Prevalence of Metabolic Syndrome in a Hemodialysis Population

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Introduction. The role of metabolic syndrome (MS) in hemodialysis population has not been thoroughly studied. This study aimed to determine the prevalence of MS and to identify its correlates among hemodialysis patients.

Materials and Methods. This cross-sectional study was conducted on patients in a hemodialysis center. The MS was defined according the Adult Treatment Panel III criteria. Clinical data of the patients were collected and blood samples were studied to measure fasting blood glucose and lipid profile.

Results. Eighty hemodialysis patients, including 47 men (58.8%) and 33 women (41.2%) with a mean age of 55.6 ± 15.6 years, were enrolled in this study. Metabolic syndrome was diagnosed in 23 patients (28.7%). Hypertension was present in 55 patients (68.8%). Fifteen patients (18.8%) were diabetic, 24 (30.0%) had a high serum triglyceride, 22 (27.5%) had a low high-density lipoprotein cholesterol, and 20 (25.0%) had evidence of abdominal obesity. Patients with MS had significantly higher body mass indexes ($P < .001$), fasting blood glucose levels ($P < .001$), and triglyceride levels ($P = .004$). Metabolic syndrome was not associated with gender, age, and duration of hemodialysis. Men showed significant abnormality in glucose metabolism ($P = .008$). Prevalence of low high-density lipoprotein cholesterol was significantly higher in the women than in the men ($P = .02$).

Conclusions. The prevalence of MS in our hemodialysis patients was relatively high, with the most common element being hypertension. We suggest that there needs to be a new set of criteria defined for MS in hemodialysis patients.

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INTRODUCTION

Metabolic syndrome (MS) is also known as *syndrome X* or *insulin resistance syndrome*. It is a complex disorder that was first described by Reaven in 1988.[1] Its characteristics include abdominal obesity, hypertriglyceridemia, low high-density lipoprotein cholesterol (HDLC) levels, high blood pressure, and high fasting blood glucose levels. The report of the Adult Treatment Panel (ATP) of the National Cholesterol Education Program stressed that because of the rising prevalence of obesity, MS should be controlled to help prevent cardiovascular disease.[2] The 2001 report of the Adult Treatment Panel (ATP III) defined MS as a condition that would at least include 3 of the following 5 criteria: waist circumference greater than 102 cm in men and greater than 88 cm in women; serum triglyceride level of 150 mg/dL

or higher; HDLC level lower than 40 mg/dL in men and lower than 50 mg/dL in women; blood pressure of 130/85 mmHg or higher and/or use of antihypertensive medications; and serum glucose level of 110 mg/dL or higher and/or use of insulin or hypoglycemic medication.[3]

According to the National Health and Nutrition Examination Survey 1999-2000,[4] age is a significant factor in the prevalence of MS in both sexes. Similar results have been reported for European and Chinese populations.[5,6] Metabolic syndrome also constitutes a major health problem in the Western World.[7-9] The prevalence of MS has also been noted to vary significantly among different ethnic groups.[10] Recent reports also indicate a very high incidence of MS in Maori and Pacific Islanders.[11,12] Multiple studies have shown that MS is a significant risk factor for cardiovascular disease, chronic kidney disease (CKD), and mortality in the general population.[3,13-16] Metabolic syndrome has been associated with an increased risk for the development of diabetes mellitus and cardiovascular disease. It further increases mortality rate in such patients.[12,17,18]

In addition, MS seems to be a risk factor for CKD progression. The prevalence rate of MS in dialysis patients is unknown. Young and coworkers reported that the overall prevalence of MS was up to 70% in hemodialysis population and was even more prevalent among diabetic, female, and white end-stage renal disease patients.[19] The aim of the present study was to determine the prevalence and correlates of MS in hemodialysis patients and to identify the most common factor of MS among those receiving dialysis in our Center.

MATERIALS AND METHODS

Study Population

We studied the prevalence of MS in 80 hemodialysis patients (58.8% men and 41.3% women; mean age, 55.6 ± 15.6 years). We included patients 16 years of age and older who had been receiving hemodialysis for more than 6 months. Patients were excluded if they were candidates for kidney transplantation before completing 6 months of hemodialysis or if they were assumed to have a life expectancy of less than 6 months. Eligible patients were divided into 2 groups according to the ATP III criteria,[3] namely hemodialysis patients with MS and those without MS.

