ORIGINAL ARTICLE

Metabolic syndrome and its components associated with chronic kidney disease

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Background: There is limited information on the relationship between metabolic syndrome (MetS) and chronic kidney disease (CKD) in the Iranian population, a group that has a high prevalence of CKD and obesity. The aim of present study was to determine the relationship between MetS and CKD in West of Iran. **Materials and Methods:** A total of 800 subjects aged more than 35 years admitted from 2011 to 2013 were enrolled in the study. MetS was defined based on the Adult Treatment Panel III criteria, and CKD was defined from the Kidney Disease Outcomes Quality Initiative practice guidelines. Waist circumference and body mass index were calculated, as well, blood samples were taken and lipid profile, plasma glucose levels, and serum creatinine were measured. Data were analyzed with SPSS version 17 (SPSS Inc., Chicago, IL, USA). **Results:** CKD was seen in 14.8% patients with MetS and 8.3% individuals without MetS. MetS was associated with an increased odds ratio (OR) for a glomerular filtration rate <60 ml/min/1.73 m^2 (OR: 1.91; 95% confidence interval [CI]: 1.22-2.99; P = 0.004). Individuals with 2, 3, 4, and 5 components of the MetS had an increased OR for CKD: 2.19 (95% CI: 0.95-3.62), 2.65 (95% CI: 1.03-4.71), 2.86 (95% CI: 1.08-5.53), and 5.03 (95% CI: 1.80-8.57), respectively, compared with individuals with none of the components. **Conclusion:** We found a high prevalence of CKD in patients with MetS compared with the subject without MetS. Our observations raised major clinical and public health concerns in Iran, where both the MetS and kidney diseases are becoming common.

Key words: Chronic kidney disease, end-stage renal disease, metabolic syndrome, serum creatinine

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INTRODUCTION

Metabolic syndrome (MetS) or X syndrome refers to a constellation of risk factors, including obesity, insulin resistance, elevated fasting glucose, elevated triglycerides (TGs), decreased high-density lipoprotein cholesterol (HDL-C), and elevated blood pressure (BP),[1] and is present in approximately 50% of adults in Iran.[2] This clinical entity has been known to increase the risk of cardiovascular disease (CVD), type 2 diabetes, chronic kidney disease (CKD), and total mortality. Globally, a rise in the incidence of CKD and end-stage renal disease in recent years has paralleled the increasing prevalence of obesity MetS and has sparked a great interest in the role of MetS as a novel risk factor for both CVD and CKD.[3] CKD is defined as the presence of kidney damage and a decrease in the level of kidney function based on the glomerular filtration rate (GFR). Previous observational studies are linked MetS with an increased risk of microalbuminuria or proteinuria, early markers of kidney injury.[4,5] In addition, high BP and hyperglycemia were the most powerful predictors of CKD in subjects with MetS.[6] The Third National Health and Nutrition Examination Survey (NHANES III) and the atherosclerosis risk in communities study both reported that MetS was independently associated with CKD in the general population.[7,8] CKD is more likely to develop in patients with MetS, and the frequency of CKD increases with the number of components of MetS.[8] However, the risk estimates for development of CKD with MetS and its individual components are differed among the studies, with some reporting a positive association and a few showing statistically insignificant associations.[8-10]

However, there are limited studies investigating the relationship between MetS and CKD in the Iranian population, a group that has a high prevalence of CKD and obesity,[11] where the genetic and environmental background differs from those in Western countries. So the aim of the present community-based study was to determine the relationship between MetS and CKD in Boroujerd, West of Iran.

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MATERIALS AND METHODS

Study design and participants

The present community-based study was a large part of the Borujerd Health and Nutrition Survey (BHNS) conducted by Lorestan University of Medical Sciences from 2011 to 2013. BHNS was a community-based descriptive program that was performed to evaluate medical history and health-related lifestyle factors of Lor population in Borujerd Province (Western Iran). In this study 25 clusters of subjects over 35 years old from urban (16 clusters) and rural (9 clusters) area of Borujerd Province were selected over a period of 2 years (June 2011 to June 2013) and a total of 800 subjects were enrolled in the study. Initially, the included patients were fully examined and questioned about demographic information (sex, age, residential area [urban/rural]).

