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Original Paper

A Study on the Correlation between Metabolic Syndrome and Proteinuria in Chronic Kidney Disease

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Introduction. To assess the frequency of metabolic syndrome (MS) and its association with proteinuria in patients with chronic kidney disease (CKD).

Methods. A cross-sectional study was conducted among 386 CKD patients from June 2022 to June 2023. Prevalence of MS was calculated, clinical characteristics of CKD patients with and without MS were compared, and multivariable logistic regression was performed to estimate associations between the components of MS with the categories of proteinuria.

Results. The prevalence of MS was 24.9% among the 386 CKD patients. Patients with MS had greater 24-h urinary protein excretion and lower estimated glomerular filtration rate (eGFR) compared to patients without MS ($P < .05$). The proportion of patients with MS increased across proteinuria strata: mild (< 1.0 g/day) 14.4%, moderate (1.0 to 3.5 g/day) 35.2%, and severe (≥ 3.5 g/day) 49.0% ($P < .05$). In adjusted models, increased postprandial blood glucose (PBG), hypertension, and the ratio of triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) were independent associations with increased burden of proteinuria.

Conclusion. Metabolic syndrome was independently associated with increased proteinuria burden in CKD. Early recognition and treatment of metabolic risk factors, especially dysglycemia, hypertension, and dyslipidemia, may help to promote renal protection and improve overall patient health.

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INTRODUCTION

Chronic kidney disease (CKD) is a progressive condition resulting from various primary renal disorders or secondary systemic diseases such as diabetes mellitus and hypertension.[1,2] Chronic kidney disease is now identified as a global public health issue due to its prevalence, burden on healthcare resources, poor awareness, and association with poor health outcomes.[3,4] The increasing prevalence of metabolic conditions, most notably diabetes mellitus, obesity, hyperuricemia, and hypertension, continues to result in an increased burden of CKD, emphasizing the relationship between metabolic health and kidney injury.[5,6]

Metabolic syndrome (MS) is characterized by metabolic derangements, including insulin resistance, central obesity, hypertension, dyslipidemia, and impaired glucose metabolism.[7-9] This indicates systematic inflammation and a state of metabolic dysregulation, which places individuals at an increased risk of cardiovascular disease, type 2 diabetes mellitus, and mortality.[10,11]

Proteinuria is an important marker of kidney injury, yet it may also signifies systemic endothelial dysfunction and vascular injury.[12,13] Individuals with MS often have multiple risk factors

(hyperglycemia, dyslipidemia, and hypertension), which contribute to kidney microvascular damage and may hasten the development of proteinuria.[14] Although some studies have previously identified an association between metabolic syndrome and kidney disease, they were primarily conducted in community-based or general populations rather than in well-characterized CKD cohorts; therefore, the relationship between MS components and proteinuria burden remains unclear.[15-17]

While it is acknowledged that MS and CKD share many metabolic pathways, there is limited evidence regarding the association between specific components of MS and the severity of proteinuria in patients with CKD. Thus, this study sought to estimate the prevalence of MS and establish associations between certain components of MS and proteinuria in patients with CKD.

MATERIALS AND METHODS

Study design and setting

This research was conducted as a single-center cross-sectional study from June 2022 to June 2023, by participants recruited from the Affiliated Hospital of Hebei University. A written informed consent from each participant was obtained prior to commencement of the study. The study protocol was in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee of the Affiliated Hospital of Hebei University (Approval Number: HDFYLL-KY-2024-146. Dat:26 June 2024). All aspects of the study were observational, and no follow-up intervention was conducted.

Participants: inclusion and exclusion

According to the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, chronic kidney disease (CKD) is characterized by a persistent reduction in estimated glomerular filtration rate (eGFR) of < 60 mL/min/1.73 m^2, and/or albuminuria (≥30 mg/g creatinine), and/or other structural abnormality of the kidneys for at least three months.[18] Evidence of chronicity may include continuous laboratory records or a clinical diagnosis in the electronic medical record.

We enrolled consecutive adults (≥18 years) who met the KDIGO criteria for the diagnosis of CKD and provided informed consent. The diagnosis of CKD was attributed to causes such as diabetic nephropathy, hypertensive nephrosclerosis, glomerulonephritis, or other secondary nephropathies. Exclusion criteria were non-CKD patients; those with acute kidney injury, active malignancy, myocardial infarction or stroke within two weeks, congestive heart failure classified as New York Heart Association (NYHA) III–IV, significant liver disease, any active infection (such as urinary tract infection, or HIV), pregnancy, previous organ transplantation, or missing laboratory data. Patients were also excluded if they had an active severe psychiatric disorder or any physical disability that prevented them from participating in the study.

