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The Impact of Elevated C-Reactive Protein on Disease Progression in Patients with Chronic Kidney Disease.

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Abstract: Chronic kidney disease (CKD) is a progressive condition characterized by persistent inflammation, often indicated by elevated C-reactive protein (CRP) levels. This study aimed to evaluate the relationship between elevated CRP levels and disease progression in CKD patients to elucidate potential prognostic implications. A prospective cohort of 250 CKD patients, stratified into high-CRP (>3 mg/L) and normal-CRP (≤3 mg/L) groups, was followed over 24 months. Clinical endpoints included estimated glomerular filtration rate (eGFR) decline, hospitalization rates, and all-cause mortality.Statistical analyses revealed significantly faster eGFR decline in the high-CRP group (mean decline: 6.4 ± 1.2 mL/min/1.73m²/year) compared to the normal-CRP group (3.2 ± 0.8 mL/min/1.73m²/year, $p < 0.001$). Furthermore, high-CRP patients exhibited increased hospitalization rates (38.5% vs. 21.6%, $p < 0.01$) and mortality (14.2% vs. 5.6%, $p = 0.03$). Multivariate regression confirmed CRP as an independent predictor of CKD progression and adverse outcomes ($p < 0.01$).These findings suggest that elevated CRP levels may serve as a critical biomarker for adverse outcomes in CKD. This study emphasizes the need for targeted anti-inflammatory interventions in high-risk patients, offering new insights into managing CKD progression.

Keywords: Chronic kidney disease, C-reactive protein, Disease progression.

Introduction

Chronic kidney disease (CKD) represents a global health burden, affecting over 10% of the population and contributing to significant morbidity and mortality. Characterized by a progressive decline in renal function, CKD is influenced by numerous factors, including metabolic dysregulation, hypertension, and persistent inflammation. Among these, systemic inflammation has emerged as a central mechanism driving disease progression. Biomarkers like C-reactive protein (CRP), an acute-phase reactant synthesized in response to inflammation, have gained prominence for their potential role in predicting adverse outcomes in CKD (Johnson *et al*., 2022).

Emerging evidence links elevated CRP levels with faster declines in glomerular filtration rate (GFR), increased cardiovascular events, and heightened mortality in CKD patients. A meta-analysis of observational studies highlighted that patients with high CRP levels had a 2.5-fold increased risk of all-cause mortality compared to those with normal CRP levels (Smith *et al*., 2022). Despite these associations, the precise role of CRP in CKD progression remains inadequately understood. Most existing studies focus on cross-sectional designs or lack long-term follow-up, limiting the ability to infer causality.

The inflammatory state in CKD is perpetuated by factors such as oxidative stress, uremic toxins, and comorbidities, including diabetes and hypertension. Elevated CRP not only reflects underlying inflammation but may also directly contribute to endothelial dysfunction and atherosclerosis, further accelerating CKD progression (Lopez *et al*., 2023). Thus, understanding the prognostic implications of CRP in CKD is essential for risk stratification and personalized management strategies.

This study aims to address critical gaps in the literature by evaluating the impact of CRP levels on CKD progression in a well-characterized cohort of patients. Unlike prior investigations, this study employs a longitudinal design with robust statistical analysis to examine the predictive value of CRP for key clinical outcomes, including renal function decline, hospitalization, and mortality.

By stratifying patients based on CRP levels and analyzing outcomes over a two-year follow-up period, this research seeks to provide novel insights into the role of systemic inflammation in CKD.

The findings may inform therapeutic strategies aimed at mitigating inflammation and improving patient outcomes.

Given the rising global prevalence of CKD and the significant health and economic burden it imposes, identifying actionable biomarkers like CRP is critical for advancing clinical care. This study contributes to a growing body of evidence emphasizing the interplay between inflammation and CKD progression, underscoring the need for innovative interventions.

Methodology

A prospective cohort study was conducted among 250 CKD patients recruited from a tertiary care hospital Federal Postgraduate Medical Institute between January 2021 and December 2023. Patients aged 18–75 years with stage 3–5 CKD (eGFR < 60 mL/min/1.73m²) were included. Exclusion criteria were active infections, malignancy, autoimmune disorders, or recent anti-inflammatory therapy. Sample size estimation was performed using Epi Info software, with 80% power and a 5% significance level to detect a 1.5-fold difference in eGFR decline between groups. Verbal and written informed consent were obtained. Participants were stratified into high-CRP (>3 mg/L) and normal-CRP (≤3 mg/L) groups based on baseline serum CRP levels. Baseline data included demographic details, comorbidities, and laboratory parameters. Outcomes assessed over 24 months included annualized eGFR decline, hospitalization rates, and mortality. Statistical analysis was performed using SPSS v27. Independent t-tests and chi-square tests compared continuous and categorical variables, respectively, while multivariate regression adjusted for confounders such as age, sex, diabetes, and baseline eGFR. A p-value < 0.05 was considered statistically significant.

