

# Study of C-Reactive Protein Significance in Chronic Kidney Disease

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## ABSTRACT

**Introduction:** Chronic kidney disease (CKD) is a worldwide major disease, both for the number of patients and cost of treatment involved. Screening for CKD at an early stage helps to initiate specific therapy to reduce the progression of renal disease and burden of end stage renal disease (ESRD). Patients with CKD and ESRD show elevated acute phase C-reactive protein (CRP) levels as a consequence of chronic inflammatory states. The aim of this research was to study the significance of CRP with objective of finding an association between the CRP and parameters of other co-morbidities.

**Material and methods:** The study was conducted in the Department of General Medicine, Civil Hospital, Aizawl. Chronic kidney disease patients admitted in the General Medicine ward were included in the study. 140 CKD patients fulfilling the inclusion and exclusion criteria were included to study the significance of CRP in CKD. CKD is defined as kidney damage or GFR < 60 ml/min/1.73 m<sup>2</sup> for 3 months or more. All the patients selected for the study was investigated for serum CRP, Albumin, Creatinine, eGFR and ankle brachial index.

**Results:** Most common past history of CKD patients was hypertension (29.3%) and diabetes mellitus (21.4%). >10 mg/L CRP patients serum albumin range (3.43±0.982 gm/dl) was significantly lower than <10 mg/L CRP patients (5.40±1.169 gm/dl). >10 mg/L CRP group eGFR range (35.74±7.54 ml/min/1.73 m<sup>2</sup>) was significantly lower than <10 mg/L CRP group (42.39±11.47 ml/min/1.73 m<sup>2</sup>).

**Conclusion:** This study shows a high rate of inflammation in CKD patients as seen by high CRP levels. High CRP levels are associated with lower eGFR and lower serum albumin levels.

**Keywords:** Chronic Kidney Disease, CRP, GFR, Albumin.

## INTRODUCTION

Globally, chronic kidney disease is the 12<sup>th</sup> cause of death and the 17<sup>th</sup> cause of disability, respectively.<sup>1</sup> It is widely prevalent in Indian population found in 785 per million population.<sup>2</sup> High sensitivity C-reactive protein (hsCRP) assay is useful for sensitive detection of inflammatory states.<sup>3</sup> CKD is defined as kidney damage or glomerular filtration rate (GFR) < 60 ml/min/1.73 m<sup>2</sup> for 3 months or more, irrespective of cause.<sup>4</sup> CRP short pentraxin is an established biomarker of inflammation in kidney disease. CRP is an acute phase protein. Since inflammation is ongoing in CKD, it promotes glomerulosclerosis. The presence of inflammatory cytokines such as IL-6, TGF-β, PDGF contribute to this process. There is an influx of monocytes, macrophages ultimately producing type 1 and 2 collagen which leads to glomerulosclerosis. Therefore CRP levels are increased in CKD.<sup>5</sup>

Annu et al reported that CRP and endothelial function could provide complementary prognostic information regarding

future cardiovascular disorders in renal patients.<sup>6</sup> CRP levels of <1 mg/L, 1-3 mg/L and >3 mg/L correspond to low, moderate and high-risk groups for future cardiovascular events respectively.<sup>7</sup> Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in CKD at all stages. The impact of CVD in CKD is illustrated by reports which find that the risk of premature cardiovascular death is much higher than the risk of progressing to dialysis/transplantation. The traditional risk factors of CVD like diabetes mellitus, hypertension and dyslipidemia have not been able to fully explain the predisposition for CVD in CKD, raising the possibility of non-traditional risk factors that may be specific to CKD. The factors that are especially relevant in CKD patients include malnutrition, low serum albumin, anemia, hyperhomocysteinemia, elevated fibrinogen, dysregulation of calcium/phosphorus, oxidative stress and inflammation.<sup>8,9</sup> CKD is associated with protein energy malnutrition. Various factors contribute in development of malnutrition in CKD include anorexia, insulin resistance, inflammation and depression. Moreover, both PEM at baseline and worsening of PEM over time are associated with a greater risk for cardiovascular death. Various studies have shown that PEM and low BMI recently have been associated with both increased oxidative stress which in turn facilitates ongoing inflammation. Excess inflammation as denoted by raised CRP levels may contribute to increased cardiovascular risk in AIDS patients.<sup>10</sup>

Study aimed to find the significance of C-reactive protein in CKD, to assess the correlation between the levels of CRP and the glomerular filtration rate, to study the correlation between levels of CRP with serum albumin in chronic kidney disease.

