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ASSOCIATION OF C - REACTIVE PROTEIN WITH SERUM PROTEIN LEVELS IN PATIENTS WITH EARLY-STAGE CHRONIC KIDNEY DISEASE

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Abstract

Background: Chronic kidney disease (CKD) is associated with metabolic, inflammatory, and nutritional disturbances that begin early in the disease course. Low-grade inflammation, reflected by elevated C-reactive protein (CRP), may contribute to alterations in serum protein levels, even in early-stage CKD.

Objective: To evaluate the association between C-reactive protein and serum protein parameters in patients with early-stage chronic kidney disease.

Materials and Methods: This prospective observational study was conducted in the Department of Biochemistry at a tertiary care hospital in Indore from May 2020 to December 2025. A total of 200 adult subjects were screened, of whom 32 were diagnosed with early-stage CKD (Stages 1–2) based on estimated glomerular filtration rate (eGFR), while 168 served as non-CKD controls. Fasting venous blood samples were collected for estimation of serum albumin, total protein, globulin, albumin-to-globulin (A/G) ratio, serum creatinine, and C-reactive protein. eGFR was calculated using the Cockcroft–Gault formula. Data were analysed using SPSS software, and Pearson's correlation coefficient was applied to assess the association between CRP and serum protein parameters.

Results: Early-stage CKD prevalence was 16%. CKD patients had lower mean serum albumin (3.41 ± 0.42 g/dL), total protein (6.12 ± 0.58 g/dL), and A/G ratio (1.28 ± 0.21) compared to non-CKD subjects. Stage-wise analysis showed a significant decline in serum albumin and A/G ratio from Stage 1 to Stage 2 CKD, with a corresponding rise in CRP levels (5.4 ± 2.1 mg/L to 7.9 ± 2.6 mg/L; $p < 0.05$). CRP showed significant negative correlations with serum total protein ($r = -0.49$), serum albumin ($r = -0.52$), and A/G ratio ($r = -0.47$).

Conclusion: Elevated CRP levels are significantly associated with reduced serum protein parameters in early-stage CKD, highlighting the role of inflammation in early nutritional and protein alterations and emphasizing the importance of early monitoring.

Key Words: C-reactive protein(CRP)

Introduction

Chronic kidney disease (CKD) is a progressive condition marked by a gradual decline in renal function and is associated with metabolic, inflammatory, and nutritional abnormalities, even in its early stages [1]. Early detection of these biochemical changes is important to prevent disease progression and related complications.

Inflammation is a key contributor to the pathogenesis of CKD. Patients with early-stage CKD often exhibit low-grade chronic inflammation, which plays a significant role in cardiovascular risk and disease advancement [2]. C-reactive protein (CRP), an acute-phase protein synthesized by the liver, is a widely used biomarker of systemic inflammation and has been reported to be elevated in CKD patients [3].

Serum proteins, particularly albumin, serve as important indicators of nutritional status and inflammatory activity. In CKD, reduced serum protein levels may result from inflammation-induced suppression of hepatic protein synthesis, increased catabolism, or urinary protein loss[4]. Hypoproteinemia has been associated with adverse clinical outcomes in patients with renal disease-[5].Several studies suggest an inverse relationship between CRP and serum protein levels, indicating that inflammation adversely affects nutritional status in CKD [6]. However, limited data are available regarding this association in patients with early-stage CKD. Therefores, the present study aims to evaluate the association between C-reactive protein and serum protein levels in early-stage CKD patients.

Material and method

Study Design and Setting

This prospective observational study was conducted in the Department of Biochemistry at a tertiary care hospital in Indore. Patients were recruited from the Nephrology and Medicine outpatient departments and admitted wards of the hospital.

Study Duration

The study was carried out over a period, from May 2020 to December 2025.

Study Population

The study population comprised adult patients diagnosed with early-stage chronic kidney disease (CKD), defined on the basis of estimated glomerular filtration rate (eGFR) values. Only patients with CKD stages 1 and 2 were included.

Inclusion Criteria

Adult patients aged 18 years and above with diagnosed early-stage CKD (Stages 1–2), stable renal function for at least three months, and willingness to participate with written informed consent were included in the study.

Exclusion Criteria

Patients with advanced CKD (Stages 3–5), acute kidney injury, those undergoing haemodialysis or peritoneal dialysis, pregnant women, and paediatric patients were excluded. Patients with chronic liver disease, malignancy, autoimmune or inflammatory disorders, or active infections were also excluded to avoid confounding inflammatory influences.