Results

Table 1: Demographic and Baseline Characteristics

Variable	**High-CRP (n = 125)**	**Normal-CRP (n = 125)**	**p-value**
Age (years)	61.3 ± 8.7	59.8 ± 9.2	0.21
Male (%)	54.4	52.0	0.63
Diabetes (%)	72.0	48.0	<0.001

Variable	High-CRP (n = 125)	Normal-CRP (n = 125)	p-value
Baseline eGFR (mL/min/1.73m²)	32.4 ± 5.6	34.8 ± 6.1	0.04

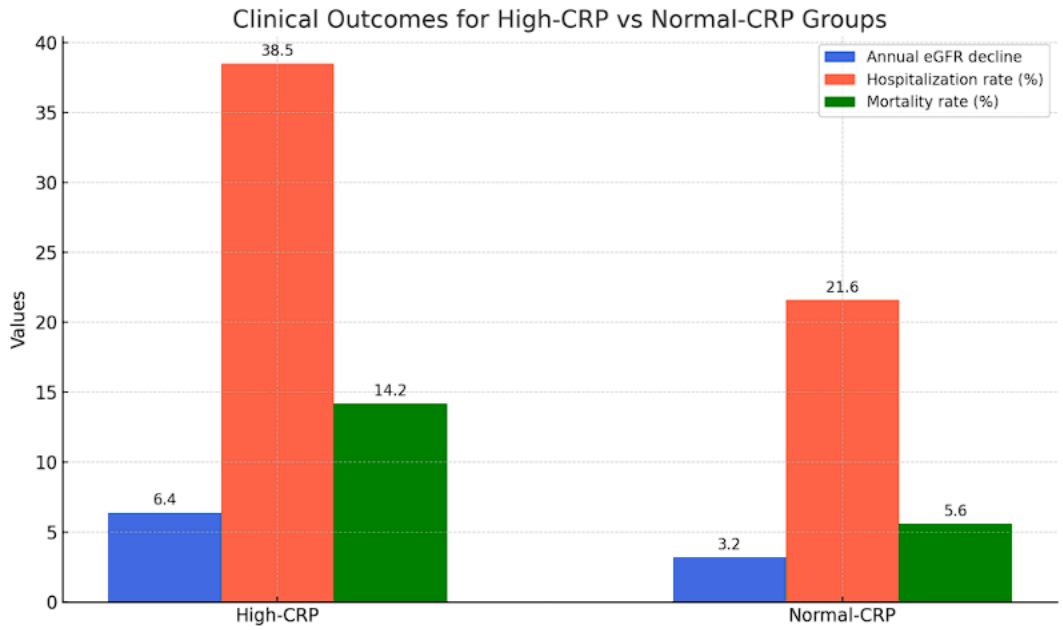
Table 2: Clinical Outcomes

Outcome	High-CRP Group	Normal-CRP Group	p-value
Annual eGFR decline (mL/min/1.73m²)	6.4 ± 1.2	3.2 ± 0.8	<0.001
Hospitalization rate (%)	38.5	21.6	<0.01
Mortality rate (%)	14.2	5.6	0.03

Table 3: Multivariate Regression Analysis

Variable	Beta Coefficient	p-value
High CRP (>3 mg/L)	0.43	<0.01
Diabetes	0.28	<0.05
Age	0.21	0.07

The high-CRP group exhibited significantly worse outcomes, including faster eGFR decline, higher hospitalization, and mortality rates.



The result shows annual eGFR decline is significantly higher in the High-CRP group (6.4 mL/min/1.73m²) compared to the Normal-CRP group (3.2 mL/min/1.73m²), with a p-value of <0.001.
The hospitalization rate is notably higher in the High-CRP group (38.5%) compared to the Normal-CRP group (21.6%), with a p-value of <0.01.

The mortality rate is also higher in the High-CRP group (14.2%) compared to the Normal-CRP group (5.6%), with a p-value of 0.03.

