Prevalence of Metabolic Syndrome according to NCEP-ATP III and IDF criteria in Patients on Hemodialysis

Authors
Marcos Kubrusly[1]
Claudia Maria Costa de Oliveira[1]
Patricia Saldanha Freire Simões[1]
Rodrigo de Oliveira Lima[1]
Paula Nathana Rabelo Galdino[1]
Pamela de Alencar Fortaleza Sousa[1]
Antônio Luíz Carneiro Jerônimo[1]

[1] Unichristus Medical School - Federal University of Ceará.

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Correspondence to:
Claudia Maria Costa de Oliveira.
Faculdade de Medicina Unichristus
Universidade Federal do Ceará.
Rua Professor Jacinto Botelho, nº 500, apto. 500, Guararapes.
Fortaleza, Ceará, Brasil.
CEP: 60810-050.
E-mail: claudiadrl@gmail.com

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Abstract

Introduction: Metabolic syndrome (MS) has a high prevalence in hemodialysis' patients and is a risk factor for cardiovascular disease, the leading cause of mortality in chronic kidney disease (CKD). **Objectives** To evaluate the prevalence of MS in patients on hemodialysis (HD) and the difference in its prevalence according to the NCEP-ATP III and IDF criteria. **Methods:** We evaluated HD patients in two outpatienclinics in Fortaleza, with dialysis vintage of aleas3 months and aged 18 + years. The patients underwenmeasuremenof waiscircumference, blood pressure (BP), dosages of glucose, triglycerides and HDL-cholesterol in fasting. **Results:** 115 patients were included and the prevalence of MS was 41.7% according to the NCEP-ATP III and 42.6% according to the IDF. Among the 48 patients with a diagnosis of MS according to the NCEP-ATP III, 87.5% were diagnosed by the IDF. Among the 67 patients withouMS by NCEP-ATP III, 89.5% were nodiagnosed by means of the IDF. The variables of MS according to the NCEP which had a higher prevalence were abnormal HDL-chol in 83.4% of patients and BP altered or use of antihypertensive drugs in 81.3%. **Conclusion:** The prevalence of MS in the study population was high, regardless of the criteria used. The variables thacontributed mosto the diagnosis of MS were dyslipidemia and blood pressure. Routine assessmenof the diagnosis of MS in HD should be implemented, since patients with MS have an increase in the number of hospitalizations and in the risk of cardiovascular events.

Keywords: diagnosis; metabolic syndrome X; renal dialysis.

Introduction

The frequent coexistence of hypertension, abnormal glucose homeostasis, obesity and dyslipidemia in certain population or individual groups led to the description of a clinical syndrome that relates and groups them. In 1988, Reaven called it the "X syndrome" which included insulin resistance, hyperinsulinemia, glucose intolerance, dyslipidemia (hypertriglyceridemia and decreased high-density lipoprotein - HDL) and arterial hypertension (AH). Currently, the "X syndrome " name was changed to "metabolic syndrome (MS)" with the clustering of risk factors for type 2 diabetes and cardiovascular disease (CVD).[1]

Recognition of this syndrome is becoming increasingly important, and it is associated with increased overall mortality by about 1.5 times and cardiovascular mortality about 2.5 times.[2] Lakka *et al.*[3] reported 12% increase in cardiovascular mortality in patients with MS, when compared to the population that did not meet the criteria for MS.

