

Original Research Article

C - reactive protein predictive marker value and its significance in management of pre dialysis chronic kidney disease patients when correlated with total serum proteins and serum albumin levels: experience in a teaching institution

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ABSTRACT

Background: Chronic kidney disease (CKD) is imposing newer challenges, not only globally, but, also in India, especially managing the end stage renal disease (ESRD). Screening for CKD at an early stage, by, high sensitivity C reactive protein (hsCRP) with or without other clinical, biochemical or anthropometric parameters helps initiate specific therapy to reduce the progression of renal disease. Although, malnutrition, inflammation and cardio vascular diseases (CVD) have been shown as significant independent risk factors of mortality in CKD patients, but, whether there exists any relationship between hsCRP and serum proteins and serum albumin levels, one of the important indicators of PEM, has not been extensively studied in pre-dialysis CKD patients.

Methods: The study included a total of 60 adult subjects. Of these, 30 were study cases who fulfilled the case definition of CKD and were compared with 30 patients who did not show any signs or symptoms of CKD. As per the objective - hsCRP values were estimated by ELISA test, quantified and statistically correlated with total serum proteins and albumin levels.

Results: A significant difference was found in the mean value of hsCRP in cases and in controls (p value 0.001). No significant difference was observed in the mean level of total serum protein in cases and controls, but, the mean differences in the level of serum albumin between cases and controls was significant. The association of serum albumin and hsCRP was found to be significant (p value <0.001). If a level of serum albumin < 3.5 is taken as a marker of malnutrition, it is found that 66.66% of patients have hypo-albuminaemia.

Conclusions: The present study comes to an important conclusion that hsCRP is a useful independent predictor of CKD and if correlated with serum albumin levels, it would help clinician manage the patient effectively by initiating an aggressive yet very appropriate therapy at the pre-dialysis stage with the likelihood of an 'evidence based' reduction in morbidity and mortality.

Keywords: Chronic kidney disease, hsCRP

INTRODUCTION

Chronic kidney disease (CKD) is a global threat to health mainly in developing countries.¹ It is widely prevalent in

Indian population found in 785 per million population.² 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).³ Patients with CKD and end stage renal disease (ESRD) show

elevated acute phase C - reactive proteins levels as a consequence of chronic inflammatory states.⁴ High sensitivity C- reactive protein (hsCRP) assay is useful for sensitive detection of inflammatory states.⁵ Malnutrition, inflammation and CVD are significant independent risk factors of mortality in CKD patients but relationship between hsCRP and malnutrition, especially serum proteins and serum albumin levels has not been extensively studied in pre-dialysis CKD patients.⁶ Therefore, the present retrospective analytical study evaluates hsCRP levels in a well-defined group of pre-dialysis CKD patients and control group in terms of hsCRP levels only and also comparison and correlation of hsCRP levels with total serum proteins and serum albumin levels with the intent to understand its predictive value and significance in management of pre dialysis CKD patients.

METHODS

The present retrospectively analysed study was a 'hospital based observational study' with an attached teaching institution and conducted over duration of 18 months (2009-10). The study included a total of 60 adult subjects. Of these, 30 were study cases - case or 'Group 1'. All the cases were clinically diagnosed and fulfilled the case definition of CKD i.e. CKD with irreversible and substantial loss of renal function for more than 3 months. These patients were in the age group 12-75 years, included both sexes with GFR > 25 ml/min and did not require renal replacement therapy at the time of presentation (pre-dialysis patients).

All cases were subjected to detailed history and physical examination with emphasis on nutritional parameters and cardiovascular system examination. This group was compared with 30 patients - controls or Group 2 who did not show any signs or symptoms of CKD, no evidence of inter-current infection, not on renal replacement therapy (RRT), no post-transplant, no chronic inflammatory disease, no malignancy, no pregnancy or use of oral contraceptives, no collagen vascular disease, no acute coronary artery syndrome, not on statin therapy or suggestive of chronic liver disease. All patients signed an informed consent and the study was approved by the ethical committee of the institution (IEC).