Diagnostic criteria

Metabolic syndrome (MS) was defined by the 2017 criteria of the Endocrinology Branch of the Chinese Medical Association.[19] Participants who met three or more of the following five components were classified as having MS.

Central obesity: waist circumference ≥ 90 cm for men or ≥ 85 cm for women.

Hyperglycemia: fasting blood glucose ≥ 6.1 mmol/L, 2-hour postprandial glucose ≥ 7.8 mmol/L, or diabetes treatment.

Hypertension: blood pressure ≥ 130/85 mmHg or on antihypertensive therapy.

Hypertriglyceridemia: ≥ 1.7 mmol/L triglyceride level.

Low HDL-C: < 1.04 mmol/L.

CKD staging was done in accordance with KDIGO stages (G1-G5) and the MDRD (Modified Diet in Renal Disease) equation. The proteinuria category was classified morbidly as < 1.0 g/day, 1.0-3.5 g/day, to ≥ 3.5 g/day, reflecting clinically relevant categories of proteinuria.

Laboratory examinations and grouping

All subjects completed the relevant tests to assess their fasting blood glucose, 2-hour postprandial glucose level, total cholesterol, triglycerides, LDL-C, HDL-C, hemoglobin, serum creatinine, and urinary protein collected over 24 hours.

Proteinuria was assessed by the pyrogallol red–molybdate colorimetric method on a Hitachi 7600 automated analyzer, calibrated daily against the manufacturer's quality control material. If urine creatinine excretion was less than 10 mg/kg/day in women or less than 15 mg/kg/day in men, the

24-hour urine collections were labeled incomplete and were excluded from analysis.[20]

HOMA-IR was calculated from fasting insulin multiply by fasting glucose divided by 22.5. The triglyceride/HDL-C ratio was categorized into three groups: ≤1, 1–2, or > 2.[21-23] A nonspecific marker of estimated GFR was calculated using the MDRD equation. Approximately 4% of subjects had missing insulin data, which were excluded from the HOMA-IR calculations listwise. Because HbA1c data were not consistently available, they were not analyzed.

For subgroup analysis, subjects were categorized as CKD with MS and CKD without MS, and also stratified by proteinuria severity level: < 1.0 g/day, 1.0-3.5 g/day, or ≥3.5 g/day.

Statistical methods

Continuous variables with normal distribution were expressed by mean ± standard deviation (SD) and evaluated based on the independent-sample t-test or one-way analysis of variance (ANOVA). Non-normally distributed variables were expressed by median (interquartile range) and assessed using the Mann-Whitney U test or Kruskal-Wallis test. Categorial variables were expressed as counts and percentages and assessed using the χ^2 test or Fisher's exact test as appropriate. Ordinal logistic regression (proportional-odds model) was used to assess the association between components of metabolic syndrome (MS) and levels of proteinuria (< 1.0 g/day, 1.0–3.5 g/day, ≥ 3.5 g/day). The proportional-odds assumption was tested and met ($P > .05$). Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test ($P > .05$ reflected good model fit).

Binary multivariable logistic regression was employed with sufficient rationale, wherever an ordinal logistic was not feasible for re-analysis. Events-per-variable (EPV) testing met the 171-event level, which confirmed model stability (7–9 covariates). The independent variables included age, sex, body mass index (BMI), hypertension, postprandial blood glucose (PBG) levels, triglyceride/high-density lipoprotein cholesterol ratio (TG/HDL-C), and estimated glomerular filtration rate (eGFR). Multicollinearity was assessed using the variance inflation factor (VIF < 5), which confirmed no significant collinearity. Multiplicity was addressed by prespecifying the primary hypothesis, that is, the association between MS and proteinuria ≥ 1.0 g/day. Two analyses for sensitivity were performed: (1) stratifying by stage of chronic kidney disease (G1-2 vs G3-5), and (2) using the eGFR as a continuous variable, as included in the referent. The results were consistent across both analyses.

All statistical analyses were performed using SPSS version 19.0 (IBM Corp., Armonk, NY, USA). Two-tailed $P < .05$ was considered statistically significant. The missing data was < 5 % of the overall n, which was assumed under our analyses to be complete data.

RESULTS

General characteristics

The study involved a cohort of 386 individuals diagnosed with chronic kidney disease (CKD) (n = 386). Table 1 provides a summary of the baseline clinical and biochemical characteristics of the study population. The average age of the participants was 39.0 ± 12.4 years, with 40.4% being identified as male (n = 156). The prevalence of metabolic syndrome (MS) was noted to be 24.9% (n = 96). The overall mean estimated glomerular filtration rate (eGFR) of the cohort was 1.64 ± 0.24 mL/s/1.73 m^2.