Study Design

This cross-sectional study was conducted between 2009 and 2010 in 2 hemodialysis centers at Valiasr Hospital and Beheshti Hospital, affiliated with Zanjan University of Medical Sciences, in the provincial capital of Zanjan, Iran. Metabolic syndrome was defined according to the ATP III criteria.[3]

All of the Patients provided informed consent prior to data collection. Data on demographic characteristics and past medical history were collected. Abdominal circumference was measured at 1 centimeter above the umbilicus level, in the sitting position and at the end of a hemodialysis session. The following laboratory values were obtained from an overnight fasting blood sample: cholesterol, triglyceride, low-density lipoprotein cholesterol, HDLC, fasting blood glucose, hemoglobin, albumin, calcium, and phosphorus levels. Participants on antidiabetic medication were considered to have diabetic mellitus. If they had 2 random glucose measurements of 200 mg/dL or higher, they would be considered as having abnormal glucose metabolism. To evaluate the efficacy of dialysis, KT/V was calculated. Individuals taking antihypertensive medications were considered to have hypertension. The level of blood pressure before and after hemodialysis was recorded. The hemodialysis protocol for all patients was 4 hours of using hemophane membrane and an average blood flow rate of 300 mL/min to 350 mL/min, with bicarbonate basis dialysis solution. All measurements and laboratory values were collected when the participants reached their dry weight after a hemodialysis session.

Statistical Analyses

Statistical analyses were performed using the SPSS software (Statistical Package for the Social Sciences, version 17.0, SPSS Inc, Chicago, Ill, USA). Descriptive statistics included means, medians, proportions, and standard deviations for all baseline characteristics. Most continuous variables were summarized as mean ± standard deviation. The chi-square test and the Fisher exact test were used to test for differences between proportions. The Student *t* test was used for comparison of means of normally distributed samples, while a Mann-Whitney U test was used for nonparametric samples. The odds ratio (OR) and 95% confidence interval

(CI) were also used to describe associations. A *P* value less than .05 was considered to be significant in all tests.

RESULTS

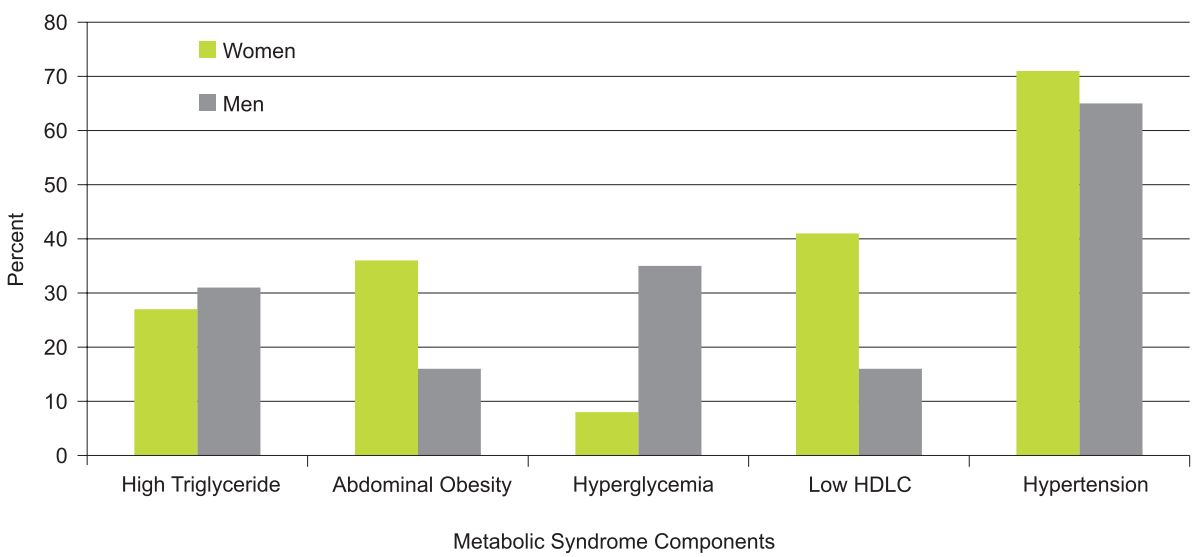
Eighty hemodialysis patients, including 47 men (58.8%) and 33 women (41.2%) with a mean age of 55.6 ± 15.6 years, were enrolled in this study. The mean duration of dialysis was 36.2 ± 35.6 months (range, 1 to 192 months). Of the 80 hemodialysis patients participating in this study, 18.8% (15 patients) were diabetic and 68.8% (55 patients) were hypertensive. The underlying causes of ESRD were as follows: hypertension, 42.5% (34 patients); diabetic nephropathy, 17.5% (14 patients); polycystic kidney disease, 6.3% (5 patients); chronic glomerulonephritis, 3.8% (3 patients); autoimmune diseases, 3.8% (3 patients); urological problems, 1.3% (1 patient); nephrotoxicity, 1.3% (1 patient); and unknown, 23.8% (19 patients). Table 1 shows the patients' demographic data.

