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Original Article

A study on correlation of serum prealbumin with other biochemical parameters of malnutrition in hemodialysis patient

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A R T I C L E   I N F O

A B S T R A C T

Background: Malnutrition is more common in patients with end stage renal disease undergoing hemodialysis. The aim of the study was to assess the relation between serum prealbumin with other biochemical markers of malnutrition in patients with end stage renal disease undergoing hemodialysis. Method: 50 controls and 47 patients with chronic kidney disease on hemodialysis were enrolled in the study. Prealbumin, albumin, urea, creatinine, total cholesterol, prothrombin time and hsCRP was estimated in serum samples. Result: The data in the present study showed significant decrease in albumin, prealbumin, and increase in urea, creatinine in chronic kidney disease on hemodialysis . Also, we found significant correlation of prealbumin level with other biochemical parameters used for assessment of malnutrition with (p value <0.05), ROC analysis showed at optimum cutoff level of 29.5 mg/dl can predict malnutrition in person subjected to hemodialysis of stage 5 chronic kidney diseases with 72 % sensitivity and 60% specificity. Conclusion: The present study concludes that Prealbumin can be used surrogate marker of malnutrition when compared to other biochemical parameters of malnutrition in CKD patient on hemodialysis.

1. Introduction

Chronic kidney disease (CKD), one of the leading causes of morbidity worldwide, (CKD) is defined as a *pathophysiologic* process with multiple etiologies resulting in decrease in nephron number and function leading to end stage renal disease (ESRD)[1]. Study by Dash et al has reported approximately 7.85 million are suffering from chronic kidney diseases (CKD) in India. Renal replacement therapies like dialysis and transplantation has increased the survival rate in patients with CKD worldwide [2].

End stage renal disease (ESRD) patients are more prone to develop various complications including malnutrition. Early detection of nutritional status is important for monitoring the diseased patients. Though albumin has been commonly used as an indicator of malnutrition in dialysis patient, it responds slowly to the nutritional interventions. Because of the shorter half life of prealbumin, many authors consider prealbumin to be a better marker of nutrition than serum albumin. [3-5]. So this study was designed to evaluate the role of prealbumin levels in predicting malnutrition in south Indian Tamil population with CKD on hemodialysis (CKD-HD).

2. Materials and Methods

The present study was conducted in Stanley medical college & hospital. A total of 97 human subjects were selected and divided into two groups: Group I includes 50 normal subjects and Group II consists of 47 CKD stage V patients [6] on twice weekly hemodialysis for more than 1 month. Ethical clearance was obtained prior to the study.Persons with impaired hepatic function, coronary heart disease, and infections in the last 3 months before the blood collection, inflammatory syndromes or any steroid intake were excluded from the study.

After getting informed consent, 5 ml venous blood was collected at fasting state, serum separated and was used for the following tests: Prealbumin was estimated by immunoturbidimetry method using UV-vis Systronic spectrophotometer at 340nm using reagent kits from Spinreact-

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Spain , hsCRP was estimated by ELISA using reagent kits from Diagnostics Biochem Canada Inc (DBC), Ontario Canada. Albumin, urea, creatinine, total cholesterol using reagent kit from Agappe diagnostic India adapted to clinical chemistry analyzer(Bayer diagnostics).

2.1. Statistical analysis

The statistical analysis of data was done using SPSS version 16. Data was presented as mean ± S.D. Correlation analysis was performed using the Pearson test. Comparison of group was analyzed using Student t test. ROC was drawn to determine the area under curve to find optimum cutoff level for prealbumin in CKD-HD and control groups. A 'p' value less than 0.05 was considered significant.

3. Results

Table I shows comparison of prealbumin with other nutritional markers between CKD-HD group and control group. Data showed significant decrease in prealbumin and albumin level in patients with CKD-HD, total cholesterol was found to be less in patients with CKD-HD patient but not significant when compared to control subjects.

Table no II shows Pearson correlation of prealbumin with other nutritional markers. Prealbumin correlates significantly and positively with albumin, creatinine and total cholesterol in CKD-HD groups. Also we found negative correlation between CRP and prealbumin.

Figure 1 shows ROC curve with optimum cutoff 29.5mg/dl of prealbumin can detect malnutrition state in CKD-HD patient with significant AUC of 0.705 sensitivity of 72% specificity 60%.

Table I: Comparison of mean values and standard deviation between CKD-HD and controls

| Parameters	Control (n=50) M/F: 37/13	CKD-HD (n=47) M/F: 34/13	'p' Value
Age (yrs)	38.62±11.07	38.11±11.16	0.82 (Ns)
Prealbumin (mg/dl)	30.90 ± 4.04	26.72±6.74 **	0.00 (s)
Albumin (gm/dl)	4.04±0.31	3.37±0.6 **	0.00(s)
Urea (mg/dl)	30.38±4.02	99.09±29.6**	0.00(s)
Creatinine (mg/dl)	0.97±0.07	7.01±2.64**	0.00(s)
Cholesterol (mg/dl)	182±22.28	170±37.57	0.051(Ns)
CRP (mg/l)	3.36±1.07	5.57±7.70*	0.015(s)
Prothrombin time(sec)	12.92±0.81	12.04±0.77	0.910(Ns)

CKD-HD: chronic kidney disease patients on hemodialysis. CRP: C reactive protein. (Ns): not significant , (s): significant .Data expressed as mean ± SD.** indicates statistically significant 'p' value <0.05

Table 2: Pearson correlations of prealbumin with other nutritional markers in

Parameters	r	p
Albumin (gms/dl)	0.805	0.00(s)
Creatinine (mg/dl)	0.409	0.003(s)
Cholesterol (mg/dl)	0.76	0.009(s)
CRP (mg/L)	-0.301	0.01(s)