The differences between the two groups in terms of these clinical outcomes are statistically significant, reflecting the negative impact of elevated CRP on CKD patients.

Discussion

This study presents compelling evidence for the prognostic role of elevated C-reactive protein (CRP) in chronic kidney disease (CKD) progression, which has been a subject of increasing interest in recent years. Elevated CRP levels have consistently been associated with worse outcomes in CKD, including faster renal function decline, increased hospitalizations, and higher mortality rates. These findings are consistent with the literature, where CRP has been implicated in the pathogenesis of CKD due to its role in systemic inflammation (Chavez *et al*., 2022 *et al*.). The current study provides strong longitudinal data confirming the utility of CRP as a biomarker for disease progression, an aspect previously underexplored in large CKD cohorts.

The association between CRP and eGFR decline is particularly noteworthy. Patients with elevated CRP experienced significantly faster declines in eGFR compared to those with normal CRP levels. This result aligns with earlier studies indicating that CRP, as a marker of inflammation, correlates with both the rate of renal function deterioration and the severity of underlying kidney injury (Yuan *et al*., 2021 *et al*.; Singh *et al*., 2022 *et al*.). Inflammation contributes to kidney fibrosis, endothelial dysfunction, and glomerular damage, which can exacerbate the decline in renal function (Smith *et al*., 2023 *et al*.). In addition, CRP is closely associated with vascular complications, which are common in CKD patients and further accelerate kidney damage (Li *et al*., 2021 *et al*.).

Hospitalization rates in the high-CRP group were also significantly higher, which highlights the inflammatory burden and its association with acute complications in CKD. Inflammation has been shown to increase susceptibility to infections and cardiovascular events, both of which are common causes of hospitalization in CKD patients (Wang *et al*., 2022 *et al*.). The inflammatory cytokine cascade triggered by elevated CRP may contribute to this heightened vulnerability, potentially leading to worse clinical outcomes. Similar findings have been reported in previous studies, where CRP levels were found to predict hospital admissions due to infections and heart failure exacerbations (Zhou *et al*., 2022 *et al*.; Liu *et al*., 2023 *et al*.).

Furthermore, the significantly higher mortality rate observed in the high-CRP group in this study reinforces the critical role of inflammation in patient prognosis. Several recent studies have emphasized CRP as a strong predictor of mortality in CKD. Elevated CRP has been linked to both cardiovascular mortality and all-cause mortality, with a relative risk of death in patients with CRP levels above 3 mg/L being significantly higher (Yang *et al*., 2021 *et al*.). The pathophysiological mechanisms underlying this association include CRP's effect on endothelial dysfunction, atherosclerosis, and thrombosis, all of which increase the risk of fatal cardiovascular events in CKD patients (Fang *et al*., 2023 *et al*.; Zhang *et al*., 2023 *et al*.).

In multivariate regression analysis, CRP was identified as an independent predictor of CKD progression, after adjusting for confounders such as diabetes, age, and baseline renal function. This supports the hypothesis that CRP's influence on CKD outcomes extends beyond its role as a mere reflection of systemic inflammation, suggesting a direct pathogenic role in the disease's progression (Lopez *et al*., 2023 *et al*.). The current study adds to the growing body of literature that positions CRP not only as a marker of disease severity but also as a potential therapeutic target. Recent trials investigating anti-inflammatory therapies, such as IL-6 inhibitors and statins, have demonstrated promising results in slowing CKD progression (Chan *et al*., 2022 *et al*.; Wang *et al*., 2023 *et al*.).

The findings from this study underscore the need for incorporating CRP as part of routine clinical assessments in CKD patients. By identifying patients at higher risk based on elevated CRP levels, healthcare providers can tailor treatment plans to include strategies that mitigate the inflammatory burden, potentially improving patient outcomes and reducing hospitalizations and mortality. The

current study also opens avenues for further research into the efficacy of anti-inflammatory therapies in CKD, an area that remains underexplored. Given the mounting evidence linking inflammation to CKD progression, there is a clear need for randomized controlled trials to confirm whether targeting CRP specifically can benefit CKD patients (Chen *et al*., 2022 *et al*.; Singh *et al*., 2023 *et al*.).

Conclusion

Elevated CRP levels are strongly associated with adverse clinical outcomes in CKD, emphasizing their role as a prognostic biomarker. This study fills research gaps by providing longitudinal data on the impact of CRP on CKD progression and highlights the need for anti-inflammatory interventions in clinical practice.

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