The overall prevalence of MS was 28.7% (23 patients). The general characteristics of the patients are presented by MS status in Table 2; patients with MS had significantly higher body mass index ($P < .001$; OR, 2.3; 95% CI, 1.4 to 6.5), fasting blood glucose ($P < .001$; OR, 2.5; 95% CI, 1.2 to 10.4), and triglyceride ($P = .004$; OR, 19.5; 95% CI, 1.1 to 97.3). Metabolic syndrome was not significantly associated with age and gender. The prevalence of MS was 29.8% in the men and 27.3%

Table 1. Demographic, Metabolic, and Laboratory Features of Hemodialysis Patients*

Variable	Value
Demographics	
Age, y	55.6 ± 15.6
Gender	
Female	33 (41.2)
Male	47 (58.8)
Metabolic features	
Diabetes mellitus	15 (18.8)
Hypertension	55 (68.8)
Systolic BP, mm Hg	139.4 ± 25.6
Diastolic BP, mm Hg	82.2 ± 11.4
Low HDLC	22 (27.5)
Abnormal glucose metabolism	20 (25.0)
Elevated triglycerides	24 (30.0)
Obesity	20 (25.0)
Body mass index, kg/m^2	23.5 ± 4.2
Serum laboratory features	
HDLC, mg/dL	49.2 ± 9.0
FBG, mg/dL	94.3 ± 17.2
Cholesterol, mg/dL	166.6 ± 47.5
Triglyceride, mg/dL	135.9 ± 76.3
Blood urea nitrogen, mg/dL	119.7 ± 66.0
Creatinine, mg/dL	8.6 ± 2.9
Sodium, mEq/L	141.2 ± 3.7
Potassium, mEq/L	5.6 ± 0.9
Calcium, mEq/L	9.4 ± 0.7
Phosphorus, mEq/L	5.0 ± 1.3
Hemoglobin, g/dL	10.8 ± 2.0
Albumin, mg/dL	4.3 ± 0.6
Ferritin, U/L	624 ± 399
KT/V	1.09 ± 0.26

*Values in parentheses are percents. BP indicates blood pressure; HDLC, high-density lipoprotein cholesterol; and FBG, fasting blood glucose.



Frequency of components of metabolic syndrome in hemodialysis patients by gender. HDLC indicates high-density lipoprotein cholesterol.

Table 2. Characteristics of Study Participants by Metabolic Syndrome Status*

Variable	Metabolic Syndrome		*P*
	Yes (n = 23)	No (n = 57)	
Demographics			
Age, y	58.9 ± 13.3	54.2 ± 16.3	.19
Gender			
Female	9 (39.1)	24 (42.1)	
Male	14 (60.9)	33 (57.9)	.99
Metabolic features			
Diabetes mellitus	12 (52.2)	3 (5.3)	< .001
Hypertension	22 (95.7)	33 (57.9)	.001
Systolic BP, mm Hg	143.8 ± 22.6	137.7 ± 26.7	.31
Diastolic BP, mm Hg	83.8 ± 10.7	81.6 ± 11.7	.43
Low HDLC	11 (47.8)	11 (19.3)	.01
Abnormal glucose metabolism	15 (65.2)	5 (8.8)	< .001
Elevated triglycerides	14 (60.9)	10 (17.5)	< .001
Obesity	14 (60.9)	6 (10.5)	< .001
Body mass index, kg/m^2	26.7 ± 4.3	22.2 ± 3.4	< .001
Serum laboratory features			
HDLC, mg/dL	46.3 ± 9.0	50.4 ± 8.0	.07
FBG, mg/dL	107.2 ± 19.9	89.2 ± 13.0	< .001
Cholesterol, mg/dL	181.6 ± 64.0	160.1 ± 36.0	.07
Triglyceride, mg/dL	177.6 ± 81.0	119.1 ± 68.0	.004
Blood urea nitrogen, mg/dL	137.4 ± 59.9	112.3 ± 57.6	.11
Creatinine, mg/dL	9.1 ± 2.9	8.5 ± 2.9	.41
Sodium, mEq/L	142.1 ± 3.4	140.9 ± 3.8	.17
Potassium, mEq/L	5.7 ± 0.8	5.6 ± 1.0	.92
Calcium, mEq/L	9.4 ± 0.7	9.4 ± 0.7	.84
Phosphorus, mEq/L	4.8 ± 1.1	5.1 ± 1.4	.31
Hemoglobin, g/dL	11.0 ± 1.3	10.7 ± 2.3	.47
Uric acid, mg/dL	6.9 ± 1.5	7.5 ± 1.6	.19
Albumin, mg/dL	4.3 ± 0.7	4.3 ± 0.6	.83
Ferritin, U/L	654 ± 425	602 ± 399	.79
KT/V	1.12 ± 0.20	1.08 ± 0.28	.53