CKD-HD: Chronic kidney diseases on Hemodialysis , (Ns) : not significant , (s): significant

Figure I. Receiver operating curve analysis of prealbumin in predicting malnutrition in CKD-HD

ROC Curve

Diagonal segments are produced by ties.
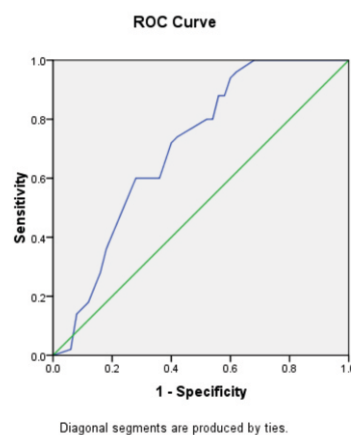
CUTTOFF LEVELS:

At 29.5mg/dl can detect malnutrition in CKD-HD

SENSITIVITY   : 72%

SPECIFICITY   : 60%

AUC   : 0.705

4. Conclusion

To conclude, prealbumin is a negative marker of inflammation level that correlates positively and significantly with other nutritional markers in ESRD patients on hemodialysis. In future serial prealbumin measurements can be incorporated in hemodialysis patients who are at high risk of malnutrition. Hence, serial prealbumin measurements may be incorporated in prospective trials of nutritional assessment.

5. Discussion

Malnutrition and wasting are present in large proportion of patients with chronic renal failure especially in patients on hemodialysis and they are unequivocally associated with mortality and morbidity. This can be due to low dietary intake pertaining to poor socio economic status, inflammation, inadequacy of dialysis, or a combination of these [7,8]. In our study, there is evidence of inflammation in CKD-HD with significant increase in CRP and decrease in albumin and prealbumin levels. Albumin and prealbumin are negative acute phase reactants that tend to decrease during inflammation. In our study we found significant negative correlation between prealbumin and CRP and this finding was similar to work done by Kaysen et al and Owen WF et al [9, 10].

Studies have shown that among various biochemical markers, serum albumin is widely used to assess malnutrition. And the level of albumin in the serum reflects the visceral protein status. But however, there are many factors which can influence the synthesis, distribution, degradation of albumin in the body. Even though albumin is well known biomarker for assessment of malnutrition because of longer half life it cannot be a sensitive indicator for nutritional therapy, and also studies have shown that albumin

levels decrease significantly as age advances when compared to prealbumin [11]. Also, albumin cannot be considered as nutrional marker during inflammation [12].

Possible role of inflammation and malnutrition during hemodialysis.

Various studies have emphasized the role of systemic inflammatory response as a cause of protein catabolism and malnutrition in dialysis patients. [10,13,14,&15]. Inflammation in CKD-HD may be due to uremia per se, infections or incomplete clearance of cytokines etc. The inflammatory response in CKD-HD is an adaptive phenomenon to stress. This adaptive response aims to satisfy the new metabolic priorities associated to stress condition. During this inflammatory response, there is release of catecholamines, cortisol, glucagon and growth hormone which inturn results in insulin resistance and mobilization of fuel stores. Cytokine activation, mainly interleukin-1 and tumor necrosis factor-alpha, promotes muscle protein degradation while interleukin-6 induces the synthesis of acute phase proteins in the liver. Hence, serum albumin, prealbumin, C-reactive protein and α-1 glycoprotein are the markers of systemic inflammatory response syndrome irrespective of etiology of stress 12, 15]. In stressed patients, the prolongation of this adaptive phenomenon can be deleterious by inducing a massive loss of muscle protein leading to malnutrition. In hemodialysis patients, inflammation and malnutrition coexist. Of course, inflammation is associated with a decrease in serum albumin, but serum albumin cannot be considered as a nutritional marker during inflammation [12]. The prevalence of C-reactive protein more than 20 mg/l was reported to be higher in patients with severe malnutrition than in patients without malnutrition or with moderate malnutrition as estimated by the Subjective Global Assessment [17]. However, whether this relationship was independent from other factors such age is difficult to be established.

The abnormalities of nutrient metabolism are responsible for an increase in energy and protein requirements. It is noteworthy that, inspite of these metabolic abnormalities, malnutrition is rare when the nutritional needs are satisfied. The data of the present study also supports the role of inflammation and inadequate feeding in the pathogenesis of malnutrition during dialysis.

Prealbumin (transthyretin) is a secretory protein from liver is important in the evaluation of nutritional deficiency and nutrition support [18] and it has been deemed as a valid and clinically useful indicator of PEM in maintenance of dialysis patients according to NKF-DOQI panel[19]. Many recent studies have shown that concentrations of albumin, transferrin and transthyretin correlate with the severity of the underlying disease rather than with anthropometric indices of malnutrition. In our study, there is decrease in prealbumin and albumin levels in CKD –HD. We found significant correlation between levels of albumin and prealbumin.

Another important thing is the half life of prealbumin which is about two to three days which is much shorter than the half life of albumin [6]. In our study we found optimum cutoff level 29.5mg/dl can be used to predict malnutrition in CKD –HD patient whereas Kaysen et al has shown that subjects above the cutoff level of 32 mg/dl of prealbumin are at increased risk of mortality . According to nutritional care consensus group, serum prealbumin 15mg/dl indicate patient are not at risk for malnutrition [20]. These variations may be due to difference in their ethnic races.

5. Discussion

To conclude, prealbumin is a negative marker of inflammation level that correlates positively and significantly with other nutritional markers in ESRD patients on hemodialysis. In future serial prealbumin measurements can be incorporated in hemodialysis patients who are at high risk of malnutrition. Hence, serial prealbumin measurements may be incorporated in prospective trials of nutritional assessment.

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