

Exploring the Relationship of Serum Albumin with Different Stages of Chronic Kidney Disease: A Cross Sectional Study in a Tertiary Care Hospital

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Abstract

Background: Chronic Kidney Disease (CKD) represents a major global health concern, leading to serious outcomes such as progression to End-Stage Renal Disease (ESRD), complications arising from reduced kidney function, and a heightened risk of Cardiovascular Disease (CVD). Serum albumin is a marker of malnutrition as well as inflammation and has been demonstrated as a strong predictor of mortality in CKD and ESRD patients. Lower serum albumin concentrations may be an under-appreciated risk factor for kidney function decline in elders. Many studies have hypothesized that lower levels and a progressive decline in serum albumin is associated with progressive CKD. The study's objective is to explore the link of serum albumin on renal progression in CKD patients.

Materials and methods: A cross-sectional study was conducted from January to December 2023 by the Department of Biochemistry, in collaboration with Department of Nephrology, at Marine City Medical College & Hospital (MCMCH). Purposive sampling method was implemented to recruit a total of 224 subjects, aged 18 years and above, following the inclusion and exclusion criteria, after obtaining approval from the Institutional Ethics Review Board (IERB). The study population was categorized into three groups based on the stages of CKD: stage III (eGFR 30–59 mL/min/1.73 m²), stage IV (eGFR 15–29 mL/min/1.73 m²), and stage V (eGFR <15 mL/min/1.73 m²). A detailed clinical profile was recorded for each of the subjects, including key biochemical parameters such as serum creatinine, serum albumin, and estimated Glomerular Filtration Rate (eGFR).

Results: The study revealed Male predominance of 54% and females comprising 46% with the mean age of the subjects being 56.22 ± 12.78 years. The mean serum creatinine level and the eGFR showed an inverse relation.

The mean serum albumin level among the study population was 3.21 ± 0.55 g/dL, with a significant difference between males and females ($p = 0.022$). Among the 224 subjects, 74.1% (166) of the subjects had decreased serum albumin levels with majority of the subjects (131) falling under the category of CKD Stage V. It was also observed that among the recruited 224 subjects, 84% (188) had oedema, of which 147 (65.6%) had low serum albumin levels. ANOVA test revealed that serum albumin levels progressively declined with advancing CKD stages, Stage III: 3.56 g/dL, Stage IV: 3.36 g/dL, Stage V: 3.11 g/dL ($F = 11.68$, $p = 0.00001$). A significant association was also found between decreased serum albumin and the presence of oedema ($\chi^2 = 10.17$, $p = 0.0014$).

Conclusion: The study demonstrated a strong relationship between decreased serum albumin levels and decline in eGFR among the CKD subjects. Thus a significant positive correlation was established between the declined eGFR and decreased serum albumin levels in the study population.

Key words: Chronic Kidney Disease (CKD); End-Stage Renal Disease (ESRD); Estimated Glomerular Filtration Rate (eGFR); Oedema; Protein Energy Wasting (PEW) Serum Albumin.

Introduction

Chronic Kidney Disease (CKD) represents a major global health burden because of its strong association with Cardiovascular Disease (CVD) and the risk of progressing to kidney failure.¹ According to 2012 report by the World Health Organization (WHO) CKD was linked to approximately 1.5% of all deaths worldwide.² In 2017, CKD resulted in 1.2 million deaths and was the 12th leading cause of death worldwide.² Therefore, preventing the progression of CKD remains a critical healthcare priority.³ Numerous studies have sought to identify predictive factors for CKD to help target patients who may benefit most from early intervention.⁴⁻⁷

Reduced kidney function especially in the elderly population is strongly and independently associated with cardiovascular disease, heart failure and mortality.^{8,9} The underlying risk factors