This syndrome has many similarities with chronic kidney disease (CKD) and the risk factors that are similar are: insulin resistance, glucose intolerance, hypertension, dyslipidemia and obesity. In addition, the MS

has a strong and significant association with the risk for CKD and albuminuria, being directly proportional to the number of its components.[4]

Despite its importance as a risk factor for CVD and CKD, the study of MS has been hampered by the lack of consensus on its definition and the cutoff points of its components, with implications in clinical practice and health policies. The National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP III) and International Diabetes Federation (IDF) have created definitions for the MS.[5,6]

NCEP-ATP III criteria requires three out of five factors to establish the diagnosis of MS, i.e. abdominal obesity (waist circumference > 88 cm for women or > 102 cm for men), increased triglycerides (TG ≥ 150 mg/dL), reduced HDL-chol (HDL-chol < 50 mg/dL for women or < 40 mg/dl for men), high blood pressure (BP ≥ 130/85 mmHg) and high fasting glucose (≥ 100 mg/dL).[5]

The IDF has published new criteria that resemble the NCEP-ATP III; however, the IDF requires the waist circumference criterion according to race. They consider abdominal obesity more strongly correlated with insulin resistance than other criteria.[6]

The prevalence of MS in the population that requires HD is not sufficiently known. A previous study using NCEP-ATP III to identify the prevalence of MS found a rate of 69.3% in chronic HD patients.[7] According to Ucar *et al.*,[8] HD patients that were evaluated according to the IDF and the NCEP-ATP III had MS prevalence of 36% as per the IDF and 51.8% as per the NCEP-ATP III, with diagnostic correlation between the criteria in only 56.5% of cases, showing divergence between the methods and higher prevalence according to the NCEP-ATP III.

CKD has become a global public health problem due to its high prevalence and the concomitant increased risk of cardiovascular disease and premature death. HD patients have a lower life expectancy and poorer quality of life when compared with individuals of the same age in the general population.[4] A better understanding of the prevalence of MS in CKD and their interrelationships can lead to measures to slow the progression of kidney disease and chronic cardiovascular disease, these are associated with mortality.

This study aims to assess the prevalence of MS in patients with CKD on HD and analyze the difference in prevalence according to NCEP-ATP III and IDF criteria.

Materials and methods

This was a cross-sectional, observational study, in which we used a quantitative approach to investigate MS prevalence and its components, according to NCEP-ATP III and IDF criteria in hemodialysis patients from two clinics in Fortaleza-CE. The study was submitted to and approved by the Research Ethics Committee of the Christus University Centre.

The population consisted of patients on hemodialysis for longer than 3 months and aged higher than or equal to 18 years. As for inclusion criteria, we selected all who agreed to participate and signed the Informed Consent form, who were able to respond to the survey questionnaire (with clinical and demographic data) and could be subject to weight and height measures and blood collection.

We measured the patients' weight, height, waist circumference (WC) and blood pressure (BP). We also dosed their glucose, triglycerides and HDL-cholesterol after proper fasting.

We used the patients' dry weight, routinely assessed in the clinics that participated in the study by a combination of clinical criteria and with the help of a multi-frequency bioelectrical impedance analysis. The patients' heights were measured with a stadiometer from a Filizola anthropometric scale, with 0.5 cm grading for height, and it was checked twice.

The waist circumference was measured after dialysis with a measuring tape, placed in the middle of the distance between the iliac crest and the lower costal margin, on the narrowest abdominal section.

The BP was assessed in the study considering the mean BP measured before each hemodialysis session during one month.

Triglycerides were measured using the enzymatic colorimetric method; glucose by the PAP colorimetric method and the HDL-col by the enzymatic method.

The use of antihypertensive, lipid-lowering, insulin or oral hypoglycemic agents, as well as the previous diagnosis of diabetes and hypertension was recorded in the survey questionnaire.

The concept of MS was defined according to the NCEP-ATP III and IDF guidelines, taking into account the high values of the following parameters: waist circumference (WC), triglycerides (TG), HDL-cholesterol, blood pressure (BP) and fasting glucose.

MS diagnosis according to the NCEP-ATP III is a modification of three or more of the above factors; while the IDF uses the increased waist circumference plus at least two other risk factors.

