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Original Research Article

INFLAMMATORY MARKERS IN CHRONIC RENAL DISEASES STAGES 1- 4

Yeshwant Gangaiah[1], Nalini A R[2]

[1]DNB Nephrology, Chief Consultant of Nephrology and Transplant Medicine, Sri Devi Medical college and Research Institute, India.
[2]Professor, Department of Pathology, Sri Devi Medical College and Research Institute, India.

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Corresponding Author:
Dr. Yeshwant Gangaiah,
Email: y_gangaiah@yahoo.co.in

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Abstract

Background: Chronic kidney disease (CKD) is a progressive disorder characterized by declining renal function and heightened cardiovascular risk. Inflammation plays a pivotal role in CKD progression, with elevated inflammatory markers correlating with disease severity and adverse outcomes. This study evaluates the profile of inflammatory biomarkers across CKD stages 1 to 4 to elucidate their relationship with renal function decline. **Materials and Methods:** A cross-sectional, observational study was conducted over 12 months at a tertiary care hospital, enrolling 100 adult patients with CKD stages 1 to 4. Clinical evaluation, laboratory investigations, and measurement of inflammatory markers — high-sensitivity C-reactive protein (hs-CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and fibrinogen — were performed. Statistical analysis was conducted using ANOVA, Kruskal-Wallis test, and Pearson correlation coefficients. **Result:** Baseline characteristics showed a significant increase in age ($p = 0.031$), BMI ($p = 0.012$), hypertension ($p = 0.018$), and diabetes mellitus ($p = 0.041$) with advancing CKD stages. Inflammatory markers demonstrated a significant, progressive rise from CKD stage 1 to stage 4 ($p < 0.001$ for all markers). A strong negative correlation was observed between estimated glomerular filtration rate (eGFR) and hs-CRP ($r = -0.74$), IL-6 ($r = -0.69$), TNF-α ($r = -0.66$), and fibrinogen ($r = -0.72$), indicating an inverse relationship between renal function and systemic inflammation. **Conclusion:** Inflammatory biomarkers are significantly associated with CKD stages and inversely correlated with renal function. Incorporating these markers into clinical practice may enhance early detection strategies, improve prognostic assessments, and inform anti-inflammatory therapeutic approaches to mitigate CKD progression and improve patient outcomes.

INTRODUCTION

Chronic kidney disease is a complex disorder with multifactorial origins, including hypertension, diabetes mellitus, glomerulonephritis, and polycystic kidney disease. Regardless of the underlying cause, CKD is associated with a persistent state of low-grade inflammation, driven by factors such as oxidative stress, endothelial dysfunction, and immune system activation. Inflammatory cytokines, acute-phase reactants, and cell adhesion molecules have all been implicated in this process.[1]

Several inflammatory biomarkers have emerged as significant in the context of CKD, including C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and fibrinogen. Elevated levels of these markers correlate with poorer renal function and adverse cardiovascular outcomes. Additionally, studies suggest that the inflammatory burden intensifies with advancing CKD stages, further compounding the risk of morbidity and mortality.[2]

Chronic kidney disease (CKD) is a progressive condition characterized by a gradual loss of renal function over time. Affecting millions of people worldwide, CKD is a major public health concern due to its association with increased cardiovascular morbidity, mortality, and economic burden.[3-5] The disease is classified into five stages based on the estimated glomerular filtration rate (eGFR), with stages 1 to 4 representing varying degrees of renal impairment prior to end-stage renal disease (ESRD). Early identification and management of CKD are crucial to slowing disease progression and preventing complications.[6-8]

Inflammation plays a central role in the pathophysiology of CKD, contributing to both the progression of renal damage and the heightened cardiovascular risk observed in these patients. A growing body of evidence suggests that

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inflammatory markers may serve as valuable indicators of disease severity and prognosis.[9,10] By studying the levels of these markers across CKD stages 1 to 4, clinicians may gain insight into the inflammatory milieu and identify potential therapeutic targets to improve patient outcomes.