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for the onset and progression of kidney disease include older age, black race, diabetes, hypertension and cardiovascular disease.¹⁰ One potentially under-appreciated risk factor for kidney function decline is low serum albumin. Previous studies have shown even small decrements in levels of serum albumin to be strongly associated with cardiovascular disease, heart failure.¹¹⁻¹³ Limited research has linked low albumin levels to kidney function decline. Investigations in the Cardiovascular Health Study found that serum albumin was independently associated with higher risk of kidney function decline.¹⁴ Tangri et al. demonstrated that serum albumin concentrations are an important component of a multi-marker predictive model for progression to End-Stage Renal Disease (ESRD) in a cohort of Canadian adults with known Chronic Kidney Disease (CKD).¹⁵

Protein Energy Wasting (PEW) is a condition characterized by metabolic and nutritional changes leading to depleted stores of protein and energy. PEW has been considered as one of the strongest indicators of death in CKD and maintenance hemodialysis patients.¹⁶⁻¹⁸ Serum albumin is a protein synthesized by the liver, whose synthesis and thereby serum levels are impacted by conditions related to both nutrition (Protein intake) and inflammation.¹⁹⁻²¹ Many studies have indicated hypoalbuminemia in CKD and End-Stage Renal Disease (ESRD) patients as a strong indicator of PEW.²² Lower serum albumin levels have been associated with higher death risk in nondialysis-dependent CKD patients.²³⁻²⁶ In maintenance hemodialysis patients, low baseline serum albumin is a potent predictor of adverse outcomes such as lower health-related quality of life and higher hospitalization rates and death risk.²⁷⁻³¹ In chronic dialysis patients, in addition to the mortality predictability of serum albumin measured at a single point in time, time-varying hypoalbuminemia independently predicts all cause and CV mortalities. Furthermore, studies examining change in serum albumin in ESRD patients found that declining albumin levels in ESRD were associated with higher mortality, whereas increasing levels reduced this risk.^{27,32-34}

Patients with advanced CKD transitioning to ESRD have particularly high mortality rates within the first months after transition.^{35,36} In this study, we hypothesized that serum albumin would be an important prognostic biomarker for CKD.

Materials and methods

A cross-sectional study was conducted in the Department of Biochemistry, in collaboration with the Department of Nephrology in MCMCH, from January to December 2023 after obtaining permission from the IERB. The study encompassed 224 participants aged 18 years and above. These subjects were stratified into three groups as CKD: stage III, stage IV and stage V. Key variables examined included Serum creatinine, Serum Albumin and eGFR. eGFR was determined using the Cockcroft and Gault equation: $eGFR = (140 - \text{Age in years}) \times \text{Weight (kg)} \times [0.85 \text{ if female}] / 72 \times [\text{Serum Creatinine (mg/dL)}]$.

Inclusion criteria

Adult subjects of 18 years and above of any gender, diagnosed with CKD stage III, stage IV and stage V were included in this study.

Exclusion criteria

Subjects with CKD undergoing dialysis, subjects exhibiting psychological instability, bedridden patients, pregnant individuals, Subjects diagnosed with malignancy, HIV positive and Individuals positive for HbsAg were excluded in this study.

Data collection utilized a pre-tested structured questionnaire encompassing all the variables of interest. Study participants were recruited from the Department of Nephrology, MCMCH. After a brief clinical history was obtained, the purpose of the study was clearly explained to each participant, and both verbal and written informed consent were secured. Participants were instructed to report to the Biochemistry Laboratory at MCMCH between 8:00 and 9:00 AM. Approximately 5 mL of venous blood was drawn from the median cubital vein under strict aseptic precautions. The blood samples were collected in plain red-top tubes, without anticoagulants and immediately transported to the Biochemistry Laboratory for analysis. Serum was separated and analyzed for serum albumin and serum creatinine concentrations.

Data analysis was performed using Microsoft Excel (Windows 10) and IBM SPSS Statistics version 23. For quantitative variables, the mean and Standard Deviation (SD) were calculated. Statistical significance across different stages of Chronic Kidney Disease (CKD) was assessed using the Student's t-test, Chi-square test and one-way ANOVA, as appropriate. Results were presented in tables, bar charts and correlation graphs.