Anthropometric and blood pressure measurements

Waist circumference (WC) was measured at the minimum circumference between lowest rib and the upper lateral border of the right iliac crest over light clothing using a flexible measuring tape without any pressure to the body surface being recorded to the nearest 0.1 cm.

After removing shoes and wearing a light dress, height (by a stadiometer using a centimeter scale) and weight (by a clinical scale) were measured. Body mass index (BMI) was calculated by body weight (kg)/height (m^2) and BMI ≥30 kg/m^2 defined as obesity.

To avoid subjective error, all measurements were taken by the same male physician for all males and the same female physician for all females.

BP was measured twice at least 30 min interval between two measurements, using a standard mercury sphygmomanometer, after a 5 min rest from the right hand in a sitting position, and the mean was recorded as BP.

Laboratory measurements

After 12 h of fasting, blood samples were taken in the morning. TG, fasting blood sugar (FBS), cholesterol, HDL, blood urea nitrogen (BUN) and serum creatinine were measured using an enzymatic colorimetric method with standard kits (Pars Azmoun, Iran) by using auto-analyzer (Hitachi, Japan).[12]

Definition of metabolic syndrome and chronic kidney disease

Patients were considered to have MetS if they had any three or more of the following criteria, according to the Adult Treatment Panel III (ATP III):[13]

1. Abdominal obesity: (WC ≥102 cm in men and ≥88 cm in women).
2. Hypertriglyceridemia: TG ≥150 mg/dl or history of drug consumption for hypertriglyceridemia.
3. Low HDL-C: HDL ≤40 mg/dl in men and ≤50 mg/dl in women or history of drug consumption.
4. High BP: BP systolic ≥130 mmHg or BP diastolic ≥85 mmHg or history of anti-hypertensive drug consumption.
5. High fasting glucose: FBS ≥100 mg/dl, history of diabetes mellitus history or using anti-diabetic drugs.

We used the definition of CKD from the Kidney Disease Outcomes Quality Initiative practice guidelines that were published by the National Kidney Foundation.[14] The estimated GFR (eGFR), an indicator of kidney function, was estimated using a simplified equation for the modification of diet renal disease (MDRD) data:

$$eGFR\ (ml/min/1.73\ m^2) = 186.3 \times (\text{serum Cr in mg/dl})^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ for women}) \times 1.212 \text{ (if patient is black)}.$$

CKD was defined as an eGFR of <60 ml/min/1.73 m^2.

Statistical analysis

All data were analyzed by SPSS version 17 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to check that the continuous variables were normally distributed. The significance of association between categorical variables was estimated by Chi-square test and the differences in significance between continuous variables were compared by the Student's *t*-test. The associations between the different traits of the MetS and CKD were analyzed by multivariate logistic regression analysis. $P < 0.05$ was considered statistically significant.

Ethical considerations

The study protocol was approved by Ethical Committee of Lorestan University of Medical Sciences, moreover all respondents voluntarily participated after the intent and the design of the study had been explained to them and signing informed consent forms prior to implementation of the study.

RESULTS

A total of 800 subjects (381 males and 419 females) entered the study. According to ATP III criteria, 344 (43%) had MetS. Characteristics of the study participants with and without MetS are compared in Table 1. Frequency of MetS was higher in females ($P < 0.0001$). GFR tended to be lower in those with MetS compared with those without the syndrome ($P < 0.0001$), while serum creatinine and BUN were not significantly different between the two groups.

CKD was seen in 14.8% patients with MetS and 8.3% individuals without MetS [Table 2]. MetS was associated with an increased odds ratio (OR) for a GFR <60 ml/min/1.73 m^2 (OR: 1.91; 95% confidence interval [CI]: 1.22-2.99; $P = 0.004$).

As shown in Table 3, abdominal obesity, low HDL, and elevated TG were associated with CKD. However, there was no association between elevated fasting glucose and elevated BP with CKD.

Table 4 shows only 5.3% of the CKD patients had no MetS component, while 22% had all 5 components. The odds for eGFR <60 ml/min/1.73 m^2 seems to vary for different components of MetS, and the risk estimate increased as the number of components of MetS increased from 1 to 5. Individuals with 2, 3, 4, and 5 components of the MetS had an increased OR for CKD: 2.19 (95% CI: 0.95-3.62), 2.65 (95% CI: 1.03-4.71), 2.86 (95% CI: 1.08-5.53), and 5.03 (95% CI: 1.80-8.57), respectively, compared with individuals with none of the components [Table 5].

