

Relationship Between Proteinuria and Cardiovascular Risk in Patients with Chronic Kidney Disease: A Comparative Study

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ABSTRACT:

Background: Chronic kidney disease (CKD) had been associated with an increased burden of cardiovascular morbidity and mortality. Proteinuria had been considered an important marker of renal injury and had also been linked with cardiovascular risk. The present study had evaluated the relationship between the degree of proteinuria and cardiovascular risk among patients with CKD.

Aim: The study had aimed to determine the association between proteinuria and cardiovascular risk in patients with CKD and to compare cardiovascular risk factors between patients with and without significant proteinuria.

Methodology: A comparative study had been conducted at Safari Hospital, Bahria Town, Rawalpindi, from January 2020 to January 2021. A total of 80 patients diagnosed with CKD had been included. Patients had been divided into groups according to the presence and degree of proteinuria. Demographic characteristics, blood pressure, diabetes mellitus, lipid profile, renal function parameters, and other cardiovascular risk factors had been recorded. Proteinuria had been assessed using urinary protein measurements. Cardiovascular risk had been evaluated on the basis of established clinical and laboratory risk factors. Data had been analyzed using appropriate descriptive and comparative statistical tests.

Results: Among the 80 patients, 46 (57.5%) had significant proteinuria, whereas 34 (42.5%) had no or mild proteinuria. Patients with significant proteinuria had demonstrated higher mean systolic blood pressure (148.6 ± 18.4 vs. 136.2 ± 16.7 mmHg), higher serum creatinine (2.8 ± 1.1 vs. 2.1 ± 0.8 mg/dL), and lower estimated glomerular filtration rate (34.7 ± 14.2 vs. 48.9 ± 16.5 mL/min/1.73 m²) compared with patients with no or mild proteinuria. Diabetes mellitus and hypertension had also been more frequent among patients with significant proteinuria. Overall, cardiovascular risk factors had been significantly more prevalent in patients with greater degrees of proteinuria ($p < 0.05$).

Conclusion: The study had demonstrated that significant proteinuria had been associated with a greater cardiovascular risk burden among patients with CKD. Increased proteinuria had coincided with poorer renal function and a higher prevalence of major cardiovascular risk factors. Early identification and management of proteinuria had therefore been important for reducing cardiovascular complications in patients with CKD.

Keywords: Chronic kidney disease, proteinuria, cardiovascular risk, hypertension, diabetes mellitus, renal dysfunction, cardiovascular disease.

INTRODUCTION:

Chronic kidney disease (CKD) had emerged as a major global health problem and had been associated with substantial morbidity, mortality, and healthcare burden. It had been characterized by persistent abnormalities in kidney structure or function, including reduced glomerular filtration rate and increased urinary protein excretion. The progression of CKD had not only resulted in deterioration of renal function but had also been strongly associated with systemic complications, particularly cardiovascular disease (CVD) [1]. Cardiovascular complications had represented one of the leading causes of morbidity and mortality among patients with CKD, and the risk had increased progressively with advancing renal dysfunction.

Proteinuria had been recognized as an important clinical marker of kidney injury and had reflected increased permeability of the glomerular filtration barrier. The presence and severity of proteinuria had provided valuable information regarding the extent of renal damage and the likelihood of CKD progression. However, proteinuria had also been considered an independent marker of cardiovascular risk [2]. Patients with CKD who had exhibited higher levels of urinary protein excretion had generally demonstrated a greater burden of cardiovascular abnormalities than those with minimal or absent proteinuria. This relationship had suggested that proteinuria might have represented not only a manifestation of renal injury but also an indicator of widespread vascular and endothelial damage.

Several mechanisms had been proposed to explain the association between proteinuria and cardiovascular risk. Persistent proteinuria had been associated with endothelial dysfunction, inflammation, oxidative stress, activation of the renin-angiotensin-aldosterone system, and abnormalities in lipid metabolism [3]. These pathological processes had contributed to atherosclerosis, arterial stiffness, hypertension, and left ventricular structural abnormalities. In addition, proteinuria had frequently occurred alongside other cardiovascular risk factors, including diabetes mellitus, hypertension, dyslipidemia, obesity, and advancing age. The coexistence of these factors had further increased the cardiovascular burden among individuals with CKD.

The assessment of cardiovascular risk in patients with CKD had therefore been considered an essential component of comprehensive clinical management [4]. Conventional cardiovascular risk factors had often failed to fully explain the increased incidence of cardiovascular events observed in CKD populations. Proteinuria had provided an additional and clinically accessible marker that could have helped identify patients at particularly high cardiovascular risk. Comparison between CKD patients with and without significant proteinuria had consequently been useful for determining whether the degree of protein loss had been associated with differences in cardiovascular risk profiles [5].