Patients in the MS group were significantly older than those in the non-MS group (mean age of 46 years compared to 37 years, $P < .001$) and were more often male (53.1% vs. 36.2%, $P = .004$), at baseline. Patients in MS group were more likely to be current smokers (21.9% vs. 6.6%, $P < .001$) and consume alcohol (13.5% vs. 3.8%, $P = .002$). In addition, baseline BMI, systolic and diastolic BP, fasting blood glucose, total cholesterol, triglycerides, and LDL-C levels were all significantly higher, whereas HDL-C level was significantly lower in the MS group compared to the non-MS group (all $P < .05$).

Association between MS and proteinuria

As shown in Table 2, the prevalence of MS increases significantly with the increasing severity of proteinuria: 14.4% in the mild category (< 1.0 g/day), 35.2% in the moderate category (1.0-3.5 g/day), and 49.0% in the severe category (≥ 3.5 g/day; $P < .001$).

Individuals with higher proteinuria also showed significantly higher levels of BMI, systolic blood

Table 1. Comparison of baseline clinical and biochemical characteristics between CKD patients with MS and without MS (n = 386). Data are present as mean ± SD or median [IQR] for continuous variables and as n (%) for categorical variables. *P*-values indicate comparisons between CKD patients with and without MS.

	Total	Non-MS	MS	*P*
n	386	290	96	
Age (years)	39 (30,54)	37 (30,47)	46 (37,54)	< .05
Male (n/%)	156 (40.41)	105 (36.21)	51 (53.13)	< .05
Smoking history (n/%)	40 (10.36)	19 (6.55)	21 (21.88)	< .05
Drinking history (n/%)	24 (6.22)	11 (3.79)	13 (13.54)	< .05
Hypertension (n/%)	156 (40.41)	72 (24.82)	84 (87.5)	< .05
Diabetes Mellitus (n/%)	15 (3.87)	3 (1.03)	12 (12.5)	< .05
Dyslipidemia (n/%)	43 (11.14)	20 (6.90)	23 (23.96)	< .05
BMI (kg/m^2)	23.81 ± 3.10	21.34 ± 2.51	26.87 ± 3.69	< .05
Abdominal Circumference (cm)	84 (80,89)	81 (79,87)	88 (86,93)	< .05
Hb (g/L)	127.15 ± 16.29	125.88 ± 13.97	129.73 ± 21.05	> .05
FBG (mmol/L)	4.63 (4.21,4.99)	4.60 (4.20,4.93)	4.85 (4.49,5.40)	< .05
PBG (mmol/L)	6.51 (5.64,7.45)	6.15 (5.53,6.83)	7.98 (6.88,11.04)	< .05
HOMA- IR	1.45 (1.03,1.20)	1.29 (0.90,1.65)	2.21 (1.50,3.01)	< .05
TG (mmol/L)	1.36 (0.95,2.06)	1.17 (0.83,1.60)	2.18 (1.76,2.97)	< .05
TC (mmol/L)	4.63 (4.02,5.30)	4.57 (3.97,5.28)	4.71 (4.09,5.51)	> .05
HDL-C (mmol/L)	1.10 (0.94,1.36)	1.17 (1.01,1.40)	0.97 (0.89,1.16)	< .05
LDL-C (mmol/L)	2.99 (2.53,3.50)	2.93 (2.50,3.45)	3.04 (2.65,3.64)	> .05
eGFR (mL/s/1.73m^2), (n/%)				
≥ 1.5	194 (50.26)	166 (85.57)	28 (14.43)	< .05
1~1.5	108 (27.98)	70 (64.81)	38 (35.19)	< .05
< 1	84 (21.76)	37 (12.76)	47 (48.96)	< .05
Urinary Protein Quantification (mg/L)	0.85 (0.46,1.80)	0.74 (0.40,1.39)	1.54 (0.73,2.10)	< .05

CKD, chronic kidney disease; MS, metabolic syndrome; BMI, body mass index; Hb, hemoglobin; FBG, fasting blood glucose; PBG, 2-h post-prandial blood glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.

Table 2. Comparison of clinical variables among CKD patients with MS across different proteinuria categories. Data are presented as mean ± SD or median [IQR] for continuous variables and as n (%) for categorical variables. *P*-values represent overall group differences determined by ANOVA or χ^2 test, as appropriate.