Sample Size

The sample size was calculated using the prevalence-based formula:

$n = Z^2 \times p \times (1 - p) / d^2$

Assuming a prevalence of early-stage CKD of 15%, a 95% confidence interval, and a 5% allowable error, the minimum sample size was estimated to be 196. A total of 200 subjects were included in the study.

Ethical Considerations
Ethical clearance was obtained from the Institutional Ethics Committee prior to commencement of the study. Written informed consent was obtained from all participants.

Sample Collection and Processing
5 millilitres of fasting venous blood was collected aseptically from each participant. Serum was separated by centrifugation at 3000 rpm for 10 minutes. Samples were analysed immediately or stored at 2–8 °C for short-term and at −20 °C for long-term storage.

Biochemical Analysis
Serum creatinine was estimated using the modified Jaffe's kinetic method. Estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft–Gault formula and used for CKD staging according to KDIGO 2020 guidelines. Serum total protein was measured by the Biuret method, and serum albumin was estimated using the Bromocresol Purple dye-binding method. Serum globulin was calculated as the difference between total protein and albumin, and the albumin-to-globulin ratio was derived accordingly. C-reactive protein (CRP) levels were measured using the latex-enhanced immunoturbidimetric method.

Statistical Analysis
Data were entered into Microsoft Excel and analysed using SPSS software. Results were expressed as mean ± standard deviation. Pearson's correlation coefficient was used to assess the association between serum CRP and serum protein parameters. A p-value of less than 0.05 was considered statistically significant.

Result
A total of 200 subjects were screened in the study, of which 32 (16%) were diagnosed with early-stage chronic kidney disease (CKD), while 168 (84%) served as non-CKD controls. Among CKD patients, the highest proportion belonged to the 46–60 years age group (13 patients, 40.6%), followed by the 31–45 years group (8 patients, 25.0%) and those aged above 60 years (8 patients, 25.0%). Males constituted 21 (65.6%) of the CKD group, whereas females accounted for 11 (34.4%).
The mean serum albumin level in CKD patients was 3.41 ± 0.42 g/dL compared to 4.21 ± 0.36 g/dL in non-CKD subjects. Mean serum total protein was also lower in the CKD group (6.12 ± 0.58 g/dL) than in controls (7.08 ± 0.64 g/dL). The A/G ratio was reduced in CKD patients (1.28 ± 0.21) compared to non-CKD subjects (1.47 ± 0.19), while serum globulin levels showed minimal variation between CKD (2.71 ± 0.44 g/dL) and non-CKD groups (2.87 ± 0.39 g/dL).
Stage-wise analysis showed a decline in serum albumin from 3.62 ± 0.38 g/dL in Stage 1 CKD (n = 14) to 3.25 ± 0.41 g/dL in Stage 2 CKD (n = 18), with a corresponding increase in serum CRP from 5.4 ± 2.1 mg/L to 7.9 ± 2.6 mg/L. The A/G ratio decreased from 1.36 ± 0.19 in Stage 1 to 1.22 ± 0.20 in Stage 2, and these differences were statistically significant ($p < 0.05$).
Correlation analysis demonstrated significant inverse relationships between CRP and serum protein parameters, with CRP showing negative correlations with serum total protein ($r = −0.49$, $p = 0.037$), serum albumin ($r = −0.52$, $p = 0.029$), and A/G ratio ($r = −0.47$, $p = 0.043$), indicating that higher inflammatory burden was associated with lower protein levels in early-stage CKD patients.

Table 1. Distribution of Study Population (n = 200)

Parameter	Number	Percentage (%)
Total screened patients	200	100
Early-stage CKD	32	16
Non-CKD (Controls)	168	84

Table 2- Demographic Distribution of Study Participants (n = 200)

Parameter	Category	CKD (n = 32)	CKD (%)	Non-CKD (n = 168)	Non-CKD (%)	Total (n)
Age Group (years)	18–30	3	9.4	42	25.0	45
	31–45	8	25.0	58	34.5	66
	46–60	13	40.6	46	27.4	59
	>60	8	25.0	22	13.1	30
Gender	Male	21	65.6	96	57.1	117
	Female	11	34.4	72	42.9	83