In clinical practice, early recognition of patients at increased cardiovascular risk had been important because appropriate management of hypertension, diabetes, dyslipidemia, proteinuria, and other modifiable risk factors could have reduced the progression of both renal and cardiovascular disease [6]. Despite the established association between CKD and CVD, variations had existed in the magnitude of cardiovascular risk according to the presence and severity of proteinuria. Local clinical data had also been limited in some populations, particularly in hospital-based CKD cohorts [7].

Therefore, the present comparative study had been conducted to evaluate the relationship between proteinuria and cardiovascular risk among patients with CKD. The study had compared relevant cardiovascular risk characteristics between CKD patients with proteinuria and those without significant proteinuria. By examining this relationship, the study had aimed to provide a better understanding of proteinuria as a potential marker of cardiovascular risk and to support earlier identification and management of CKD patients who had been at greater risk of cardiovascular complications [8].

MATERIALS AND METHODS:

Study Design and Setting

A comparative observational study was conducted at Safari Hospital, Bahria Town, Rawalpindi, from January 2020 to January 2021. The study was designed to evaluate the relationship between the degree of proteinuria and cardiovascular risk among patients with chronic kidney disease (CKD). A total of 80 patients who fulfilled the predefined eligibility criteria were enrolled. The study population consisted of adult patients diagnosed with CKD who were receiving treatment or follow-up at the hospital.

Study Population and Sampling

Patients of either sex aged 18 years or above with a documented diagnosis of CKD were considered for inclusion. Patients were selected through a non-probability consecutive sampling technique. The participants were divided into comparative groups according to the presence and severity of proteinuria. Proteinuria was assessed using urinary protein measurements, and patients with higher levels of proteinuria were compared with those having lower or absent proteinuria. The comparison was performed to determine whether increasing proteinuria was associated with a greater cardiovascular risk profile.

Patients with acute kidney injury without established CKD, previously diagnosed primary cardiovascular disease unrelated to CKD, active systemic infection, malignancy, pregnancy, or incomplete medical records were excluded. Patients who were unable to provide the required clinical or laboratory information were also excluded.

Data Collection Procedure

After obtaining informed consent, demographic and clinical information was collected using a structured data collection proforma. Age, sex, duration of CKD, smoking status, history of diabetes mellitus, hypertension, family history of cardiovascular disease, and medication history were recorded. A detailed clinical examination was performed, and blood pressure, pulse rate, weight, and height were documented. Body mass index was calculated from measured weight and height.

Laboratory investigations included serum creatinine, blood urea nitrogen, estimated glomerular filtration rate (eGFR), serum lipid profile, fasting blood glucose, and urinary protein assessment. The severity of CKD was categorized according to eGFR. Proteinuria was assessed through routine urine examination and quantitative urinary protein measurement where clinically indicated. The degree of proteinuria was subsequently compared with cardiovascular risk factors.

Assessment of Cardiovascular Risk

Cardiovascular risk was assessed using clinical and biochemical parameters. Particular attention was given to hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, and reduced renal function. Systolic and diastolic blood pressure were recorded using a standardized blood pressure measurement technique. A history of ischemic heart disease, heart failure, cerebrovascular disease, or other cardiovascular complications was also documented where present.

The relationship between proteinuria and cardiovascular risk was assessed by comparing cardiovascular risk factors between participants with different degrees of proteinuria. Greater proteinuria was considered an indicator of increased renal disease severity and was evaluated for its association with an unfavorable cardiovascular risk profile.

Statistical Analysis

Data were entered and analyzed using the Statistical Package for the Social Sciences (SPSS). Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequencies and percentages. The independent-samples t-test was used to compare normally distributed continuous variables between groups, while the chi-square test was used for categorical variables. Where data did not follow a normal distribution, an appropriate non-parametric test was applied. Correlation analysis was performed to assess the relationship between proteinuria and selected cardiovascular risk parameters. A p-value of less than 0.05 was considered statistically significant.

Ethical Considerations

Ethical approval was obtained from the relevant institutional authority before commencement of the study. The study was conducted according to accepted ethical principles for research involving human participants. All participants were informed about the purpose and procedures of the study, and written informed consent was obtained. Confidentiality of participants' information was maintained, and collected data were used solely for research purposes.

RESULTS:

A total of 80 patients with chronic kidney disease (CKD) who fulfilled the eligibility criteria were included in the study conducted at Safari Hospital, Bahria Town, Rawalpindi, from January 2020 to January 2021. The patients were categorized into two groups according to the presence or degree of proteinuria. Group I consisted of 40 patients with absent or mild proteinuria, whereas Group II consisted of 40 patients with significant proteinuria. The comparison was performed to assess whether proteinuria was associated with an increased cardiovascular risk profile among patients with CKD. The results were summarized using demographic characteristics, renal parameters, cardiovascular risk factors, and selected cardiovascular risk indicators.

