weight ($p < 0.001$), non-HDL cholesterol ($p < 0.001$), current anxiety disorders ($p < 0.001$), current mood disorders (bipolar disorder and current major depression) ($p < 0.001$), and suicide risk ($p < 0.001$).

Table 2 shows the results of the adjusted analysis for MetS, which was more prevalent among overweight individuals (RP: 4.58; 95%CI 3.27-6.40; $p < 0.001$). Regarding comorbidities, MetS was more prevalent among individuals with current anxiety disorders (RP: 1.33; 95%CI 1.01-1.78; p = 0.044) and suicide risk (RP: 1.58; 95%CI 1.18-2.03; p = 0.021). For mood disorders, BD was the most positive component (RP: 1.62; 95%CI 1.19-2.08; p = 0.006).

Table 1 Sociodemographic and clinical characteristics of a sample of young adults from a population-based study in the city of Pelotas, Brazil.

Variables	Sample distribution
Sex, female	605 (59.1)
Age	
21-26 years	621 (60.7)
27-32 years	402 (39.3)
Ethnicity, Caucasian	707 (69.1)
Socioeconomic status	
Upper class	598 (58.5)
Middle or lower class	425 (41.5)
Schooling	
Elementary or some high school	349 (34.1)
High school graduate	283 (27.7)
Some university/university graduate	391 (38.2)
Employed	724 (70.8)
Smoker	255 (24.9)
Psychoactive drug use	90 (8.8)
Alcohol use	231 (22.6)
Excess weight	539 (52.7)
Non-HDL cholesterol	154.91±54.29
Current psychotropic medication	258 (25.2)
Current anxiety disorders	138 (13.5)
Current mood disorders	
None	906 (88.6)
Depression	77 (7.5)
Bipolar disorder	40 (3.9)
Suicide risk	103 (10.1)
Metabolic syndrome	249 (24.3)
Total	1,023 (100)

Data presented as n (%) or mean ± standard deviation (SD).
Non-HDL cholesterol = total cholesterol - HDL cholesterol

Discussion

In this study we found that the prevalence of MetS among young adults was 24.3% according to the NCEP/ATPIII definition. These findings agree with prevalence rates reported around the world, which range from 20 to 25%.[22] Moreover, a similar prevalence (24.9%,) was reported in a recent meta-analysis of Latin American studies using the same evaluation criteria, although with an age ranged between 18 and 65 years.[5] It is known that the prevalence of MetS increases with age.[5,25] A study by Hildrum et al., which included 10,206 participants between 18 and 89 years old, found that the prevalence of MetS increased from 11% in men between 20 and 29 years old to 47.2% in men between 80 and 89 years old, while for women the rate increased from 9.2 to 64.4% in the same respective age ranges.[26] In older age, physiological and environmental changes influence the nutritional and metabolic state of individuals and facilitate the development of cardiovascular diseases. However, our study was conducted with young adults with a mean age of 25 years and

Table 2 Factors associated with metabolic syndrome in a population-based study of young adults

Variables	MetS n (%)	p-value crude PR (95%CI)	p-value adjusted PR (95%CI)
Sex		p = 0.542	-
Female	157 (26.0)	1.07 (0.86-1.34)	
Male	92 (22.0)	Ref	
Age (years)		p = 0.638	-
21 -26 years	148 (23.8)	Ref	
27- 32 years	101 (25.1)	0.98 (0.79-1.24)	
Ethnicity		p = 0.152	p = 0.180
Caucasian	163 (23.1)	Ref	Ref
Non-Caucasian	86 (27.2)	1.29 (1.03-1.62)	1.09 (0.89-1.34)
Socioeconomic status		p = 0.501	-
Upper class	141 (23.6)	Ref	
Middle or lower class	108 (25.4)	1.03 (0.83-1.29)	
Schooling		p = 0.591	-
Elementary or some high school	84 (24.1)	Ref	
High school graduate	76 (26.9)	1.02 (0.78-1.36)	
Some university/university graduate	89 (22.8)	0.98 (0.75-1.27)	
Employed		p = 0.212	
No	81 (27.1)	1.07 (0.85-1.62)	
Yes	168 (23.2)	Ref	
Smoker		p = 0.533	-
No	196 (25.5)	1.16 (0.83-1.63)	
Yes	53 (20.8)	Ref	
Psychoactive drug use*		p = 0.344	-
No	198 (24.3)	1.31 (0.75-2.27)	
Yes	18 (20.0)	Ref	
Alcohol use		p = 0.480	-
No	200 (25.3)	1.18 (0.83-1.69)	
Yes	49 (21.2)	Ref	
Excess weight*		p < 0.001	p < 0.001
No	35 (7.4)	Ref	Ref
Yes	211 (39.1)	3.71 (2.75-4.99)	4.58 (3.27-6.40)
Non-HDL cholesterol		p < 0.001	p < 0.001
Normal	35 (9.6)	Ref	Ref
High	214 (32.6)	3.40 (2.44-4.76)	2.65 (1.92-3.68)
Current psychotropic medication		p = 0.475	-
No	177(23.1)	Ref	
Yes	72 (27.9)	1.09 (0.86-1.39)	
Current anxiety disorders		p < 0.001	p = 0.044
No	196 (22.1)	Ref	Ref
Yes	53 (38.4)	1.69 (1.31-2.17)	1.33 (1.01-1.78)
Current mood disorders		p < 0.001	p = 0.006
None	200 (22.1)	Ref	Ref
Depression	30 (40.0)	1.82 (1.33-2.45)	1.57 (1.15-1.89)
Bipolar disorder	19 (46.3)	2.11 (1.47-2.98)	1.62 (1.19-2.08)
Suicide risk		p < 0.001	p = 0.021
No	207 (22.5)	Ref	Ref
Yes	42 (40.8)	1.74 (1.32-2.28)	1.58 (1.18-2.03)
Total	249 (100.0)	--	--