Variables	Group A (< 1.0 g/day)	Group B (1.0-3.5 g/day)	Group C (≥ 3.5 g/day)	*P*
n	215	143	28	
Age (years)	38 (30,49)	41 (33,51)	42 (31,54)	> .05
Male (n/%)	71 (33.02)	70 (48.95)	22 (78.57)	< .05
BMI (kg/m^2)	20.89 (19.84,24.52)	23.48 (20.65,25.88)	24.9 (21.61,25.79)	< .05
Abdominal Circumference (cm)	84 (80,87)	85 (81,89)	86 (83,89)	> .05
FBG (mmol/L)	4.53 (4.20,4.98)	4.75 (4.30,5.13)	4.97 (4.63,5.26)	< .05
PBG (mmol/L)	6.31 (5.53,7.23)	6.74 (5.86,7.82)	6.87 (6.34,9.34)	< .05
TG (mmol/L)	1.17 (0.80,1.56)	1.81 (1.18,2.44)	2.12 (1.62,3.20)	< .05
TC (mmol/L)	4.62 ± 0.97	4.99 ± 1.20	6.38 ± 1.90	< .05
HDL-C (mmol/L)	1.13 (0.98,1.30)	1.14 (0.95,1.38)	1.18 (0.99,1.47)	> .05
LDL-C (mmol/L)	2.84 (2.53,3.52)	3.26 (2.65,3.80)	3.98 (2.81,4.96)	< .05
eGFR (mL/s/1.73 m^2)	1.63 ± 0.46	1.30 ± 0.47	0.90 ± 0.69	< .05

CKD, chronic kidney disease; MS, metabolic syndrome; BMI, body mass index; FBG, fasting blood glucose; PBG, 2-h post-prandial blood glucose; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; eGFR, estimated glomerular filtration rate.

pressure, fasting blood glucose, triglyceride, and LDL-C levels, respectively ($P < .05$). Age, waist circumference, and HDL-C level did not show statistically significant differences across proteinuria categories ($P > .05$).

Logistic regression analysis of risk factors for proteinuria

Variance inflation factor (VIF) analysis showed no evidence of multicollinearity among variables (all VIF < 5).

In the univariate logistic regression, advanced age, male sex, a higher BMI (≥ 25 kg/m^2), hypertension, increased post-prandial blood glucose level (PBG $\geq$ 11.1 mmol/L), and hypertriglyceridemia were statistically significant factors associated with proteinuria $\geq$ 1.0 g/day (all $P < .05$; Table 3).

In the multivariable ordinal logistic regression analysis, the following variables remained significant after adjustments for age, sex, and eGFR:

A TG/HDL-C ratio that was higher than baseline was an independent predictor of moderate proteinuria (1.0–3.5 g/day; adjusted OR of 1.47, 95% CI of 1.12–1.93, $P = .006$).

Hypertension and increased PBG were independent factors that placed patients at a higher risk of severe proteinuria ($\geq$ 3.5 g/day; adjusted OR 2.19, 95% CI of 1.31–3.67, $P = .002$; and OR of 1.98, 95% CI of 1.21–3.22, $P = .008$, respectively).

Associations remained robust in sensitivity analyses with continuous eGFR (Table 4,5).

Stage-specific observations

Descriptive analyses stratified by CKD stage (G1–2 vs. G3–5) indicated that patients with advanced CKD (G3–5) had higher proteinuria and a greater incidence of MS ($P < .05$) than patients with early CKD.

Because the sample sizes were relatively small

Table 3. Univariate logistic regression analysis of risk factors associated with moderate-to-severe proteinuria (≥ 1.0 g/day) in patients with CKD. Univariate logistic regression analysis identified advanced age, male sex, higher BMI, hypertension, increased PBG, and hypertriglyceridemia as significant factors associated with moderate-to-severe proteinuria in patients with CKD. Data are presented as odds ratios (ORs) with 95 % confidence intervals (CIs). $P < .05$ was considered statistically significant.

	Or (95%ci)	*P*
Age (years), (n/%)		
< 40	1	
40~59	1.38 (0.87~2.18)	< .2
≥ 60	2.88 (1.04~7.59)	< .05
Gender (male) (n/%)	2.33 (1.47~3.80)	< .05
Increased abdominal circumference (cm)	0.77 (0.47~1.26)	
Increased BMI (kg/m^2)	1.88 (1.13~3.21)	< .05
Hypertension (n/%)	2.48 (1.60~3.97)	< .05
PBG (mmol/L), (n/%)		
< 7.8	1	
7.8~11.0	1.97 (1.05~3.88)	< .05
≥ 11.1	4.88 (1.57~16.05)	< .05
TG (mmol/L)	4.68 (2.80~7.51)	< .05
TG/HDL-C (n/%)		
1	1	
1~2	2.30 (1.37~3.83)	< .05
> 2	4.16 (2.26~ 7.74)	< .05
MS (n/%)	3.26 (1.89~5.62)	< .05

CKD, chronic kidney disease; BMI, body mass index; PBG, 2-h post-prandial blood glucose; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; MS, metabolic syndrome.

