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Relationship between Serum Levels of Albumin and C - reactive protein (CRP) In Patients with Chronic Kidney Disease

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Abstract: Protein- energy malnutrition, wasting and inflammation are frequent complication among patient with Chronic kidney disease (CKD). Malnutrition is associated with cardiac co-morbidity, inflammation and poor survival in CKD patients. Serum albumin is a well-known negative acute phase protein, marker of nutrition in CKD patients. C-reactive protein (CRP), the major acute phase response (APR) protein is elevated in these patients. High CRP levels are linked to the degree of atherosclerosis in coronary, peripheral, and extracranial brain arteries. The aim of the present study was to investigate nutritional factor (albumin) and CRP levels in CKD patients. This cross –sectional study was carried out in the Department of Biochemistry in collaboration with the Department of Medicine, Guru Gobind Singh Medical College & Hospital, Faridkot .Study involved 100 pre dialysis CKD patients (age 40.5 ± 12.3 years) admitted indoor and attending outdoor .Following investigations were carried out –CRP by fluorescence immunoassay method utilizing latex particles coated with CRP monoclonal antibodies (I-chroma). Serum albumin levels on fully automated chemistry analyzer Renal function by estimated glomerular filtration rate (eGFR). The data was later statistically analyzed. The study patients included 57 males (57%) and 43 females (43%) with average age of 40.5±12.3 years. The mean GFR was 38.3 ± 16.4 ml/min/1.73m2. The mean value of CRP was 10.93 ± 1.42 mg /dl. 67% of patients had elevated CRP (> 6 mg/L) with low serum albumin levels were present with mean value (3.02 ± 0.17 gm/dL). This study showed that low albumin and high CRP levels are the main predictors for death. There was a significant difference between CRP and albumin levels in CKD patients (P<0.001). Measuring CRP as a marker of inflammation can be helpful in managing these patients and Low levels of albumin are a marker of poor nutritional status in CKD patients. Our results indicate that CRP(as marker of inflammation) and albumin(as marker of nutritional status) were very closely related to each other ,as the levels of CRP increased the albumin goes on decreasing due to degree of inflammation , malnutrition and decreased synthesis by liver exists in pre-dialysis CKD patients.
Keywords: CKD, CRP, Albumin

INTRODUCTION

Chronic kidney disease is characterized by an irreversible worsening of renal function that slowly leads to end-stage renal disease (ESRD). A set of diverse pathophysiological processes related with atypical kidney function and progressive turn down in glomerular filtration rate <60mL/min/1.73m2 for 3 months, irrespective of the primary cause. Despite the remarkable advances in the field of dialysis within the last 20 years, the mortality rate in patients with chronic kidney disease (CKD) is quite high. Cardiovascular diseases, with a mortality rate of 9%, are the major cause of death in this group; this rate is 10–20 times higher than the normal population even after age, gender, race, and diabetes mellitus adjustments. Such a high rate indicates the presence of an accelerated atherogenesis process[1] .In addition to traditional risk factors of arthrosclerosis, uremia and dialysis-related factors may also release the pre-inflammatory cytokines and disturb the endothelial performance. It may also produce an acute or chronic systemic inflammatory response increase in the C-reactive protein [CRP] level and other proathrotrombic factors, consequently accelerating the arthrosclerosis process. Therefore, inflammation has a major role in arthrosclerosis in CKD patients [2].

C-reactive protein has the most important role in the inflammatory response and is the most common index for diagnosing inflammation. An elevated serum

CRP is reported in 20–65% of ESRD patients (pre-dialysis and those under hemodialysis and peritoneal dialysis). This increase in serum CRP and other acute-phase proteins are caused by underlying factors that lead to acute phase responses and the activation of the inflammatory cascade[3]. However, a reduction in renal clearance of pre-inflammatory cytokines in addition to diseases and their accompanying complications, like cardiac failure and advanced glycation end product (AGEs) accumulation, as well as dialysis factors can cause inflammation and increase the serum CRP levels in ESRD patients.[4] Several studies have proved the relationship between an elevated serum CRP levels and renal function (GFR reduction), arthrosclerosis, malnutrition, low serum albumin, anemia, low hemoglobin resistant to erythropoietin, and frequent hospitalizations, as well as general morbidity and mortality due to cardiovascular diseases in patients undergoing hemodialysis or peritoneal dialysis[5].