Altered TG values (≥ 150 ml/dl), BP (≥ 130/85 mmHg), glucose (≥ 100 mg/dL) and HDL-col (< 40 mg/dL for men and < 50 mg/dl for women) are the same for both criteria. Waist circumference adopted by the NCEP-ATP III is > 102 cm for men and > 88 cm for women; while the IDF considers ≥ 90 cm for men and ≥ 80 cm for women, values that are proposed for the South Americans.

Statistical analysis

The variables collected were organized in a database using the Epi Info version 3.5.1 software. Continuous variables were expressed as mean ± standard deviation and categorical variables were expressed in frequency. We used the Student *t*-test to compare two mean values (variables with normal distribution) or the Mann Whitney (variables with abnormal distribution) and the comparison of 3 or more mean values by the ANOVA and Kruskal Wallis tests.

The association between categorical variables was assessed using the chi-square test or the Fisher's exact test.

We assessed whether the two methods estimated the same MS prevalence using the McNemar test (test to evaluate the correlation between the MS- yes/no diagnosis) and the correlation between the diagnosis of MS by the two methods was tested by means of the kappa coefficient index, using the interpretation suggested by Bland-Altman (1986).[9]

Statistical analysis was carried out using the SPSS 16.0 software. A p value < 0.05 was considered significant.

Results

The study included 115 patients with a mean age of 50.2 ± 14.7 years (from 21 to 88 years) and the median time on HD was 42.7 months, and 50.4% were females. In the study population, 68.7% (n = 79) were on anti-hypertensive drugs and 13% (n = 15) were on oral hypoglycemic agents. Clinical, anthropometric and laboratory characteristics of the study population are depicted on Table 1.

Metabolic syndrome was present in 41.7% according to the NCEP-ATP III, and 42.6% according to the IDF (McNemar = 1.0, both methods estimated the same prevalence of MS). Furthermore, 87.5% of patients with MS, according to NCEP-ATP III, also had this diagnosis according to the IDF; and 89.5% of those without MS, in accordance with the NCEP-ATP III also did not have it according to IDF (p = 0.000), showing agreement between the two methods. The MS diagnosis agreement between the methods was good (kappa = 0.768) (Table 2).

The variables studied according to the presence or absence of metabolic syndrome according to the NCEP ATP III and IDF are shown in Tables 3 and 4, respectively. There was no statistically significant difference in the prevalence of MS as far as gender is concerned, according to the NCEP-ATP III (p = 0.291) and the IDF (p = 0.627), as well as, according to the duration of dialysis < 5 years *versus* ≥ 5 years

Table 1 Clinical, anthropometrical and laboratorial characteristics of the study population

Variable	Mean	Standard deviation	Minimum	Maximum
Weight (Kg)	60.36	13.14	31.5	101.5
Height (cm)	1.60	0.09	1.35	1.9
BMI	23.54	4.59	14.55	37.48
WC (cm)	89.56	12.96	54	122
Pre-HD SBP	134.28	16.31	104	182
Pre-HD DBP	81.55	7.45	62	113
Glycaemia (mg/dl)	84.73	50.39	32	433
Total cholesterol	167.16	86.17	72	944
HDL-col	43.28	14.16	13.3	93.7
TG	163.20	128.68	44	779

BMI: Body Mass Index; WC: Waist Circumference; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HD: Hemodialysis; TG: Triglycerides.

Table 2 Agreement in the diagnosis of metabolic syndrome according to the criteria from NCEP-ATP III and IDF

	IDF		
NCEP-ATP III	Yes	No	Total
Yes	42	6	48
No	7	60	67
Total	49	66	115

p = 0.000; kappa index = 0.768.