Table 3. Serum Protein Profile and Albumin–Globulin Status in CKD and Non-CKD Subjects

Parameter	Normal Reference Range	CKD (n = 32)	Non-CKD (n = 168)
Serum Albumin (g/dL)	3.5 – 5.0	3.41 ± 0.42	4.21 ± 0.36
Serum Globulin (g/dL)	2.0 – 3.5	2.71 ± 0.44	2.87 ± 0.39
A/G Ratio	1.2 – 2.2	1.28 ± 0.21	1.47 ± 0.19
Serum Total Protein (g/dL)	6.0 – 8.0	6.12 ± 0.58	7.08 ± 0.64

Table 4- Biochemical Variation with CKD Stage (n = 32)

Parameter	Stage 1 (n = 14) Mean ± SD	Stage 2 (n = 18) Mean ± SD	p-value
Serum Albumin (g/dL)	3.62 ± 0.38	3.25 ± 0.41	0.032
Serum CRP (mg/L)	5.4 ± 2.1	7.9 ± 2.6	0.008
A/G Ratio	1.36 ± 0.19	1.22 ± 0.20	0.041

Table 5- Pearson's Correlation between C - reactive protein and Serum Protein Parameters in Early-Stage CKD Patients

Parameters Correlated	r- value	p-value
CRP vs Serum Total Protein	−0.49	0.037
CRP vs Serum Albumin	−0.52	0.029
CRP vs A/G Ratio	−0.47	0.043

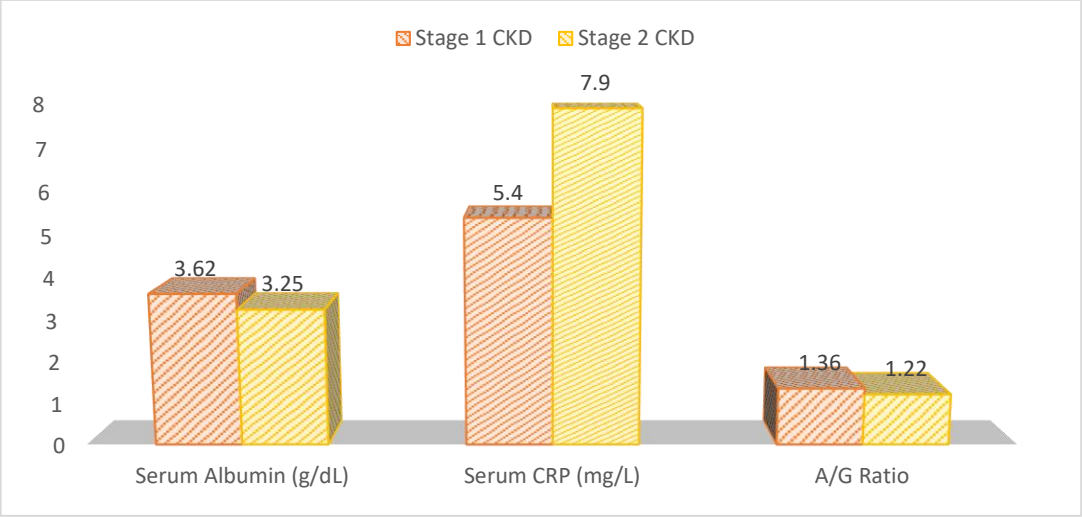


Figure - Biochemical Variation with CKD Stage (n = 32)

