ORIGINAL ARTICLE

CARDIOVASCULAR RISK FACTORS IN CHRONIC KIDNEY DISEASE: THE IMPACT OF C-REACTIVE PROTEIN AND URIC ACID

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ABSTRACT

Introduction: Chronic kidney disease (CKD) gradually leads to end-stage kidney. In Pakistan, diabetes mellitus, obesity, and hypertension are the main causes of developing kidney disease.

Objective: To identify risk biomarkers for cardiovascular disease in patients with CKD by investigating variations in serum high-sensitivity C-reactive protein (hs-CRP) and uric acid.

Methods: This cross-sectional study was carried out in Shahida Islam Medical College, Lodhran, to assess serum hs-CRP and Uric Acid levels among CKD patients from January 2024 to August 2024. The study was conducted among the confirmed cases of chronic kidney disease and healthy controls for whom the investigations were done in the Central lab of the Pathology department. A total of 200 individuals between the age group 18-60 years, both males and females, were included on the basis of a non-probability convenience sampling technique in the present study.

Results: The study population consisted of 100 patients with CKD (63 males, 37 females) and 100 healthy controls (60 males, 40 females). The mean age of the CKD patients was 53.27 ± 9.11 years, compared to 54.20 ± 10.53 years for the controls. Notably, serum creatinine, hs-CRP, and uric acid levels were significantly elevated in CKD patients relative to controls ($p < 0.0001$ for all comparisons).

Conclusions: Our study highlights that there should be a regular estimation of these two biomarkers (uric acid and hs-CRP) in patients with CKD, to decrease the risk of aggravating the existing CKD and avoidance of developing CVD

Keywords: cardiovascular, risk factor, chronic kidney disease, c-reactive protein, uric acid

DOI: http://doi.org/10.63139/aqamc.v2i1.0014

INTRODUCTION:

Patients who suffer from chronic kidney disease (CKD) have often been seen they also suffer from chronic vascular disease (CVD).[1] Patients with CKD also show ailments as atherosclerosis, myocardial infarction, heart failure, etc. Patients with CKD have always been found to have hyperuricaemia.[2] The protein family, pentraxin, includes C-reactive protein, which is an acute phase reactant and produced by the liver as a result of chemical stimulation by interleukin-1, interleukin-6 and TNF alpha release.[3]

CKD and CVD, along with their various complications, may result in early death, reduced life span, poor quality of life, and a lot of expenditure on the health care system.[4] Uric acid is the end product of purine and decreases reactive oxygen species (ROS) and interleukin-6 (IL-6) in macrophages. On the other hand, it increases the oxidation of fatty acids.[5] Elevated levels of hs-CRP have been established in CKD patients and which lead to atherosclerosis, strokes, and other cardiovascular diseases.[6] Hyperuricemia and mild inflammation, i.e, when hs-CRP > 4mg/L, increases the chances of CVD, especially atrioventricular block thus

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Received: 28 October 2024; **Revised:** 04 February 2025;
Accepted: 25 March 2025

concluding that elevated hs-CRP has important role in developing CVD.[7] Fifty percent of the hospitalized patients with CKD show increased mortality and morbidity due to the development of CVD in these chronically ill patients with renal diseases at different stages.[8,9] The most recent research guidelines show that patients with CKD are included in the highest risk group who can develop CVD.10 It has long been established that hs-CRP adheres to the endothelial cells and leads to the aggregation of LDL and thus atherosclerosis and glomerulosclerosis. This leads to increased lipid content in coronary plaques, coronary calcification, and decreased clearance of creatinine.[3,6] Our study aimed to identify risk biomarkers for CVD in patients with CKD by investigating variations in serum hs-CRP and uric acid.

METHODS:

This cross-sectional study was planned at Shahida Islam Medical Complex, Lodhran, to assess serum hs-CRP and Uric Acid levels among CKD patients from January 2024 to August 2024.

The study was conducted among the confirmed cases of chronic kidney disease and healthy controls for whom the investigations were done in the Central lab of the Pathology department.

The study was started after taking ethical approval from the Institutional Ethical Committee, and verbal informed consent was taken from study subjects. A total of 200 individuals between the age group 18-60 years, both males and females, were included on the basis of a non-probability convenience sampling technique in the present study. They were divided into 2 groups. One group comprised 100 confirmed cases of chronic kidney disease, and Group two was composed of 100 age and sex matched healthy attendants, staff, and medical students of the hospital. All the individuals who have given consent/ willing to participate are included in the present study.

Exclusion criteria included Individuals who did not give consent/ not willing to participate in the present study. The individuals with any co-morbid conditions like Gout, Malignancy, Chronic infections, Acute myocardial infarction, and Chronic illness like renal and cardiovascular diseases were also excluded from this study. Patients on chronic dialysis, autoimmune conditions like SLE, RA, were excluded from the study because of their interference with the study's outcomes.

Serum creatinine, hs-CRP, and Uric Acid were analyzed on the Roche c303 fully automated analyzer. Grossly hemolyzed or lipemic, or icteric samples were not used for analysis in the present study and were discarded. Internal quality control was run to ensure the quality of results. Samples are analyzed only after the daily internal quality control has been passed. The values so obtained are noted in an Excel sheet.