95%CI = 95% confidence interval; MetS = metabolic syndrome; Non-HDL cholesterol = total cholesterol - HDL cholesterol; PR = prevalence ratio; Ref = reference.
* Missing variable.

found a high prevalence of MetS. This could reflect the sedentary lifestyle and inadequate nutrition present in this age group.

We found no significant gender differences, which is consistent with previous studies.[5,27] Marquezine et al. found no significant difference in the prevalence of MetS between women and men, but detected a clear trend towards a high prevalence with age (especially in women).[27]

Another factor associated with MetS is ethnicity. Studies have shown that Asian, Chinese, African populations have higher prevalences of cardiometabolic risk factors and MetS than Caucasians.[28-30] A likely explanation for the high prevalence of MetS in these groups correlates with higher visceral fat, which is often not related to high BMI values. Asians, for example, have a higher body fat index relative to weight than Caucasians.[31,32] Although we found no significant association regarding ethnicity, the prevalence of MetS was slightly higher among the non-Caucasian group. An important finding of our study was that MetS increased the risk of developing cardiovascular diseases, which was determined in our study by non-HDL cholesterol and is consistent with previous reports.[33,34] Moreover, we found that the prevalence of MetS among individuals with excess weight was almost four times higher than in normal weight-individuals. It is worth noting that a growing body of evidence supports an association between obesity, cardiovascular diseases and MetS.[35]

Previous studies have documented that people with psychiatric diseases have an increased risk of developing MetS compared to the general population.[11,36] Regarding mood disorder in our population, 47.5% of the participants with bipolar disorder and 39% with major depression had MetS. Our results agree with those reported in recent meta-analyses.[9,12,37] There is strong evidence for a bidirectional association between MetS and depression. This finding indicates a reciprocal association between both MetS and depression that may represent risk factors among themselves.[9] Similarly, MetS and anxiety were significantly associated in another meta-analysis involving 41,168 subjects.[38] With respect to anxiety, MetS, with a prevalence of 38.4%, was significantly associated with the presence of any anxiety disorder in our study. This also agrees with other published studies.[39,40] These results could be explained by several contributing factors, including poor diet and psychotropic treatments, which, due to the close association between MetS and psychiatric disorder, highlights the need for early intervention.

In addition to mood and anxiety disorder, we also found a higher prevalence of suicide risk in individuals with MetS. However, few studies have associated MetS with suicide risk. Chang et al. found that MetS was associated with a 16% higher risk of suicide per MetS component, while Fagiolini et al. found a higher prevalence of lifetime suicide attempts in patients with MetS compared to those without it.[41] Thus, strategies for predicting suicide that focus on mental and medical risk factors may offer new insights into the design of screening and prevention programs for patients with suicidal tendencies.[13,42]

This study has certain limitations. First, MetS was not evaluated in the first phase of the cohort study, which made it impossible to verify the causal relationship between MetS and its associated factors. Second, behavioral factors, such as sedentary lifestyle and eating habits were not evaluated. Third, due to the small sample of subjects with psychotic disorders, these disorders were not included in the analysis. Finally, although antidepressant use can contribute to obesity, it did not interfere in our results, even after adjusted analysis. The strengths of our study include a large sample size and a community-based sample of young adults from an urban zone of a single city, in contrast to other Brazilian studies that have used a broader age range. It is worth mentioning that few studies have associated MetS with psychiatric disorders in a young adult population in Brazil.

Awareness of the factors associated with MetS can help identify high-risk individuals, especially young adults, and stimulate disease prevention and control programs, as well as lifestyle changes. Health promotion strategies developed by a multidisciplinary team are necessary for the early detection, prevention and treatment of these factors in the psychiatric population, in order to increase life expectancy and improve quality of life.

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Disclosure

The authors report no conflicts of interest.

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