Malnutrition of visceral proteins often occurs in many chronic illnesses such as chronic renal failure, protracted infections and cancer. Clinical assessment of malnutrition is most commonly done by biochemical indicators of nutrition .Serum albumin is a well-known marker of nutrition in ESRD patients. There is a linear increase in death rate with declining serum albumin levels in the dialysis patients.[6] Low serum albumin levels may reflect poor nutrition. Presence of an inflammatory reaction, old age and degree of hydration could also cause hypoalbuminemia. Although several approaches have been used to assess nutrition, serum albumin is probably still the most commonly used nutritional marker in CKD patients. Several studies have shown that inflammation is another cause of problems attributed to malnutrition [7]. Thus, in the present study, the serum CRP levels and its correlation with renal function and nutritional factor albumin was studied in patients with chronic renal failure

MATERIALS AND METHODS

It is a descriptive hospital cross sectional study done in the Department of Biochemistry in collaboration with the Department of Medicine, Guru Gobind Singh Medical College & Hospital, Faridkot .Study involved 100 pre dialysis CKD patients (age 40.5 ± 12.3 years) admitted indoor and attending outdoor. Informed consent was taken from all patients. The clinician examined the patients thoroughly, and demographic data, past medical history (cardiovascular diseases), and administered medications were recorded.

Exclusion criteria were age >70 years and not willing to participate in this study. Also clinically unstable patients and those with tumors, diabetes mellitus, inflammatory diseases (such as diabetic ulcers of chronic pulmonary disease, systemic lupus erythematosus, rheumatoid arthritis, tuberculosis, and infection) or those treated with immunosuppressive drugs were excluded.

Laboratory findings, including albumin, creatinine, BUN, CRP, CBC, lipid profile were done. eGFR was calculated in each patient using Cockcroft-Gault formula. Serum albumin and CRP were measured using Bromocrosol Green and fluorescence immunoassay method, respectively.

Statistical analysis was done with IBM SPSS version 22. All results were given in mean ± SD. Linear regression was used to study the Pearson's correlation between the two quantitative variables; CRP and Albumin and a p-value of <0.05 was considered to be significant.

RESULTS

Chronic kidney disease had emerged as a serious public health problem especially in developing countries. The study patients included 57 males (57%) and 43 females (43%) with average age of 40.5±12.3 years. Hypertension (65%), diabetes (33%), the most common causes of CKD in our cases .The mean GFR was 38.3 ± 16.4 ml/min/1.73m2. The mean value of CRP was 10.93 ± 1.42 mg /dl. 67% of patients had elevated CRP (> 6 mg/dl) with low serum albumin levels were present with mean value (3.02 ± 0.17 gm/dl) . This study showed that low albumin and high CRP levels are the main predictors for death. There was a significant difference between CRP and albumin levels in CKD patients (P<0.001).

Table-1: The demographic data and laboratory findings of the enrolled patients

Variables	Mean ± Standard deviation	Range
Age (years)	40.5±12.3	25-68
GFR(ml/min//1.73m2)	38.3 ± 16.4	5.2-72.5
Albumin (g/dl)	3.02 ± 0.17	2.2 - 5.5
Triglycerides(mg/dl)	180.90 ± 95.23	88 -520
Cholesterol (mg/dl)	194.66 ± 52.42	80 - 380
HDL (mg/dl)	40.81 ±21.20	15-180
Hemoglobin (g/dl)	10.95 ± 2.43	5.2-15.1
CRP (mg/dl)	10.93 ± 1.42	1.0-35.5

Table-2: The correlation between different laboratory findings and CRP level

Variables	Pearson CC	*p value*
Age(years)	0.14	0.064
GFR(ml/min//1.73m2)	-0.20	0.020
Albumin(g/dl)	-0.14	0.001
Triglycerides(mg/dl)	-0.08	0.573
Cholesterol(mg/dl)	-0.18	0.054
HDL(mg/dl)	-0.04	0.654
Hemoglobin(g/dl)	-0.14	0.145