DISCUSSION

We investigated the association between MetS and CKD for the general population of Iran. Our study established a positive and significant relationship between MetS and CKD and indicates that the association between MetS and CKD may be explained by risk conferred by individual components of the syndrome, such as abdominal obesity, low HDL and elevated TG. Also, decreased kidney function is more common in individuals with the MetS than in those without it.

Our findings showed that the prevalence rate of CKD was 14.8% in patients with MetS and results are consistent with previous studies that revealed a significant association between MetS and CKD. Prevalence of CKD in a Chinese population aged 40 years and older with MetS was 15.4% compare to 8.3% in participants without MetS.[15] Chen *et al*.[5] in the NHANES III showed CKD was present in 1.2% of the subjects without multiple sclerosis (MS) and 6.0% of the subjects with MetS. Per their analysis, MetS was found to be independently associated with an increased risk of CKD. Based on a study conducted by Zhang *et al*.[15] on Chinese study participants, MetS was found to be significantly associated with CKD in Northern China. Third Korea National Health and Nutrition Examination Survey study showed the prevalence of CKD among those with MetS was 9.0% whereas among those without MetS was 5.6%. People with MS had a 1.77 times greater risk of CKD than those without MS.[16]

Tanaka *et al*.[17] in a study in Okinawa, Japan showed that MetS was a significant determinant of CKD (OR: 1.537; 95% CI: 1.277-1.850, $P < 0.0001$). Another study in Japan showed the 5-year cumulative incidence of CKD was significantly

Table 1: Comparing baseline characteristics of the study participants with and without the MetS

Characteristic	MetS		*P*
	Yes (*n* = 344)	No (*n* = 456)	
Age (years)	55.51±10.88	54.37±13.09	0.195*
BMI (kg/m^2)	28.98±4.79	25.06±4.29	<0.0001*
Gender (%)			
Males	91 (26.5)	290 (63.6)	<0.0001†
Females	253 (73.5)	166 (36.4)	
Systolic blood pressure (mmHg)	136.26±20.16	119.87±18.65	<0.0001*
Diastolic blood pressure (mmHg)	83.51±12.06	76.16±10.68	<0.0001*
Waist circumference (cm)	98.26±10.14	87.73±10.94	<0.0001*
Total cholesterol (mg/dl)	211.52±38.98	178.35±35.81	<0.0001*
TG (mg/dl)	221.94±134.67	117.07±60.36	<0.0001*
LDL (mg/dl)	126.31±41.17	107.83±35.41	<0.0001*
HDL (mg/dl)	40.46±5.73	46.73±6.69	<0.0001*
Fasting blood glucose (mg/dl)	123.59±53.12	102.09±26.23	<0.0001*
Uric acid (mg/dl)	7.11±4.72	6.84±2.74	0.328*
Serum creatinine (mg/dl)	0.91±0.21	0.94±0.23	0.123*
BUN (mg/dl)	15.72±7.23	15.61±4.69	0.796*
GFR (mL/min/1.73 m^2)	77.57±17.09	84.61±18.11	<0.0001*

*t-test statistics; †Chi-square statistics; BMI = Body mass index; LDL = Low-density lipoprotein; HDL = High-density lipoprotein; BUN = Blood urea nitrogen; GFR = Glomerular filtration rate; MetS = Metabolic syndrome; TG = Triglyceride

Table 2: Cross-prevalence of CKD and MetS

CKD	MetS present (%)	MetS absent (%)
CKD present	51 (14.8)	38 (8.3)
CKD absent	293 (85.2)	418 (91.7)

CKD = Chronic kidney disease; MetS = Metabolic syndrome

Table 3: Associations of MetS components with CKD

Components	OR	95% CI	*P*
Abdominal obesity	2.06	1.32-3.22	0.001
Elevated fasting glucose	1.38	0.88-2.16	0.151
Elevated blood pressure	1.47	0.94-2.29	0.086
Low HDL	1.80	1.13-2.86	0.012
Elevated TG	1.56	1.01-2.43	0.047