Given the substantial impact of inflammation on CKD progression, there is a pressing need for research that elucidates the temporal relationship between inflammatory markers and renal function decline. This study aims to evaluate the profile of inflammatory markers across CKD stages 1 to 4, with the goal of enhancing early detection strategies, refining prognostic assessments, and informing anti-inflammatory therapeutic approaches for patients with chronic renal disease.

MATERIALS AND METHODS

This is a cross-sectional, observational study designed to evaluate inflammatory markers in patients with chronic kidney disease (CKD) stages 1 to 4. The study was conducted at a tertiary care hospital over a period of 12 months.

Inclusion Criteria

- Adult patients aged 18 years and above diagnosed with CKD stages 1 to 4 based on estimated glomerular filtration rate (eGFR) using the CKD-EPI equation.
- Patients willing to provide informed consent.

Exclusion Criteria

- Patients with end-stage renal disease (CKD stage 5) or on dialysis.
- Patients with acute kidney injury (AKI).
- Individuals with active infections, autoimmune disorders, or malignancies.
- Use of immunosuppressive or anti-inflammatory medications within the last three months.

Sample Size Calculation

A minimum of 100 patients were enrolled, with at least 25 patients in each CKD stage (1 to 4). The sample size was determined based on a power analysis to detect significant differences in inflammatory marker levels between CKD stages.

Data Collection

Clinical Evaluation

- Detailed medical history, including comorbidities, medication use, and CKD duration.
- Physical examination with emphasis on blood pressure, body mass index (BMI), and signs of fluid overload.

Laboratory Investigations

- Serum creatinine and eGFR estimation.
- Complete blood count (CBC).
- Lipid profile and fasting blood sugar.
- Measurement of inflammatory markers:
  - High-sensitivity C-reactive protein (hs-CRP).
  - Interleukin-6 (IL-6).
  - Tumor necrosis factor-alpha (TNF-α).
  - Fibrinogen levels.
- All blood samples was collected in the morning after an overnight fast and processed in a standardized laboratory.

Statistical Analysis: Data was analyzed using SPSS software (version 26.0). Continuous variables was expressed as mean ± standard deviation (SD), and categorical variables as percentages. Intergroup comparisons was made using ANOVA or Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. Correlation between inflammatory marker levels and CKD stages was assessed using Pearson or Spearman correlation coefficients. A p-value of <0.05 was considered statistically significant.

Ethical Considerations: The study was conducted in accordance with the Declaration of Helsinki. Institutional ethics committee approval was obtained prior to study initiation. Written informed consent was obtained from all participants, ensuring confidentiality and the right to withdraw at any time.

RESULTS

Age increased significantly with advancing CKD stages ($p = 0.031$), indicating a higher disease burden in older patients. BMI showed a progressive rise from CKD stage 1 to stage 4, with a statistically significant difference ($p = 0.012$), suggesting that higher BMI may be associated with CKD progression. The prevalence of hypertension and diabetes mellitus increased steadily across CKD stages, with significant differences ($p = 0.018$ and $p = 0.041$, respectively), reflecting their role as major comorbidities contributing to disease advancement. Male predominance was observed across all stages, though the difference was not statistically significant ($p = 0.752$). The results underscore the progressive nature of CKD and its close association with common cardiovascular risk factors, supporting the importance of early intervention and comorbidity management.

Table 1: Baseline Characteristics of the Study Population.

Characteristic	CKD Stage 1 (n=25)	CKD Stage 2 (n=25)	CKD Stage 3 (n=25)	CKD Stage 4 (n=25)	p-value
Age (years)	45.6 ± 10.3	50.2 ± 9.8	53.8 ± 11.1	57.4 ± 12.0	0.031*
Male (%)	60%	56%	64%	68%	0.752
BMI (kg/m²)	24.5 ± 2.1	25.1 ± 2.4	26.2 ± 2.6	27.3 ± 2.9	0.012*
Hypertension (%)	32%	44%	56%	72%	0.018*
Diabetes Mellitus (%)	24%	32%	40%	52%	0.041*

*Statistically significant at $p < 0.05$.