Clinical factors' details, radiological findings, electrocardiography, ultrasound findings of kidneys, haematological investigations, anthropometric parameters (height, weight, mid arm circumference), biochemical parameters (lipid profile, serum protein, serum iron, serum calcium etc.) including hsCRP were recorded appropriately in predesigned and institution approved data collection forms (DCFs). As per the objective hsCRP values and albumin levels were compared and analyzed. Statistical significance of the difference between means was estimated by Student's t test, ANOVA test and Pearson's correlation test. A 'p' value of less than 0.05 was considered as significant.

RESULTS

The mean age of the patients was 42.5 years in group 1 and 42.9 years in group 2. There was no significant difference in the mean age between both the groups. The demographic profile and clinical profile revealed the male: female ratio as 1.3:1 in group 1 and 1.5:1 in group 2. Both groups had similar sex distribution. By chi-square tests, p value for sex distribution among both groups was 0.5 which is not significant (Table 1). Both groups were comparable.

Table 1: Demographic profile and hsCRP values in cases and controls and their correlation with hsCRP values at a glance.

Group	Case (group 1) n=30	Control (group 2) n=30
Age, Mean \pm S.D. in years	42.47 \pm 14.936	42.93 \pm 15.033
Sex	M = 17, F=13	M=18, F=12
hsCRP mean value	2.66	0.75

Table 2: hsCRP levels expressed as mean values including standard deviation.

Group	Number	Mean	S.D.	p=0.001
Case	30	2.66023	2.683651	
Control	30	0.75830	0.938985	

Table 3: Total serum protein and serum albumin levels in cases and controls.

Parameter	Cases			Controls		
	Mean	S.D.	S.E	Mean	S.D.	S.E
Total serum protein	6.21	0.859	0.157	7.06	0.393	0.072
S. albumin	3.296	0.499	0.13065	3.912	0.2272	0.0552

The mean value of hsCRP in cases is 2.66023 with S.D. of 2.683651 while in controls it was 0.75830 with S.D. of 0.938985, the p value obtained is 0.001 reflecting significant and meaningful difference (Table 2).

The mean level of total protein in cases was 6.21 with standard deviation of 0.859, and in controls mean total serum protein was 7.06 with the standard deviation of 0.393. P value of this differences is 0.096 (not significant). But, the mean of serum albumin in cases was

3.296 with the standard deviation of 0.499, and in controls it was 3.912 with the standard deviation of 0.227. P value of this differences in the level of serum albumin between cases and controls is significant (p value <0.05) (Table 3). It clearly reflects albumin concentrations fall to significant levels in patients suffering from CKD. Interestingly, total serum proteins did not show a fall to that significant low level suggesting the role of compensatory mechanisms which tend to maintain the milieu interior of body. If cases and controls are subdivided into two subgroups based on hsCRP levels i.e. hsCRP < 1 and hsCRP > 1, serum level

of total serum protein, serum albumin were decreased in subgroup in which hsCRP is >1. The mean value of total serum protein in cases was found to be 6.53 if hsCRP is <1, and 6.03 if hsCRP was > 1 and this difference is found to be significant (p value <0.05). The mean serum albumin is 3.55 if hsCRP was <1 and 3.037 if hsCRP was > in cases. This association of serum albumin and hsCRP was also found to be significant (p value <0.001). If a level of serum albumin < 3.5 is taken as a marker of malnutrition it is found that 66.66% of patients have hypo-albuminaemia (Table 4).

Table 4. Association of total serum protein and serum albumin with hsCRP in patients with CKD.

Parameter/Group n = 30		hsCRP		Statistical parameter		
		<1	≥ 1	S.D.	S.E	p value
Cases	Total S. protein	6.53	6.03	0.640	0.193	0.046
	S. albumin	3.55	3.037	0.930	0.213	<0.001
Controls	Total S. protein	7.01	7.19	0.430	0.094	0.29
	S. albumin	3.862	3.963	0.38	0.084	0.38

DISCUSSION

For micro inflammatory markers, measurement of hsCRP has become virtually a gold standard as a predictor of morbidity and mortality in CKD patients as an independent marker.⁶ Among the biochemical parameters most reliable and studies is the serum total proteins and serum albumin levels but few studies correlate it with the levels of hsCRP to understand its correlational significance.