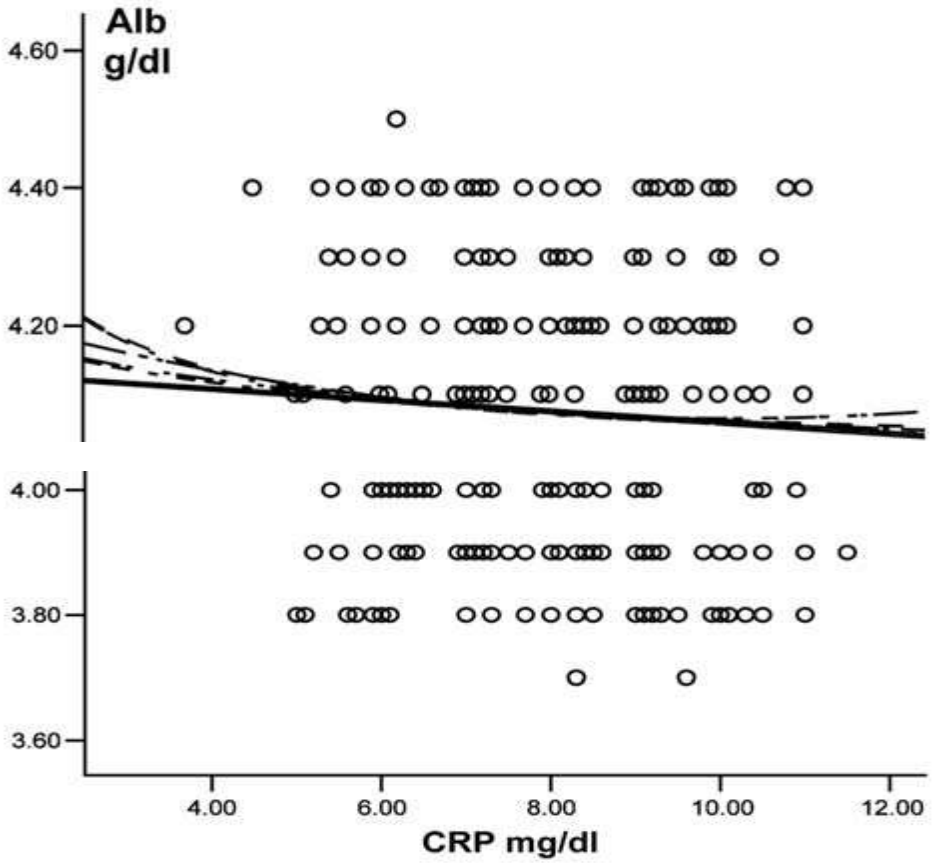

Fig-1: Scatter chart showing relationship between CRP and seum albumin levels in CKD patients (*P*<0.001)

DISCUSSION

Activated acute phase response is shown to be prevalent in dialysis patients; however, few researches have studied the increase of serum CRP in pre-dialysis patients. C -reactive protein is an acute phase reactant that belongs to the protein family known as pentraxin. It is synthesized by the liver in response to cytokines such as interleukin-1, interleukin-6, tumour necrosis factor-alpha released from macrophages and adipocytes[8].

Various rates of increase have been shown in these studies. Stenvinkel *et al*. stated that 32% of their patients (mean creatinine clearance of 7 ± 1 mL/min) to have an elevated serum CRP level (≥10 mg/ L) [9]. Panichi *et al*. reported the increased serum CRP (>5 mg/L) in 42% of the patients (mean creatinine clearance of 36.3 ± 23.1 mL/min)[10]. The frequency of serum CRP levels reported in the present study was lower than the previous ones. Several reasons may explain such discrepancy. The serum CRP was quantitatively measured using the nephelometry method in previous studies; thus, various figures were considered as the normal value. In the present study, the amounts less than 6 mg/dl were considered as normal; this justifies the lower frequency of patients with elevated serum CRP levels. Here in present study serum CRP levels were quantitatively measured using fluorescence immunoassay method utilizing latex particles coated with CRP monoclonal antibodies (I-chroma).

In our study, a negative correlation found between the serum CRP and GFR levels. This indicates that any decrease in CRP clearance may activate the acute phase response. Indeed, the inflammatory process

and the elevated serum CRP levels in patients with chronic renal failure reduce GFR. Ates and Panichi[10] also found a negative correlation between the serum CRP and GRF levels.

Elevated serum C-reactive protein (CRP) levels have been shown to be linked with the development of atherosclerosis in CKD patients. Chronic kidney disease is a chronic inflammatory state caused by both patient and dialysis related factors. These factors include the uremic milieu, infection, oxidative stress, co-morbidities, obesity, genetic or immunologic factors, exposure to dialyzer membrane and dialysate in those on dialysis.[11] The levels of inflammatory markers like fibrinogen, homocysteine, several pre-inflammatory cytokines (IL-6, TNF-α, INF-β, INF-γ, IL-1) and CRP are high in CKD patients with coronary heart disease (CHD).Consequences of chronic inflammation in CKD patients include malnutrition, anaemia, hypo-responsiveness to erythropoietin, CVD and increased mortality[12].

Albumin is among the negative acute phase proteins, the synthesis of which reduces during the inflammation. On the contrary, ferrtin and fibrinogen are positive acute phase proteins[13].Hypoalbuminemia is a well-known marker for morbidity and mortality in ESRD population. Lowrie and Lew documented a linear increase in death rate with declining serum albumin levels at the initiation of dialysis as well as during the course of maintenance dialysis[14].Hypoalbuminemia is frequently associated with cardiac co-morbidity. Thus hypoalbuminemia is not simply a marker of malnutrition but also reflects inflammation and co-morbidity, therefore its regular assessment in very important in ESRD patients[15].

In conclusion this study shows that elevated CRP and reduced levels of negative acute phase protein albumin are the main predictive markers of inflammation in CKD patients. They both are associated with each other and showed a strong relation as the level of CRP increased the albumin goes on decreasing due to the effect of pro-inflammatory cytokines. It is also noted that reduced levels of albumin also a marker for malnutrition .Also Elevated serum C-reactive protein (CRP) levels have been shown to be linked with the development of atherosclerosis in CKD patients. Reducing inflammation plus routine measurement of CRP in these patients may improve the nutritional and cardiovascular condition and consequently slow down the renal failure process and extend the patients' lifespan

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