(p = 0.699 according to the NCEP and p = 0.753 according to the IDF). As far as age goes, we found that only 29.3% of patients younger than 50 years were classified as MS carriers according to the NCEP-ATP III, *versus* 54.4% of patients aged older than or equal to 50 years (p = 0.006). According to the IDF, 29.3% of patients younger than 50 years had MS, compared to 56.1% of those older than or equal to 50 years of age (p = 0.004)

Discussion

MS is the joint presence of risk factors for cardiovascular disease, mortality in the general population and CKD progression.[10] These

Table 3 Prevalence of the study variables according to having metabolic syndrome or not, as per the NCEP-ATP III

NCEP-ATP III	MS-yes	MS-No	p
TG ≥ 150 ml/dl	81.6%	18.4%	0.000
TG < 150 ml/dl	22.1%	77.9%	
Altered HDL-col	59.7%	40.3%	0.000
Normal HDL-col	16.7%	83.3%	
BP ≥ 130/85 mmHg	42.8%	57.1%	0.636
BP < 130/85 mmHg	37.5%	62.5%	
Fasting glycaemia ≥ 100 mg/dl	77.3%	22.7%	0.000
Fasting glycaemia < 100 mg/dl	33.3%	66.7%	
Altered WC	82.1%	17.9%	0.000
Normal WC	21.1%	78.9%	

TG: Triglycerides; BP: Blood Pressure; WC: Waist Circumference.

Table 4 Prevalence of the study variables according to having MS or not according to the IDF

IDF	MS-yes	MS-no	p
TG ≥1 50 ml/dl	78.9%	21.1%	0.000
TG < 150 ml/dl	24.7%	75.3%	
Altered HDL-col	58.2%	41.8%	0.000
Normal HDL-col	20.8%	79.2%	
BP ≥ 130/85 mmHg	54.9%	45.1%	0.302
BP < 130/85 mmHg	33.3%	66.7%	
Fasting glycaemia ≥ 100 mg/dl	77.3%	22.7%	0.000
Fasting glycaemia < 100mg/dl	34.4%	65.6%	
Altered WC	69.1%	30.9	0.000
Normal WC	0.00	100.00	

TG: Triglycerides; BP: Blood pressure; WC: Waist circumference.

factors are abdominal obesity, dyslipidemia (characterized by increased triglycerides and decreased HDL-cholesterol), hypertension and blood glucose elevation. Several study groups have developed diagnostic criteria for MS, the NCEP-ATP III and IDF stand out due to their wide use.[11]

This study aimed to evaluate the diagnosis of MS in HD patients and its frequencies, using the NCEP-ATP III and IDF criteria, which are considered current methods and easy to use.[5]

Regarding the prevalence of MS, 41.7% of patients were diagnosed according to the NCEP-ATP III, and 42.6% according to the IDF, with good agreement between the methods (kappa = 0.768). Among the 48 patients diagnosed with MS, according to NCEP-ATP III, 42 (87.5%) were also diagnosed by the IDF. Among the 67 patients without MS by NCEP-ATP III, 60 (89.5%) did not have it according to the IDF. These results differ from a study carried out by Ucar *et al.*,[8] who used the same criteria in a Turkish population undergoing HD; however, the authors showed a lower correlation between the criteria, showing divergences between the methods and a higher prevalence when using the NCEP-ATP III.

MS prevalence in the present study was higher than the one found in study done by Nakazone *et al.*[12] who evaluated a Brazilian population and found 35.5% of MS according to the NCEP-ATPIII. This difference may be explained by the fact that all the patients in this study had CKD, which is one of the risk factors for MS. This same difference between the general population and patients with CKD was observed in the study by Young *et al.*,[13] who found a prevalence of 69.3% of MS when evaluating 202 patients starting renal replacement therapy. Probably the study by Young *et al.* found higher values than ours because they replaced two MS parameters: waist circumference for BMI and fasting plasma glucose for a diagnosis of diabetes, use of antidiabetic or random blood glucose ≥ 200 mg/dL, by doing this they may have increased the method's sensitivity.