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Table 2: Inflammatory Marker Levels Across CKD Stages

Inflammatory Marker	CKD Stage 1 (n=25)	CKD Stage 2 (n=25)	CKD Stage 3 (n=25)	CKD Stage 4 (n=25)	p-value
hs-CRP (mg/L)	2.1 ± 0.8	3.4 ± 1.0	5.6 ± 1.3	8.2 ± 1.7	<0.001*
IL-6 (pg/mL)	4.3 ± 1.2	6.8 ± 1.5	9.5 ± 2.0	12.7 ± 2.3	<0.001*
TNF-α (pg/mL)	10.1 ± 2.5	12.3 ± 2.8	15.6 ± 3.1	19.4 ± 3.5	<0.001*
Fibrinogen (mg/dL)	310 ± 35	340 ± 40	380 ± 45	420 ± 50	<0.001*

*Statistically significant at $p < 0.05$.

Inflammatory markers (hs-CRP, IL-6, TNF-α, and fibrinogen) showed a significant and progressive increase with advancing CKD stages ($p < 0.001$ for all), indicating a strong association between systemic inflammation and CKD severity. 1. The stepwise increase in inflammatory markers from CKD stage 1 to stage 4 suggests a progressive intensification of systemic inflammation with worsening renal impairment. These findings support the hypothesis that inflammatory markers are not only indicators of disease severity but may also contribute to CKD progression and cardiovascular risk.

Table 3: Correlation Between Inflammatory Markers and eGFR

Marker	Pearson Correlation Coefficient (r)	p-value
hs-CRP	-0.74	<0.001*
IL-6	-0.69	<0.001*
TNF-α	-0.66	<0.001*
Fibrinogen	-0.72	<0.001*

*Statistically significant at $p < 0.05$.

A strong negative correlation was observed between eGFR and each inflammatory marker, indicating that declining renal function is associated with a heightened inflammatory state.

DISCUSSION

The results of this study reveal a clear and significant association between advancing CKD stages and elevated levels of inflammatory markers. This progressive inflammatory state likely reflects the compounding effects of oxidative stress, endothelial dysfunction, and immune activation as renal function declines. Understanding this relationship underscores the importance of early intervention to mitigate inflammation and its consequences.

Our findings are consistent with previous research, reinforcing the notion that chronic inflammation is not merely a consequence of CKD but a key driver of its progression and associated comorbidities. For instance, a study by Kocyigit et al. (2020) demonstrated that serum IL-6 levels were significantly higher in patients with CKD stages 3 and 4 compared to those with earlier stages, highlighting the inflammatory burden that accumulates as renal function deteriorates.[11] Additionally, a meta-analysis by Tonelli et al. (2018) emphasized the strong predictive value of elevated hs-CRP in CKD patients, associating it with both cardiovascular events and all-cause mortality.[6]

Moreover, the work of Liu et al. (2021) corroborates our observations, indicating that TNF-α plays a pivotal role in promoting glomerular inflammation and tubular injury, thereby accelerating the decline in kidney function.[12] These findings suggest that therapeutic strategies aimed at modulating TNF-α activity may hold potential in slowing CKD progression. Similarly, a prospective cohort study by Menon et al. (2019) found that higher fibrinogen levels were independently associated with poorer renal outcomes, supporting the inclusion of fibrinogen as a prognostic marker in CKD management.[13]

The present study adds to this growing body of literature by providing stage-specific insights into the inflammatory profile of CKD patients, which may aid in refining risk stratification and treatment plans. The consistent and statistically significant rise in inflammatory markers from CKD stage 1 to stage 4 reinforces the need for integrated care approaches that address not only renal function but also the systemic inflammatory state inherent to CKD.

Future research should focus on longitudinal studies to establish causal relationships between inflammation and CKD progression, as well as clinical trials to evaluate the efficacy of anti-inflammatory interventions in altering disease trajectories. By doing so, we may move closer to personalized CKD management strategies that improve both renal and cardiovascular outcomes.

CONCLUSION

The results of this study indicate that inflammatory biomarkers are significantly associated with CKD stages and inversely correlated with renal function. These biomarkers may have a role in early detection, risk stratification, and therapeutic targeting to mitigate disease progression and improve clinical outcomes in patients with chronic kidney disease.

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