CKD = Chronic kidney disease; MetS = Metabolic syndrome; CI = Confidence interval; OR = Odds ratio; HDL = High-density lipoprotein; TG = Triglyceride

Table 4: MetS components frequency in all participants and by CKD status

MetS score	CKD present (%)	CKD absent (%)	All participants (%)
0	6 (5.3)	107 (94.7)	113 (100)
1	11 (7.3)	140 (92.7)	151 (100)
2	21 (10.9)	171 (89.1)	192 (100)
3	21 (13)	141 (87)	162 (100)
4	17 (13.8)	106 (86.2)	123 (100)
5	13 (22)	46 (78)	59 (100)

CKD = Chronic kidney disease; MetS = Metabolic syndrome

Table 5: Multivariate OR of CKD associated with several components of MetS

MetS score	OR	95% CI	*P*
0	1		1
1	1.41	0.51-3.91	0.519
2	2.19	0.95-3.62	0.047
3	2.65	1.03-4.71	0.042
4	2.86	1.08-5.53	0.033
5	5.03	1.80-8.57	<0.0001

CKD = Chronic kidney disease; MetS = Metabolic syndrome; OR = Odds ratio; CI = Confidence interval

greater in subjects with than without MS (10.6% vs. 4.8%; $P < 0.01$).[18] While Hanai *et al*.[19] showed decreased GFR is not independently associated with MetS.

Also, Gatti *et al*.[20] established that in obese nondiabetic individuals the risk of CKD is independent of the MetS, and MetS is not a risk factor for kidney dysfunction in these subjects. Emem-Chioma *et al*.[21] showed CKD was more common in subjects with MetS compared with those without (4.8% vs. 2.9%), but the difference was not statistically significant.

Previous studies have suggested that the risk for CKD increased as the number of MetS components increased.[22,23] Each of the components of the MetS has been identified to be associated with CKD;[5,8,24-26] thus, the diagnosis may reflect additive effects of the individual components on CKD risk. The risk conferred by each component, however, is probably not equal. In addition, patients with MetS have a higher risk for development of higher urinary protein excretion.[10,27] Interestingly, our study showed that abdominal obesity, low HDL and elevated TG had an association with CKD. However, there was no association between elevated fasting glucose and elevated BP with CKD. Similar to our findings, some studies in the USA[5] and Iran have indicated that obesity is associated with CKD.[5,28] Hypertension is one of the most common underlying causes of CKD. The relationship between hypertension and progression of CKD has been established in several epidemiologic studies.[23,29-31] But as it showed in our study there was no association between high BP with CKD. Our finding was consistent with Chen *et al*.[32] and Emem-Chioma *et al*.[21] that showed no significant difference between elevated BP and CKD. Our finding was consistent with studies that concluded that low HDL and high TG levels had association with CKD and appeared to be a risk factor for developing CKD[5,31,33] whereas inconsistent with the aforementioned studies in China,[32] Japan,[10] and Nigeria.[21]

Limitations of our present study should be noted. In our analysis, we employed the use of eGFR as opposed to directly measuring GFR to define CKD. GFR, based on the MDRD study equation, has not been validated for use with the Iranian population. The MDRD-equation might have overestimated or underestimated the actual GFR in the Iranian population because it was developed primarily in populations in the US.

In this study, we elevated the prevalence of CKD among subjects with MetS among Iranian general population and provided new and important information regarding the relationship between the MetS and risk of CKD. In conclusion, we found a high prevalence of CKD in our patients with MetS compared with the subject without MetS. In addition, there is a graded relationship between the number of the MetS components and risk of CKD. Based on the fact that approximately a half of Iranian population has MetS, the risk of CKD would be considered high in Iran resulting in higher medical cost. Our observations raise major clinical and public health concerns in Iran, where both the MetS and kidney disease are becoming common.

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AUTHOR'S CONTRIBUTIONS

AM provided conception and design and contributed to administrative, technical and material support, MM supervised and revised it critically for important intellectual content, NR participated in data acquisition, drafting the article, data analysis and interpretation, MM revised it critically for important intellectual content and participated in data acquisition, and EY Abdolmaleki contributed to statistical analysis and revised it.

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