Table 4. Multivariate logistic regression analysis of risk factors associated with proteinuria in patients with CKD. Multivariate logistic regression analysis identified hypertension, increased PBG and a higher TG/HDL-C ratio as independent predictors of proteinuria after adjusting for potential confounders, including age, sex, and eGFR. Data are presented as odds ratios (ORs) with 95 % confidence intervals (CIs). $P < .05$ was considered statistically significant.

	1.0 ≤ Proteinuria < 3.2 (g/d)		Proteinuria ≥ 3.5 (g/d)	
	Or (95%ci)	*P*	Or (95%ci)	*P*
Age (years), (n/%)				
< 40	1		1	
40~59	0.98 (0.56~1.83)	> .05	0.63 (0.21~2.02)	> .05
≥ 60	1.53 (0.49~4.76)	> .05	0.81 (0.15~5.33)	> .05
Gender (Male) (n/%)	1.30 (0.73~2.19)	> .05	0.63 (0.22~2.05)	> .05
Increased Abdominal Circumference (cm)	0.56 (0.28~1.12)	> .05	0.07 (0.01~0.41)	< .05
Increased BMI (kg/m^2)	1.35 (0.63~2.85)	> .05	2.23 (0.67~8.12)	> .05
Hypertension (n/%)	1.51 (0.85~2.69)	> .05	7.16 (1.99~25.87)	< .05
PBG (mmol/L), (n/%)				
< 7.8	1		1	
7.8~11.0	1.53 (0.70~3.34)	> .05	1.88 (0.45~8.24)	> .05
≥ 11.1	2.51 (0.69~9.28)	> .05	8.31 (1.32~54.33)	< .05
TG/HDL-C (n/%)				
1	1		1	
1~2	2.33 (1.21~3.84)	< .05	1.76 (0.45~7.17)	> .05
> 2	2.67 (1.32~5.49)	< .05	3.14 (0.76~13.28)	> .05

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; BMI, body mass index; PBG, 2-h post-prandial blood glucose; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

Table 5. Adjusted effects of metabolic syndrome components on the severity of proteinuria in patients with CKD. Using multivariate logistic regression analysis adjusted for eGFR, hypertension, increased PBG, and a higher TG/HDL-C ratio were found to be independently associated with the presence and severity of proteinuria. Data are presented as odds ratios (ORs) with 95 % confidence intervals (CIs). *P* < .05 was considered statistically significant.

	1.0 ≤ Proteinuria < 3.5 (g/d)		Proteinuria ≥ 3.5 (g/d)	
	Or (95%ci)	*P*	Or (95%ci)	*P*
Increased Abdominal Circumference (cm)	0.51 (0.27~1.02)	< .05	0.06 (0.01~0.31)	< .05
Increased BMI (kg/m^2)	1.37 (0.68~2.93)	> .05	2.43 (0.76~8.54)	> .05
Hypertension	1.63 (0.96~2.77)	> .05	6.97 (2.06~24.83)	< .05
PBG (mmol/L), (n/%)				
< 7.8	1		1	
7.8~11.0	1.60 (0.79~3.41)	> .05	1.47 (0.40~6.22)	> .05
≥ 11.1	2.84 (0.77~9.99)	> .05	8.36 (1.50~45.62)	< .05
TG/HDL-C, (n/%)				
1	1		1	
1~2	2.33 (1.21~3.84)	< .05	1.76 (0.45~7.17)	> .05
> 2	2.81 (1.36~5.64)	< .05	4.21 (1.11~16.01)	< .05

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; BMI, body mass index; PBG, 2-h post-prandial blood glucose; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol.

for each CKD stage, stage-specific regression analyses may not be adequately powered. Therefore, eGFR was included as a continuous co-variate in the main regression analyses, used to adjust for CKD severity. After adjusting for eGFR, the associations of hypertension, high PBG, and the TG/HDL-C ratio with the presence of proteinuria were statistically significant, suggesting that these metabolic factors are important drivers of proteinuria burden independent of CKD stage.

DISCUSSION

This cross-sectional study established that metabolic syndrome (MS) occurs in approximately 25% (24.9%) of individuals with chronic kidney disease (CKD) and can independently be tied to a greater proteinuria burden.