*Values in parentheses are percents. BP indicates blood pressure; HDLC, high-density lipoprotein cholesterol; and FBG, fasting blood glucose.

in the women (Table 3).

The Figure depicts the unadjusted prevalence of individual abnormalities related to MS among hemodialysis patients. The most common element of MS was hypertension in 68.8% (55 patients), followed by elevated triglycerides in 30.0% (24 patients), low HDLC in 27.5% (22 patients), abnormal glucose metabolism in 25% (20 patients), and a waist circumference greater than normal in 25.0% (20 patients). Table 4 presents a breakdown of the number of MS components among hemodialysis patients.

The prevalence of various MS components among males and females is shown in the Figure. The men showed a significantly more frequent abnormality in glucose metabolism compared with the women (P = .008). A low HDLC was significantly more frequent in the women (42.4% versus 17%; P = .02; Table 2). Diabetes mellitus was more frequent in the men (27.7%) compared with the women (P = .01).

Metabolic syndrome was not significantly associated with serum cholesterol, blood urea nitrogen, serum creatinine, serum calcium, serum phosphorus, serum albumin, hemoglobin, or KT/V. Therefore, anemia and disorder in bone mineral metabolism were less likely to affect development of MS in these hemodialysis patients.

DISCUSSION

Results of the present study indicated that MS, as defined by the ATP III criteria, was present in 28.7% of the hemodialysis patients, and it was not significantly associated with gender or age. Overall, 28.7% of the study population showed 3 or more

Table 3. Metabolic and Laboratory Factors of Hemodialysis Patients by Gender*

Variable	Women (n = 33)	Men (n = 47)	*P*
Metabolic syndrome	9 (27.3)	14 (29.8)	> .99
Age, y	57.8 ± 14.2	54.0 ± 16.5	.2
Diabetes mellitus	2 (6.1)	13 (27.7)	.01
Hypertension	24 (72.7)	31 (66)	.62
Systolic BP, mm Hg	134.0 ± 21.8	143.2 ± 27.7	. 1
Diastolic BP, mm Hg	81.5 ± 10.4	82.8 ± 12.2	.6
Low HDLC	14 (42.4)	8 (17.0)	.02
Abnormal glucose metabolism	3 (9.1)	17 (36.2)	.008
Elevated triglycerides	9 (27.3)	15 (31.9)	.8
Obesity	12 (36.4)	8 (17.0)	.06
Body mass index, kg/m^2	23.3 ± 5.1	23.6 ± 3.4	.7
HDLC, mg/dL	50.7 ± 9.8	48.2 ± 8.4	.2
FBG, mg/dL	89.5 ± 16.7	97.7 ± 17.0	.03
Cholesterol, mg/dL	177.0 ± 47.0	159.0 ± 46.0	.1
Triglyceride, mg/dL	143.7 ± 77.0	130.5 ± 75.0	.4
Blood urea nitrogen, mg/dL	114.9 ± 63.9	123.0 ± 68.0	.5
Creatinine, mg/dL	8.0 ± 3.0	9.1 ± 2.7	.1
Sodium, mEq/L	141.0 ± 3.7	141.3 ± 3.7	.8
Potassium, mEq/L	5.5 ± 1.0	5.8 ± 0.9	. 2
Calcium, mEq/L	9.5 ± 0.7	9.3 ± 0.7	.1
Phosphorus, mEq/L	4.9 ± 0.6	5.1 ± 1.6	.4
Hemoglobin, g/dL	11.0 ± 1.9	10.7 ± 2.1	.5
Uric acid, mg/dL	6.9 ± 1.0	7.6 ± 1.8	.08
Albumin, mg/dL	4.5 ± 0.7	4.1 ± 0.5	.06
Ferritin, U/L	793 ± 431	691 ± 394	.1
KT/V	1.06 ± 0.31	1.11 ± 0.22	.4

*Values in parentheses are percents. BP indicates blood pressure; HDLC, high-density lipoprotein cholesterol; and FBG, fasting blood glucose.