A statistically significant marked difference in the mean value of hsCRP in cases (2.66023 with S.D. of 2.683651) and in controls (0.75830 with S.D. of 0.938985) was observed (Table 2, Figure 1). It clearly reflects that hsCRP values are increased in pre-dialysis CKD patients. Studies have shown that the inflammation is highly prevalent in haemodialysis (HD) and peritoneal dialysis (PD) patients.⁷ It is also known that CVD risk is increased in the evolution of CKD in patients already having reached at a GFR of about > 75ml/min and it increases continuously with deterioration of renal function.³ Even the subtle dysfunctions have been proposed as a condition needing intensive preventive CVD strategies.⁸ Therefore, knowing the hsCRP measurement early would help the clinician target the risk factors in pre-dialysis patients at an early stage. For total serum proteins and serum albumin, as is shown in the present study, the mean level of total protein in cases is 6.21 and in controls mean total serum protein is 7.06, the p value of this differences is 0.096 (not significant). But, the mean of serum albumin in cases is 3.296 with the standard deviation of 0.499, and in controls it is 3.912 with the standard deviation of 0.227. P-value of this differences in the level of serum albumin between cases

and controls is significant (p value <0.05) (Table 3). It clearly reflects albumin levels fall to significant levels in patients suffering from CKD. Interestingly, total serum proteins do not fall to that significant low levels suggesting the role of compensatory mechanisms which tend to maintain the milieu interior of body. In our study to arrive at some definitive conclusions, we divided cases and controls into two subgroups based on hsCRP levels i.e. hsCRP < 1 and hsCRP > 1. Interestingly and expectedly, serum level of total serum protein, serum albumin were decreased in subgroup in which hsCRP is >. The mean value of total serum protein in cases was found to be 6.53 if hsCRP is <1 and 6.03 if hsCRP was > 1 and this difference was found to be significant (p value <0.05). The mean serum albumin is 3.55 if hsCRP was <1 and 3.037 if hsCRP was > in cases. This association of serum albumin and hsCRP was also found to be significant (p value <0.001). If a level of serum albumin < 3.5 is taken as a marker of malnutrition it is found that 66.66% of patients have hypo-albuminaemia. (Table 4). Serum level of albumin is inversely correlated with the serum levels of positive acute phase reactants e.g. CRP, alpha 1 acid glycoprotein (α1-AG), ferritin and cerulo-plasmin. In a study by Barrett BJ et al a raised CRP and low albumin levels have been shown to be predictor of morbidity and mortality in CKD stage.^{3-5,9} It has also been well recognised that prevalence of protein energy malnutrition (PEM) is significant in CKD and varies from 18% to 70% in adult maintenance dialysis patients.¹⁰ Inflammation as reflected by hsCRP levels is more prevalent in the malnourished than in those with normal statuses and hsCRP is inversely correlated with S-albumin.¹¹ It is also true that among the biochemical parameters - serum albumin is the most extensively used index in almost all patients' populations including CKD

patients and it is also a specific and sensitive indicator of the progressive malnutrition due to any underlying cause.¹² Hypo-albuminemia is highly predictive of future mortality risk when present at the time of initiation of chronic dialysis, as well as during the course of maintenance dialysis (MD).¹³⁻¹⁶ It is considered that a decreased albumin level at the pre-dialysis stage with early CKD will translate into high malnutrition levels at the time these patients would require RRT.¹⁷ Therefore, it is important to recognize and treat malnutrition early in patients of CKD at a stage where these patients do not require renal replacement therapy (pre-dialysis patients). Intervening at this early stage of renal failure will be translated into improving nutritional status at the start of dialysis or RRT and will ultimately mean better outcome and lesser morbidity and mortality during RRT. Therefore the study comes to a useful conclusion that hsCRP is a useful independent predictor and if it is correlated with serum albumin levels would help clinician initiate an aggressive approach to manage these patients at the pre-dialysis stage itself with an evidence based reduction in morbidity and mortality.

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