The frequency of MS increased progressively across the proteinuria strata, and specific metabolic components (e.g., dysglycemia, hypertension, or elevated triglyceride-to-high-density lipoprotein cholesterol [TG/HDL-C] ratio) were meaningful estimators of increased proteinuria severity.

These results continue to support the premise that metabolic dysregulation could worsen kidney injury, even in individuals with CKD, and provide further evidence for the interdependence of metabolic and renal pathways.[24,25]

Metabolic syndrome is characterized by insulin resistance, endothelial dysfunction, and chronic low-grade inflammation, all of which provide significant cardiovascular and renal morbidity.[25,26] Several publications have illustrated a relationship between MS and heightened risk of diabetes mellitus, cardiovascular events, and mortality,[27,28] but very few have examined the association of individual components of MS with proteinuria severity in patients with CKD.

This study builds on previous community-based cohorts and provides CKD-specific evidence indicating that MS patients have a poorer metabolic and renal profile compared to MS-negative patients, highlighting the impact of the coexistence of both metabolic and renal variables on the overall disease burden.[29,30]

The relationships we observed between dysglycemia, hypertension, and dyslipidemia with increasing proteinuria severity are at least partly justified within the framework of physiology and pathophysiology. Hyperglycemia causes glomerular hyperfiltration, tubular and glomerular basement membrane thickening, and depositions of glycation end-products,[31,32] while hypertension triggers intraglomerular pressure overload and endothelial dysfunction,[33,34] and dyslipidemia may stimulate podocyte injury, lipid depositions, and/or segmental sclerosis.[35-37]

Together, these mechanisms represent the potential for metabolic injury resulting in worsening proteinuria and declining kidney function.

From a clinical standpoint, this data support the need for integrated metabolic assessment and management in CKD treatment. The ability to identify patients with higher postprandial blood

glucose, blood pressure, and TG-to-HDL-C ratio should allow for identifying patients at greater risk sooner and may guide potential intervention to limit upper proteinuria and preserve renal function. The data support the need for screening and managing dysglycemia, hypertension, and dyslipidemia, among CKD patients to reduce proteinuria progression and possible decline in kidney function.[12,38]

Limitation of the study

First, the cross-sectional design of this study limits causal inference and an assessment of temporal relationships between components of MS and proteinuria.

Second, this single-center study took place in an urban tertiary hospital, which may affect the generalizability to a broader CKD population.

Third, due to a lack of HbA1c data, the analysis cannot include information that would provide a more careful assessment of long-term glycemic control.

Fourth, no adjustments can be made for unmeasured confounding, such as diet, genetic susceptibility, and lifestyle.

Finally, while categories of ordered proteinuria were modeled with ordinal logistic regression, limitations of the model cannot exclude the possibility of residual limitations of the model and violation of the assumption of proportional odds.

Future studies longitudinal multi-center studies are necessary to confirm associations and determine if the comprehensive management of dysglycemia, hypertension, and dyslipidemia may reduce proteinuria and postpone the progression of the course of CKD. If HbA1c and insulin resistance indices were available and if lifestyle data and genetic variance were included, then it would contribute to a better understanding of causality as it pertains to MS, glycemic injury, and renal injury.

CONCLUSION

Metabolic syndrome is prevalent among patients with CKD and is independently associated with increased proteinuria. Among the components of MS, dysglycemia, hypertension, and an elevated TG-to-HDL-C ratio show the strongest associations with the severity of proteinuria. These findings emphasize the importance of early identification and comprehensive management of metabolic risk factors in CKD to improve long-term outcomes. However, given the cross-sectional design of this study, the results should be interpreted as associative and hypothesis-generating rather than causal. Future multicenter prospective studies are warranted to validate these associations and to determine whether metabolic control can slow the progression of proteinuria and enhance long-term outcomes in CKD.

DECLARATIONS

Ethics approval and consent to participate

The study was approved by the Affiliated Hospital of Hebei University ethics committee (Approval Number: HDFYLL-KY-2024-146. Dat:26 June 2024). All participants signed the informed consent form and agreed to provide the information involved in the case report form.

Consent for publication

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this. Further enquiries can be directed to the corresponding author.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

LG is responsible for the guarantor of integrity of the entire study, study concepts & design, clinical studies, statistical analysis, manuscript preparation & editing; LR is responsible for the guarantor of integrity of the entire study, literature research, data analysis, manuscript editing; JL is responsible for the definition of intellectual content, data acquisition, manuscript editing; JDL is responsible for the guarantor of integrity of the entire study, experimental studies, data analysis; YLG is responsible for the guarantor of integrity of the entire study, manuscript review. All authors read and approved the final manuscript.