When analyzing MS diagnosis components of the NCEP-ATP III and the IDF, we found a positive and significant association between MS diagnosis and dyslipidemia, evaluated by hypertriglyceridemia and low HDL-C. Banerjee *et al.*[14] also showed the importance of dyslipidemia, since in their study hypertriglyceridemia was a predictive factor of MS in CKD patients. Dyslipidemia is secondary to many changes in lipid metabolism, among them, the excess hepatic production of VLDL and its clearance deficit.[15] This can also lead to insulin resistance (IR),[16] a much prevalent factor in CKD patients, which leads to changes in plasma lipid make up, coagulation, endothelial function and vascular resistance, as well as changes in the endocrine system and obesity, besides increasing the risk of developing high blood pressure and accelerated atherosclerosis.[17,18] Although the IR cause is multifactorial in CKD, insulin abnormalities have been recognized as predominant causes, as well as a defective post-insulin receptor primarily affecting glucose uptake into the skeletal muscle.[18]

On the analysis regarding blood glucose level changes and MS, we found a relationship between blood glucose higher than 100 mg/dL and the diagnosis of MS by the NCEP-ATP III, in which 77.3% of patients with high blood glucose had MS, compared to only 33.3% of patients with blood glucose lower than 100 mg/dL (p = 0.000). This relationship was also found when the diagnosis was made by the IDF, with MS in 77.3% of patients with high blood glucose and only 34.4% of those with blood glucose lower than 100 mg/dL (p = 0.0005). Corroborating our results, Rasic-Milutinovic *eal.*[19] also found a strong relationship between high glucose and MS in patients on HD.

Unlike dyslipidemia and glucose levels, in the present study we found no association between hypertension and MS according to NCEP-ATP III or the IDF. In a cross-sectional population-based study carried out in the city of Vitória, which evaluated data from 1,655 individuals from the general population, the MS prevalence was 32.9% and of these 71.0% had hypertension; on the other hand, among individuals with hypertension, 50% did not meet the criteria for the diagnosis of MS.[20] In our sample, among patients with MS according to the IDF, 54.9% had high blood pressure; however, 45.1% of individuals with hypertension did not have MS.

There was no direct relationship between having hypertension and MS, probably because this comorbidity is highly prevalent in the population, even in patients without additional

MS criteria. Another justification for not having a relationship between MS and hypertension may result from the direct effect of reduced renal function in high blood pressure, increasing the prevalence of hypertension, regardless of MS.[21]

Given the deviations stemming from the MS detection using various recommended diagnostic criteria, there is a current trend in unifying the existing parameters. There was a meeting between large organizations (American Heart Association, World Heart Federation, International Atherosclerosis Society), in 2009, which suggested a new criterion for MS: 3 abnormal findings among 5 with the same variables and cutoff points, except waist circumference (WC), which would follow national or regional cutoffs (≥ 80 cm for women and ≥ 94 cm for European and Caucasian men; ≥ 88 cm and ≥ 102 cm for Americans). In this new criterion, WC is not mandatory.[22]

Besides the absence of specific criteria for MS in the dialysis population, the MS mortality risk in dialysis patients remains in question, while in the general population the MS increased mortality from cardiovascular causes and from all other causes. A study by Park *et al.*[23] investigated the MS effects on the time of life of patients on peritoneal dialysis and found a significant decrease in the 5-year survival rate in patients with MS compared to those without MS. Furthermore, the study by Pérez de José *et al.*,[24] who analyzed the effects of MS on cardiovascular events in HD patients, found no difference in mortality between patients with or without MS; however, they reported a higher hospitalization rate due to all causes in patients with MS.

Conclusion

Given the above, when analyzing the prevalence of MS according to the two criteria, NCEP-ATP III and IDF, we concluded that the prevalence was high and similar in both groups, and therefore are equivalent regarding the MS diagnosis. The variables most strongly associated to the diagnosis of MS were dyslipidemia and glycaemia; therefore, emphasis should be given to the critical analysis of lipid and glycemic evaluation, as these may represent the initial screening for MS in patients on hemodialysis.

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