Table 4. Number of Criterions of Metabolic Syndrome Present in Hemodialysis Patients

Criteria	Patient (%)	Cumulative Percent
0	5 (6.3)	6.3
1	31 (38.8)	45.0
2	21 (26.3)	71.3
3	19 (23.8)	95.0
4	2 (2.5)	97.5
5	2 (2.5)	100

of the criteria. Thirty-eight percent presented only 1 criterion and 26.3% had 2 criteria. High blood pressure was the most common element of MS. In addition, MS was prevalent among diabetics and patients who had higher BMI and triglyceride levels. This study also showed that MS was not related with serum cholesterol, blood urea nitrogen, serum creatinine, serum calcium, serum potassium, serum albumin, leukocyte count, hemoglobin level, or KT/V. Male subjects were significantly more likely to show abnormality in glucose metabolism, while the prevalence of low HDLC was significantly higher in females.

Even though MS seems to be a risk factor for CKD progression, it is not known whether dialysis in general influences the risk of acquiring MS. Another question is whether MS could itself predict morbidity and mortality in advanced CKD.

Chen and colleagues[14] observed that in patients with CKD, the prevalence of metabolic syndrome was 2.6% higher compared with those without it. Also, the prevalence of MS in stage 4 and 5 of CKD was considerably higher (31%) than that in the Australian general population, which was less than 20%.[12] Furthermore, previous studies reported much higher rates of MS in kidney transplant recipients (55%).[20,21] Elsaid and coworkers reported that the incidence of MS in hemodialysis patients was 62%, with being more common among women (74.4%) than men (52.7%).[22]

In a study, Stoli R et al. demonstrated that about 30% of patients on HD had advanced MS. The older and more obese men with increased levels of triglyceride and glucose in their serum were more likely to be among the severe cases. Diabetes mellitus was a pronounced etiological factor of kidney failure in these patients.[23]

Young and colleagues, in a retrospective cross-sectional study of 202 dialysis patients, assessed the rate of MS at the start of renal replacement therapy.[19] Overall, the prevalence of MS was 69.3% in the studied population, being especially prevalent among diabetic, female, and white patients. They concluded that MS is highly prevalent in patients who are just beginning the dialysis process.

The most common element of MS is usually hypertension since it affects up to 85% of patients, while diabetes mellitus affected 46% of them.[24-26] The individual components that showed the highest risk of CKD were hypertension and hyperglycemia. This finding is in congruity with the evidence that both of these factors seem to be involved in the pathogenesis of CKD, regardless of MS.[27] It has also been observed that a graded response exists between the number of MS risk factors and the risk of CKD.[27] Similar findings have recently been reported by Kurella and colleagues and Tanaka and coworkers.[28,29] Individual MS risk factors, such as blood pressure, body mass index, and serum cholesterol concentration, have been shown to have

a paradoxical and even opposite association with mortality rate in dialysis population, a phenomenon labeled as "reverse epidemiology.[30]"

Johnson and colleages[31] showed that metabolic syndrome occurred in 30.5% of stages 4 and 5 CKD patients and was associated with older age, peritoneal dialysis, ethnicity, increased oxidative stress, lower serum adiponectin concentrations, and a significantly increased risk of future cardiovascular events. The researchers demonstrated that intervention strategies targeting hypercholesterolemia, hyperhomocysteinemia, anemia, and mineral metabolism bone disorder may not be effective in explaining the increase in cardiovascular risk of CKD patients with MS.[31]

CONCLUSIONS

The present study was limited by the number of patients it had access to. Furthermore, the prevalence rates of MS in the general population and in the early stage of CKD patients were not available to us for comparison. However, according to the above literature review and our findings, our understanding of the role of the MS in ESRD patients is growing. Certainly, further studies are needed to help us understand the heightened cardiovascular risk of CKD patients with MS. We must also pay special attention to the phenomenon of reverse epidemiology in hemodialysis population. Thus, it is unclear whether MS could potentially result in a favorable, neutral, or harmful influence on patients' condition in severe CKD. We even think that the criteria of MS for hemodialysis patients might need to be revised.

CONFLICT OF INTEREST

None declared.

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