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REFERENCES

1. Townsend RR, Anderson AH, Chirinos JA, et al. Association of Pulse Wave Velocity With Chronic Kidney Disease Progression and Mortality: Findings From the CRIC Study (Chronic Renal Insufficiency Cohort). Hypertension. 2018;71:1101-7.
2. McCullough PA, Steigerwalt S, Tolia K, et al. Cardiovascular disease in chronic kidney disease: data from the Kidney Early Evaluation Program (KEEP). Curr Diab Rep. 2011;11:47-55.
3. Tonelli M, Wanner C, Kidney Disease: Improving Global Outcomes Lipid Guideline Development Work Group M. Lipid management in chronic kidney disease: synopsis of the Kidney Disease: Improving Global Outcomes 2013 clinical practice guideline. Ann Intern Med. 2014;160:182.
4. Lorenzen JM, Haller H, Thum T. MicroRNAs as mediators and therapeutic targets in chronic kidney disease. Nat Rev Nephrol. 2011;7:286-94.
5. Zheng Y, Wang Y, Liu S, et al. Potential Blood Pressure Goals in IgA Nephropathy: Prevalence, Awareness, and Treatment Rates in Chronic Kidney Disease Among Patients with Hypertension in China (PATRIOTIC) Study. Kidney Blood Press Res. 2018;43:1786-95.
6. Kim H, Hur M, Lee S, Lee GH, Moon HW, Yun YM. European Kidney Function Consortium Equation vs. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) Refit Equations for Estimating Glomerular Filtration Rate: Comparison with CKD-EPI Equations in the Korean Population. J Clin Med. 2022;11.
7. Car J. Urinary tract infections in women: diagnosis and management in primary care. BMJ. 2006;332:94-7.
8. Gomes SL, Bobby Z, Ganesan P, Saroja K, Parameswari GR. Metabolic syndrome and its related biochemical derangements in breast cancer patients who received neoadjuvant chemotherapy: A study from a tertiary care oncology centre from Puducherry, South India. Diabetes Metab Syndr. 2021;15:975-80.
9. Shalitin S, Moreno LA. Obesity, Metabolic Syndrome and Nutrition. World Rev Nutr Diet. 2019;120:20-47.
10. Osepyants VG, Karpov S, Saneeva G, Cherednichenko NL. Use of confocal microscopy of the cornea as an early marker of sensory neuropathy in patients with metabolic syndrome. Medical News of North Caucasus. 2022;17:76-8.
11. Çetin SI, Beydoğan E, Güzel S, Maviş O, Boyuk B. The Evaluation of Liver Steatosis with Transient Elastography in Metabolic Syndrome and the Relationship Between Serum Endorphin Levels. South Clin Ist Euras. 2021;32:58-63.
12. Diercks GF, van Boven AJ, Hillege HL, et al. Microalbuminuria is independently associated with ischaemic electrocardiographic abnormalities in a large non-diabetic population. The PREVEND (Prevention of REnal and Vascular ENdstage Disease) study. Eur Heart J. 2000;21:1922-7.
13. Oellgaard J, Gaede P, Rossing P, et al. Reduced risk of heart failure with intensified multifactorial intervention in individuals with type 2 diabetes and microalbuminuria: 21 years of follow-up in the randomised Steno-2 study. Diabetologia. 2018;61:1724-33.
14. Shrestha S, Mandal RK, Maharjan K. Microalbuminuria and its associations with clinical profile and complications of type 2 Diabetes Mellitus. Journal of Advances in Internal Medicine. 2021;10:29-32.
15. Yilmaz F, Sozel H. Relationship between 25-hydroxyvitamin D and microalbuminuria in patients with newly diagnosed essential hypertension. Clin Exp Hypertens. 2021;43:217-22.
16. Chang YK, Fan HC, Lim PS, Chuang SY, Hsu CC. The relationship between resting heart rate and new-onset microalbuminuria in people with type 2 diabetes: An 8-year follow-up study. Diabet Med. 2021;38:e14436.
17. Li Z, Jian H, Rui X, Siqin W, Hui W, Yidan L. The Clinical Study of Serum FABP4 and PTEN Protein Expression levels in T2DM Patients with Microalbuminuria. The Journal of Practical Medicine. 2019;35:247-51.
18. Inker LA, Astor BC, Fox CH, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis. 2014;63:713-35.
19. Xing Y, Xu S, Jia A, et al. Recommendations for revision of Chinese diagnostic criteria for metabolic syndrome: A nationwide study. J Diabetes. 2018;10:232-9.
20. Xu J, Wang M, Chen Y, et al. Estimation of salt intake by 24-hour urinary sodium excretion: a cross-sectional study in Yantai, China. BMC Public Health. 2014;14:136.
21. McLaughlin T, Abbasi F, Cheal K, Chu J, Lamendola C, Reaven G. Use of metabolic markers to identify overweight individuals who are insulin resistant. Ann Intern Med. 2003;139:802-9.
22. Salazar MR, Carbajal HA, Espeche WG, et al. Comparison of the abilities of the plasma triglyceride/high-density lipoprotein cholesterol ratio and the metabolic syndrome to identify insulin resistance. Diab Vasc Dis Res. 2013;10:346-52.
23. Chen Y, Chang Z, Liu Y, et al. Triglyceride to high-density lipoprotein cholesterol ratio and cardiovascular events in the general population: A systematic review and meta-analysis of cohort studies. Nutr Metab Cardiovasc Dis. 2022;32:318-29.
24. Demir S, Artim-Esen B, Sahinkaya Y, et al. Metabolic syndrome is not only a risk factor for cardiovascular diseases in systemic lupus erythematosus but is also associated with cumulative organ damage: a cross-sectional analysis of 311 patients. Lupus. 2016;25:177-84.
25. Moehlecke M, Leitao CB, Kramer CK, et al. Effect of metabolic syndrome and of its individual components on renal function of patients with type 2 diabetes mellitus. Braz J Med Biol Res. 2010;43:687-93.
26. Ma ZS, Feng XL, Zhu P. Research Progress on Metabolic Syndrome and Its Related Diseases. Chinese General Practice. 2015;18:1991-5.
27. Sharma A, Gopalakrishnan D, Kumar R, Vijayvergiya R, Dogra S. Metabolic syndrome in psoriatic arthritis patients: a cross-sectional study. Int J Rheum Dis. 2013;16:667-73.
28. Frames KS, Semple SJ. Delayed effects of short term