Results

The study population comprised 224 individuals, with a male predominance of 54% (n = 121) and females accounting for 46% (n = 103) [Figure 1]. The mean age of the subjects was 56.22 ± 12.78 years [Table I]. The mean Serum Creatinine concentration was 6.69 ± 4.46 mg/dL, while the mean eGFR was 13.35 ± 10.81 mL/min/1.73 m², demonstrating an inverse relationship between the two parameters. The mean serum albumin level among all subjects was 3.21 ± 0.55 g/dL, with a significant difference between males (3.31 ± 0.52 g/dL) and females (3.12 ± 0.56 g/dL) (p = 0.022) [Table II]. ANOVA analysis revealed a progressive decline in serum albumin levels with advancing CKD stages; Stage III: 3.56 g/dL, Stage IV: 3.36 g/dL, and Stage V: 3.11 g/dL. This trend was highly significant (F: 11.68, p = 0.00001) [Table III]. A total of 166 subjects (74%) exhibited hypoalbuminemia, of whom 131 were in Stage III CKD [Table IV]. Among the 224 CKD patients, 188 (84%) presented with oedema, and of these, 147 (65.6%) had low serum albumin levels. A significant association was also observed between decreased serum albumin and the presence of oedema ($\chi^2 = 10.17$, p = 0.0014) [Table V]. In addition to the fact that decreased serum albumin levels were associated with both lower eGFR and oedema, a strong positive correlation was found between decreased serum albumin and progressive decline in eGFR (r = 0.34, p = 0.001) [Figure 2].

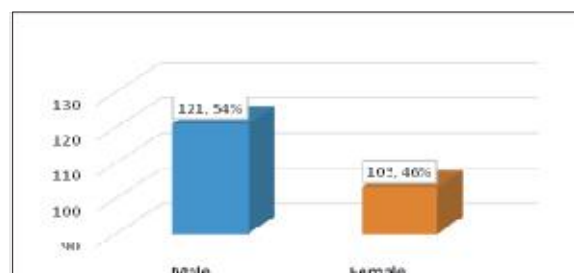


Figure 1 Bar Diagram showing the gender distribution in study subjects (n=224)

Table I Baseline characteristics of the study cases (n = 224)

Variables	Mean± SD	Range
Age (Years)	56.22 ± 12.78	18-85
S. Creatinine (mg/dl)	6.69± 4.46	1.42-21.5
eGFRml/min/1.73m ²	13.35± 10.81	2.0-50.9
Serum Albumin (g/dl)	3.21± 0.55	1.7-4.8

Table II Serum Albumin concentrations between male and female cases (n = 224)

Variables	Male	Female	Significance
	Mean± SD	Mean±SD	
	(Range)	(Range)	
S. Albumin (gm/dl)	3.31± 0.52	3.12± 0.56	p=0.022
	(2.2-4.8)	(1.7-4.6)	

Table III Distribution of serum albumin level according to CKD stages with ANOVA test significance (n = 224)

Variable	CKD Stage	Number (n=224)	Mean± SD	Range	Significance
S. Albumin (gm/dl)	Stage III	28	3.56 ± 0.71	2.2- 4.8	F = 11.68
	Stage IV	43	3.36 ± 0.49	2.6 – 4.6	p=0.00001
	Stage V	153	3.11 ± 0.48	1.7- 4.6	

Table IV Percentage distribution of low albumin level in the study cases (n = 224)

S. Albumin (gm/dl)	Stage III (n=28)	Stage IV (n=43)	Stage V (n=153)	Total (n)	Percentage (%)
Normal	17	19	22	58	25.9%
Decreased	11	24	131	166	74.1%

Table V Association of serum albumin with presence of oedema of the study cases (n = 224)

Groups	Low (<3.5 g/dl)	Serum Albumin Normal (3.5-5.5 g/dl)	Total	Significance
Oedema Present	147 (65.6%)	41 (18.4%)	188 (84%)	$\chi^2 = 10.17$
Oedema Absent	19 (8.4%)	17 (7.6%)	36 (16%)	p = 0.0014
Total	166 (74.1%)	58 (25.9%)	224 (100%)	