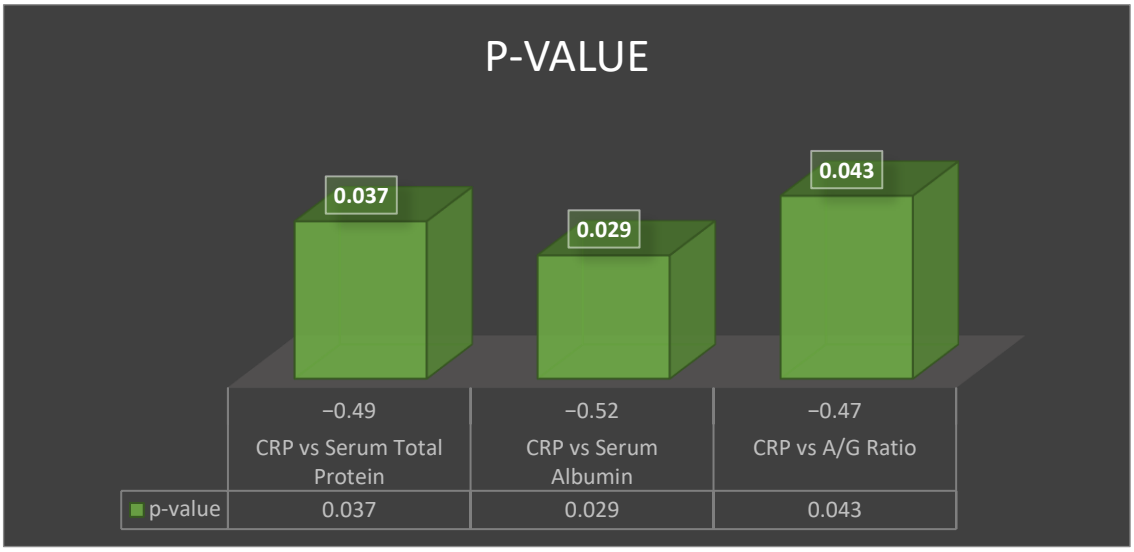


Figure 2 - Pearson's Correlation between C - reactive protein and Serum Protein Parameters in Early-Stage CKD Patients

Discussion

The present study evaluated the association between C-reactive protein (CRP) and serum protein parameters in patients with early-stage chronic kidney disease (CKD). Among the total study population, 16% were identified as having early-stage CKD, highlighting a considerable burden of undiagnosed or early renal dysfunction. Similar prevalence rates of early CKD have been reported in Indian population-based studies by Singh et al. (2018) [7] and Agarwal et al. (2020) [8], emphasizing the growing public health concern of CKD in developing countries.

In the current study, CKD patients demonstrated significantly lower serum albumin, total protein, and A/G ratio compared to non-CKD controls. These findings are consistent with observations reported by Kalantar-Zadeh et al. (2003) [9], who described hypo albuminemia as a common biochemical abnormality in CKD, even in early stages, largely driven by inflammation and protein catabolism. Gupta et al. (2019) [10] also reported significantly reduced serum albumin and total protein levels in early CKD patients, attributing these changes to low-grade inflammation and early renal protein loss.

When biochemical parameters were analysed according to CKD stage, a progressive decline in serum albumin and A/G ratio was observed from Stage 1 to Stage 2 CKD, accompanied by a significant rise in CRP levels. This stage-wise deterioration indicates that inflammatory activity intensifies as renal function declines, even before advanced CKD develops. Similar trends were documented by Menon et al. (2011) [11], who reported increasing CRP levels and declining nutritional markers with worsening CKD stage. Rao et al. (2017) [12] also observed significantly higher CRP levels in Stage 2 CKD compared to Stage 1, supporting the role of inflammation early in disease progression.

Correlation analysis in the present study revealed a significant inverse relationship between CRP and serum total protein, albumin, and A/G ratio. These findings suggest that elevated inflammatory burden adversely affects protein synthesis and nutritional status in early CKD patients. Stenvinkel et al. (2005) [13] demonstrated a strong negative correlation between CRP and serum albumin in CKD, proposing inflammation-mediated suppression of hepatic albumin synthesis as a key mechanism. Similar inverse correlations were reported by Kaysen et al. (2004) [14], who identified inflammation as a major determinant of hypoalbuminemia independent of dietary protein intake.

The observed reduction in A/G ratio with rising CRP levels in this study further reflects chronic inflammatory activity, as globulin levels tend to remain normal or elevated while albumin declines. This finding is in agreement with studies by Prakash et al. (2016) [15] and Sharma et al. (2021) [16], who reported altered A/G ratios in early CKD patients and suggested its utility as a simple marker of inflammation and renal protein imbalance.

Overall, the findings of the present study align well with existing literature and reinforce the concept that inflammation and nutritional derangements begin early in CKD. Measurement of CRP along with serum protein parameters may therefore serve as a valuable tool for early risk stratification and monitoring of disease progression. Early identification and management of inflammation could potentially improve nutritional status and slow the progression of CKD.

Conclusion

Early-stage CKD is associated with elevated CRP levels and reduced serum protein parameters, indicating early inflammatory and nutritional disturbances. Serum albumin and A/G ratio decline with disease progression from Stage 1 to Stage 2. The inverse correlation between CRP and serum protein levels highlights inflammation as a key contributor in early CKD.

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