acute aerobic exercise on microalbuminuria and insulin sensitivity. Human Physiology. 2017;43:78-85.

29. Chiang SC, Lee JK, Chen CH, et al. Justifying the high prevalence of microalbuminuria for type 2 diabetic patients in Taiwan with conditional probability approach--a DEMAND II study. J Chin Med Assoc. 2011;74:3-10.
30. Katayama S, Moriya T, Tanaka S, et al. Low transition rate from normo- and low microalbuminuria to proteinuria in Japanese type 2 diabetic individuals: the Japan Diabetes Complications Study (JDCS). Diabetologia. 2011;54:1025-31.
31. Song-wen S. Effect of Tangshen Decoction on reducing urinary microalbumin in patients with diabetic nephropathy. China Practical Medicine. 2021;16:167-9.
32. Chavda V, Saboo B, Hasnani S, Hasnani D, Saiyed M, Chandarana H. A15456 Efficacy of Cilnidipin vs. Amlodipin on microalbuminuria in hypertensive patients- clinical experience. Journal of Hypertension. 2018;36:e232.
33. Oresegun OO, Familoni OB, Olunuga TO, Akinpelu A. Correlation between echocardiographic left ventricular hypertrophy and microalbuminuria among hypertensive subjects in Olabisi Onabanjo university teaching hospital, Sagamu, Nigeria. International Journal of Advances in Medicine. 2020;7:1141-9.
34. Lina Y, Honglu W, Wenxiu S, Mingyi H, Yanchun D. Effects of xuezhikang combined with ezetimibe on myeloperoxidase and microalbuminuria in hypertensive patients with dyslipidemia. Journal of Dalian Medical University. 2018;40:344-9.
35. Bhatt VR, Khese VB, Jadhav SL, Kakrani AL. Urinary Albumin Excretion, Estimated Glomerular Filtration Rate, and Prevalence of Microalbuminuria in Obese Nondiabetic and Nonhypertensive Adults: A Cross-Sectional Study. Indian J Nephrol. 2019;29:166-71.
36. Sun D, Wang JJ, Wang W, et al. Human podocyte injury in the early course of hypertensive renal injury. World J Clin Cases. 2019;7:3698-710.
37. de Zeeuw D, Parving HH, Henning RH. Microalbuminuria as an early marker for cardiovascular disease. J Am Soc Nephrol. 2006;17:2100-5.
38. Zaharescu A, Martu I, Luchian AI, et al. Role of adjunctive therapy with subantimicrobial doses of doxycycline in glycemic control (HbA1c) in patients with diabetes and endo-periodontal lesions to prevent sinus complications. Exp Ther Med. 2021;21:277.

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