## MATERIAL AND METHODS

This cross sectional observational study was conducted in the Department of General Medicine, Civil Hospital, Aizawl from October 2016 to September 2017. 140

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Chronic kidney disease patients admitted in the General Medicine ward were included in present study. Patients were selected by using simple random sampling method. Due permission from the institutional ethical committee and review board, written informed consent of patients had been obtained.

**Inclusion Criteria:** Patients diagnosed as chronic kidney disease according to national kidney foundation definition.

**Exclusion Criteria:** Patients not willing to be a part of the study and patients in sepsis.

All the patients selected for the study was investigated for serum CRP, serum Albumin, serum Creatinine, eGFR and ankle brachial index.

CKD is defined as kidney damage or GFR < 60 ml/min/1.73 m<sup>2</sup> for 3 months or more. Kidney damage is defined as pathological abnormalities or markers of damage including abnormalities in blood or urine test or on imaging studies.

C-reactive protein is measured with the help of CRP latex test kit. This test is based on an immunologic reaction between CRP as an antigen and latex particles have been coated with mono specific anti-human CRP. Latex slide test has the advantage of rapid performance in comparison to other tests for detection of CRP. Normal range: < 10 mg/L. Among all 140 CKD patients, 74 patients had CRP >10mg/L and 66 patients had CRP < 10mg/L.

Serum Albumin is measured by Bromocresol Green Method (BCG). Normal range: 4.0–5.0 gm/dl. At a slightly acidic pH, serum albumin combines with BCG to produce a glaucous complex. The absorbency increase is directly proportional to the concentration of albumin.

**eGFR:** GFR calculation based on modification of diet in renal

disease equation, GFR (ml/min/1.73 m<sup>2</sup>) = 175 x (Scr)<sup>1.154</sup> x (Age)<sup>-0.203</sup> x (0.742 if female). Scr = Serum creatinine (mg/dl).

**Serum Creatinine:** The modification of diet in renal disease (MDRD) study equation use creatinine measured by a modified Jaffe method. Normal Range: 0.5 – 1.2 mg/dl. At an alkaline solution, creatinine combines with picric acid to form an orange-red colored complex. The absorbency increase is directly proportional to the concentration of creatinine.

**Ankle Brachial Index (ABI):** Atherosclerosis is measured clinically by ABI. Higher systolic reading of the left and right arm brachial artery is generally used in the assessment. The pressures in each foot posterior tibial artery and dorsalis pedis artery are measured with the higher of the two values used as the ABI for that leg. A normal resting ABI is 1.00 to 1.40. If the ABI is 0.91 to 0.99, it is considered borderline abnormal. Resting ABI value of 0.90 or lower are diagnostic of peripheral artery disease (PAD).

## STATISTICAL ANALYSIS

Continuous variables were presented as mean or SD or median if the data is skewed. Categorical variables were expressed as frequencies and percentages. Nominal categorical data between the groups was compared using Chi-square test. P<0.05 was taken to indicate a significant difference.

## RESULTS

Most common past history of CKD patients was hypertension (29.3%) and diabetes mellitus (21.4%) (table-1).

>10mg/L CRP group serum albumin range was (3.43±0.982 gm/dL) lower than <10mg/L CRP group (5.40±1.169 gm/dL). This relation was statistically significant. (P<0.05). >10mg/L CRP group eGFR range was 35.74±7.54mL/min/1.73m<sup>2</sup>, which was lower than <10mg/L CRP group (42.39±11.47 ml/min/1.73m<sup>2</sup>). This relation was statistically significant (P<0.05) (table-2).

More than 50% of >10 mg/L serum CRP group patients ABI was Low which was indicative of atherosclerosis. All patients (100%) with high ankle brachial index was found in <10mg/L CRP group (table-3).