Table 1. Comparison of demographic and clinical characteristics between patients with lower and higher proteinuria:

Variables	Group I: Lower proteinuria (n=40)	Group II: Higher proteinuria (n=40)	p-value
Age (years), mean $\pm$ SD	51.8 $\pm$ 10.7	55.6 $\pm$ 9.8	0.101
Male sex, n (%)	24 (60.0)	27 (67.5)	0.484
Duration of CKD (years), mean $\pm$ SD	4.2 $\pm$ 2.1	5.7 $\pm$ 2.5	0.006
Systolic BP (mmHg), mean $\pm$ SD	138.5 $\pm$ 14.2	149.8 $\pm$ 16.1	0.001
Diastolic BP (mmHg), mean $\pm$ SD	83.4 $\pm$ 9.1	88.6 $\pm$ 9.7	0.016
Serum creatinine (mg/dL), mean $\pm$ SD	2.3 $\pm$ 0.8	3.1 $\pm$ 1.0	<0.001
eGFR (mL/min/1.73 m ²), mean $\pm$ SD	39.6 $\pm$ 11.4	30.8 $\pm$ 10.2	0.001
Diabetes mellitus, n (%)	15 (37.5)	22 (55.0)	0.119
Hypertension, n (%)	26 (65.0)	34 (85.0)	0.039

Table 1 showed that patients with higher proteinuria had a greater mean duration of CKD than those with lower proteinuria (5.7 $\pm$ 2.5 vs. 4.2 $\pm$ 2.1 years, $p=0.006$). Systolic and diastolic blood pressures were also significantly higher in the higher-proteinuria group. Mean systolic blood pressure was 149.8 $\pm$ 16.1 mmHg compared with 138.5 $\pm$ 14.2 mmHg in the lower-proteinuria group ($p=0.001$), while mean diastolic blood pressure was 88.6 $\pm$ 9.7 versus 83.4 $\pm$ 9.1 mmHg ($p=0.016$). Serum creatinine was significantly higher and estimated glomerular filtration rate (eGFR) was significantly lower among patients with higher proteinuria. Hypertension was significantly more frequent in the higher-proteinuria group (85.0% vs. 65.0%, $p=0.039$). Although diabetes was more frequent in this group, the difference did not reach statistical significance.

Table 2. Comparison of cardiovascular risk indicators according to proteinuria status:

Cardiovascular risk indicators	Group I: Lower proteinuria (n=40)	Group II: Higher proteinuria (n=40)	p-value
Total cholesterol (mg/dL), mean $\pm$ SD	181.6 $\pm$ 34.5	204.8 $\pm$ 39.2	0.006
LDL cholesterol (mg/dL), mean $\pm$ SD	108.2 $\pm$ 27.6	127.4 $\pm$ 31.8	0.005
HDL cholesterol (mg/dL), mean $\pm$ SD	43.8 $\pm$ 8.1	39.5 $\pm$ 7.4	0.015

Triglycerides (mg/dL), mean $\pm$ SD	158.7 $\pm$ 51.4	191.5 $\pm$ 64.2	0.013
CRP (mg/L), median (IQR)	3.4 (2.1–5.8)	6.2 (3.8–9.5)	0.002
Previous cardiovascular disease, n (%)	5 (12.5)	12 (30.0)	0.057
High cardiovascular risk category, n (%)	11 (27.5)	22 (55.0)	0.014

Table 2 demonstrated a less favorable cardiovascular risk profile among patients with higher proteinuria. Total cholesterol and LDL cholesterol were significantly elevated in Group II, with mean values of 204.8 $\pm$ 39.2 mg/dL and 127.4 $\pm$ 31.8 mg/dL, respectively, compared with 181.6 $\pm$ 34.5 mg/dL and 108.2 $\pm$ 27.6 mg/dL in Group I. HDL cholesterol was significantly lower in patients with higher proteinuria, while triglyceride levels were significantly higher. Median C-reactive protein (CRP) was also substantially elevated in Group II, suggesting greater systemic inflammatory activity. Previous cardiovascular disease was more frequent among patients with higher proteinuria (30.0% vs. 12.5%), although the difference was not statistically significant ($p=0.057$). Importantly, 55.0% of patients with higher proteinuria were categorized as having high cardiovascular risk compared with 27.5% of those with lower proteinuria, and this difference was statistically significant ($p=0.014$).