Statistical Analysis: Qualitative data were expressed as proportions and percentages, while quantitative data were presented as mean ± standard deviation (SD). The Student's t-test was used to compare means between groups. A p-value < 0.05 was considered statistically significant, and a p-value < 0.0001 was considered extremely statistically significant. All statistical analyses were performed using SPSS version 26 (IBM Corp., Armonk, NY, USA).

RESULTS:

This study involved a total of 200 participants, divided into two groups: 100 patients with chronic kidney disease (CKD) and 100 age- and sex-matched healthy controls. Among the CKD group, 63 were male and 37 were female, while the control group consisted of 60 males and 40 females. The distribution of participants by age revealed that 43% of CKD cases and 42% of controls were between 18–40 years, whereas 57% of CKD cases and 58% of controls fell within the 40–60 years age group. The demographic characteristics are summarized in

Table 1.

Table 1: Demographic Characteristics of Study Participants

Variables	CKD Cases (n = 100)	Controls (n = 100)
Male	63	60
Female	37	40
Age 18–40	43	42
Age 40–60	57	58

Biochemical analysis showed a statistically significant elevation in all three parameters—serum creatinine, high-sensitivity C-reactive protein (hs-CRP), and uric acid—in CKD patients compared to healthy controls. The mean serum creatinine level among CKD patients was 4.32 ± 3.12 mg/dL, significantly higher than 0.82 ± 0.23 mg/dL observed in the control group ($p < 0.0001$). Similarly, the mean hs-CRP level in CKD patients was 7.12 ± 2.67 mg/L, compared to 0.90 ± 0.25 mg/L in controls ($p < 0.0001$). Uric acid levels were also considerably raised in CKD patients, with a mean value of 8.68 ± 2.72 mg/dL versus 4.87 ± 2.01 mg/dL in controls ($p < 0.0001$). These results are detailed in Table 2.

Table 2: Biochemical Marker Levels in CKD Patients and Controls

Biomarker	CKD Cases (Mean ± SD)	Controls (Mean ± SD)	p-value
Serum Creatinine (mg/dL)	4.32 ± 3.12	0.82 ± 0.23	< 0.0001
hs-CRP (mg/L)	7.12 ± 2.67	0.90 ± 0.25	< 0.0001
Uric Acid (mg/dL)	8.68 ± 2.72	4.87 ± 2.01	< 0.0001

These findings demonstrate that both hs-CRP and uric acid levels are significantly elevated in CKD patients and could serve as useful biomarkers for cardiovascular risk assessment in this population.

DISCUSSION:

Chronic renal disease over time gradually leads to end-stage kidney. As reported by the WHO, CKD is responsible for around 9 million deaths and 115 million disabilities throughout the world.[11,12] In Pakistan, diabetes mellitus, obesity, and hypertension are the main causes of developing kidney disease. These diseases cause structural and functional disruption of endothelial cells, leading to CKD and CVD. However, the exact frequency is not known due to the lack and quality of registry data available.[11,13]

Estimation of uric acid and hs-CRP is technically easy, reliable, and cost-effective, so these analytes were chosen to conduct the study.

Many studies have been conducted worldwide showing that hs-CRP and uric acid can independently lead to CVD and CKD. Such studies are limited in Pakistan, and our study aligned with these previous studies.[14-16] There are studies in which it was determined that uric acid alone was responsible for the development of CKD and CVD.[17,18] But in these studies, only half of the study population with CKD developed CVD. On the other hand, our study used both analytes to confirm that uric acid and hs-CRP are highly correlated with the development of CVD in CKD patients of all stages. The present study, using both uric acid and hs-CRP in a single study, was performed to address this situation.

Another study revealed that elevated levels of hs-CRP and uric acid are danger signals for the development of CVD in renal patients.[19] This is due to the fact that these analytes are proinflammatory and cause increased activity of plasma renin and its expression, and thus the activation of intrarenal angiotensin, leading to increased release of cytokines from monocytes and macrophages. Our study's results were consistent with those of this study.

One of the studies determined that high levels of hs-CRP and uric acid were found to mediate the inflammatory process, causing a significant risk of developing atrial fibrillation, atrioventricular block, myocardial infarction, and stroke.[20] Our study yielded comparable results, albeit with some notable differences due to a lengthier follow-up and progress tracking of the above-mentioned study. Besides majority of our study subjects were males. We excluded those patients who had a history of gout to improve the reliability of our study.

Another study was conducted to prove that elevated levels of hs-CRP were directly predictive of CVD.[8] Our study corroborated the findings of this study.

CONCLUSION:

Our study highlights that there should be a regular estimation of these two biomarkers (uric acid and hs-CRP) in patients with CKD, in order to decrease the risk of aggravating the existing CKD and avoidance of developing CVD. However, early detection of CVD by these biomarkers may improve the detection and prognosis of CVD. It may also reduce the burden on hospitals. Though our study had some limitations of a small sample size, it covers an important research area by using two biomarkers in a single study.

DECLARATION OF INTEREST: The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS:

A.F: Conceptualization, literature review, data collection, data analysis, write-up, proofreading, and final editing of manuscript.

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