Past History	Frequency	Percentage
Hypertension	41	29.3
Diabetes Mellitus	30	21.4
CVD	20	14.3
Diabetes and Hypertension	10	7.1
OTHERS	39	27.9
Total	140	100.0

**Table-1:** Distribution of study subjects according to past history:

Serum Coding	CRP >10(mg/L) (n=74)	CRP <10(mg/L) (n=66)	P Value
Serum CRP (mg/L)	11.94 ± 1.48	5.40±1.95	P = 0.077
Serum Albumin (gm/dL)	3.43 ± 0.98	5.40±1.16	P = 0.013
eGFR (mL/min/1.73m <sup>2</sup> )	35.74±7.54	42.39±11.47	P<0.05

**Table-2:** Association of serum CRP with serum albumin and EGFR:

ABI class	Serum CRP				Total	
	<10 mg/L		>10 mg/L		Number	%
	Number	%	Number	%		
Low	27	47.4	30	52.6	57	100.0
Normal	36	45.0	44	55.0	80	100.0
High	3	100.0	0	0	3	100.0
Total	66	47.1	74	52.9	140	100.0

**Table-3:** Association between serum CRP with ABI class:

## DISCUSSION

Measurement of CRP has become virtually a gold standard as a predictor of morbidity and mortality in CKD patients as an independent marker. Among the biochemical parameters most reliable and studied is the serum total proteins and serum albumin levels but few studies correlate it with the levels of CRP to understand its co relational significance.<sup>11</sup> The present study was conducted among 140 CKD patients to “study the significance of C-reactive protein in chronic kidney disease.”

Hypertension (29.3%) and diabetes (21.4%) were the most common morbidities in our study (Table 1). This is similar to a study by Adejumo et al<sup>12</sup> which showed diabetic nephropathy (37.5%) and hypertensive nephropathy (28.8%). Studies by Alebiosu et al<sup>13</sup> and Ulasi et al<sup>14</sup> also had similar findings.

Recent data from the MDRD study showed that high serum CRP was an independent risk factor for all-cause mortality in patients with CKD stages 3 and 4. In another study Zimmermann et al<sup>15</sup> showed that high serum CRP was an independent predictor of 2-year all-cause mortality in 280 stable hemodialysis patients. In the current study we observed that a majority n=74 (52.85%) of patients were showing CRP >10mg/L (Table 2).

In our study, half of the patients with elevated CRP peripheral artery disease was present as depicted by low ABI in Table 3. This is similar to a study by Garimella PS et al<sup>16</sup> which showed that persons with CKD are at a higher risk of developing PAD and its adverse health outcomes than individuals in the general population who have normal renal function.

In the present study there was significant correlation between CRP and eGFR as shown in Table 2. Estimated GFR was also found to be a significant predictor of CRP levels in CKD in this study. This study also showed that inflammation as measured by CRP level increases with declining renal function in CKD patients. This is similar to the studies by Adejumo et al<sup>12</sup>, Annuk et al<sup>6</sup>, Pravin et al<sup>17</sup> and Abraham G et al<sup>2</sup> which all showed rising CRP levels associated with deteriorating condition in CKD patients.

Hypoalbuminemia is a well-known marker for morbidity and mortality in ESRD population. In our study CRP showed significant correlation with serum albumin, > 10 mg/L CRP group mean serum albumin (3.43±0.98 g/dl) was less compared to < 10 mg/L CRP group mean serum albumin 5.40±1.16 g/dl (Table 2). This was also observed in study by Dashti N et al.<sup>18</sup> In a study by Abraham G et al<sup>2</sup> found that patients with high CRP levels showed lower serum albumin levels but without the presence of other markers of malnutrition like lower BMI.

These data support the hypothesis that protein energy malnutrition and anorexia due to uremia may be part of a malnutrition inflammation complex mediated by cytokines and this process begins in subjects with reduced GFR. However, serum albumin level may reflect the nutritional status and as a negative acute phase reactant. It is thus difficult to ascertain whether the relationship between CRP and

albumin is caused by an association between inflammation and malnutrition or an association between one marker of inflammation and another.

## CONCLUSION

High CRP levels are associated with lower eGFR and serum albumin levels. This study shows a high rate of inflammation in CKD patients as seen by high CRP levels. It is possible that inflammatory processes precipitated by uremia per se could play a role in the development of malnutrition and atherosclerosis in patients with kidney disease.

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