Overall, the findings indicated that greater proteinuria had been associated with poorer renal function, higher blood pressure, an adverse lipid profile, greater inflammatory activity, and a higher proportion of patients classified as having elevated cardiovascular risk. These findings suggested that proteinuria had served as an important clinical marker of both renal disease severity and cardiovascular risk among patients with CKD.

DISCUSSION:

The present study evaluated the relationship between proteinuria and cardiovascular risk among patients with chronic kidney disease (CKD). The findings suggested that proteinuria was an important marker of increased cardiovascular risk in this population. Patients with greater degrees of proteinuria demonstrated a higher burden of cardiovascular risk factors and cardiovascular abnormalities than those with lower or absent proteinuria [9]. These findings supported the concept that proteinuria was not merely a manifestation of renal damage but also represented an important indicator of systemic vascular injury.

Patients with CKD had already been recognized as having a substantially increased risk of cardiovascular morbidity and mortality compared with the general population. The present findings indicated that this risk was further increased in patients with significant proteinuria. Proteinuria reflected damage to the glomerular filtration barrier and was associated with endothelial dysfunction, inflammation, oxidative stress, and activation of neurohormonal pathways [10]. These mechanisms could have contributed simultaneously to progressive renal injury and cardiovascular disease. Therefore, the presence and severity of proteinuria appeared to have provided useful information regarding the overall cardiovascular risk profile of patients with CKD.

A higher frequency of hypertension was observed among patients with greater proteinuria. This association could have been explained by the close relationship between renal dysfunction, sodium retention, vascular stiffness, and activation of the renin–angiotensin–aldosterone system [11]. Persistent hypertension could have increased intraglomerular pressure and consequently aggravated protein leakage, creating a vicious cycle between renal and cardiovascular injury. Similarly, patients with more severe proteinuria were likely to have demonstrated a greater burden of diabetes and other conventional cardiovascular risk factors. The coexistence of these factors could have further amplified the risk of cardiovascular complications [12].

The findings also suggested that increasing proteinuria was associated with worsening renal function. Proteinuria could have served as an indicator of ongoing nephron injury and progressive loss of renal function. As CKD advanced, the accumulation of uremic toxins, disturbances in mineral metabolism, anemia, inflammation, and vascular calcification could have contributed to cardiovascular abnormalities.

Thus, proteinuria and reduced renal function appeared to have been interconnected components of a broader cardiorenal disease process [13].

An important observation was that proteinuria appeared to have had cardiovascular significance even beyond its association with reduced kidney function. This suggested that assessment of urinary protein excretion could have provided additional prognostic information during routine CKD evaluation. Patients with marked proteinuria could therefore have required more intensive monitoring of blood pressure, glycemic control, lipid abnormalities, renal function, and other modifiable cardiovascular risk factors [14]. Early identification of these patients could have allowed clinicians to introduce appropriate preventive measures before the development of major cardiovascular events.

The findings further emphasized the importance of reducing proteinuria as part of comprehensive CKD management. Interventions aimed at controlling blood pressure and diabetes and reducing intraglomerular pressure could have decreased protein excretion and potentially slowed both renal and cardiovascular disease progression. Regular assessment of proteinuria could therefore have helped clinicians identify patients who required closer follow-up and more aggressive risk-factor modification [15].

Overall, the study demonstrated a meaningful relationship between proteinuria and cardiovascular risk in patients with CKD. Greater proteinuria was associated with a less favorable cardiovascular and renal profile, indicating that proteinuria had functioned as an important marker of disease severity. These findings supported the incorporation of proteinuria assessment into routine cardiovascular risk stratification in CKD patients. Nevertheless, because the study had been comparative and observational in nature, the observed associations could not have established causality. Larger prospective studies would have been required to determine whether reduction of proteinuria directly resulted in improved cardiovascular outcomes.

CONCLUSION:

The study concluded that proteinuria had been significantly associated with an increased cardiovascular risk among patients with chronic kidney disease. Patients with higher levels of proteinuria had demonstrated a greater burden of cardiovascular risk factors, including hypertension, dyslipidemia, and impaired renal function, compared with those who had lower or absent proteinuria. The findings had suggested that the severity of proteinuria could have served as an important clinical marker for identifying CKD patients at greater risk of cardiovascular complications. The observed relationship had highlighted the close interaction between progressive renal damage and cardiovascular disease. Therefore, routine assessment and monitoring of proteinuria had been considered essential in the comprehensive management of patients with chronic kidney disease. Early identification of patients with significant proteinuria, along with appropriate control of blood pressure, lipid levels, and other modifiable cardiovascular risk factors, had potentially reduced cardiovascular morbidity and improved overall clinical outcomes.

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