Discussion

Serum albumin concentration is a well-established predictor of mortality among patients with CKD. While several studies have demonstrated its association with mortality often mediated by cardiovascular events, few have explored serum albumin as an independent risk factor for the development or progression of CKD. In one notable study among eight inflammatory markers, serum albumin was the only laboratory measure significantly associated with kidney function decline. However, to date, limited research has investigated its role in predicting incident CKD,

rapid kidney function decline and progression to ESRD, especially in diverse elderly populations after accounting for inflammatory factors and urinary albumin excretion.^{37,38}

Because serum albumin is a widely available laboratory measurement, it may serve as a useful clinical marker for identifying individuals at higher risk of CKD development. There is, however, no direct physiological basis suggesting that low serum albumin causes CKD. Rather, serum albumin levels may decrease due to chronic liver disease, inflammation (As a negative acute-phase reactant), or persistent albuminuria. Severe malnutrition particularly kwashiorkor, though rare in developed settings can also lead to low serum albumin.^{37,38}

The study population demonstrated male predominance with a mean age of 56.22 ± 12.78 years. Serum creatinine and eGFR demonstrated an inverse relationship, with 74.1% of participants exhibiting decreased serum albumin levels. Oedema was present in 84% of subjects, and 65.6% of those had low serum albumin levels. Analysis of variance (ANOVA) revealed a significant association between decreased serum albumin levels and both reduced eGFR and presence of oedema. However, no statistically significant correlation was found between serum albumin and eGFR when analyzed directly. These findings are consistent with prior studies conducted by Joshua Lang et al. and Cheng et al.^{37,38} Serum albumin may therefore serve as a valuable marker for clinicians in risk stratification of patients prone to kidney disease progression.

Song et al. discovered that serum was negatively associated with renal prognosis in 1138 patients with CKD (HR = 0.75, 95%CI: 0.56–0.98, $p < 0.05$) after adjusting for confounding variables in a recent retrospective study.³⁹ Another Australian study showed that serum albumin was associated with an annual decline in eGFR and renal outcomes in CKD patients after adjustment for adjusted for gender, Urine Albumin Creatinine Ratio (UACR) triglycerides, age, diabetes, C-Reactive Protein (CRP) total cholesterol, BMI, Waist-Hip Ratio (WHR) and alcohol consumption. They discovered that each additional g/L of serum albumin increase could

lead to the annual eGFR decline decreasing 0.31 mL/min/1.73 m²/year ($\beta = -0.31$, 95%CI -0.18 to -0.44).⁴⁰ Although there were differences in the study populations of interest and statistical methods used, with similar sample sizes, our findings are consistent with the studies mentioned above. The observed relationship between low serum albumin and kidney function decline may reflect broader pathophysiological processes involving inflammation, thrombosis and microvascular dysfunction, which remain incompletely understood.

Limitations

However, the study did not have concurrent measures of urine albumin concentrations, so it could not discern the contribution of urine losses of albumin which is an established prognostic marker of kidney disease and potential confounder

Conclusion

In summary, our study demonstrates that lower serum albumin levels are strongly and independently associated with eGFR decline, thus establishing a strong relationship with decline in eGFR in CKD subjects. The study also revealed a significant association of declined serum albumin level with oedema. Thus a significant correlation was established between decline in eGFR and decreased serum albumin concluding that lower serum albumin is a diagnostic marker for prognosis of renal dysfunction.

Recommendations

Additional studies are required to understand the biological mechanisms linking low serum albumin with decline in kidney function. Further multicenter studies in large scale is required to establish a validated result. The sample size could be increased substantially so that a generalized conclusion could be made. Study on different tertiary level hospital of different parts of Bangladesh involving a large population size will be more representative of entire country.

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Contribution of authors

FH-Acquisition of data, data analysis, drafting & final approval.

PDK-Conception, design, interpretation of data, critical approval & final approval.

Disclosure

All the authors declared no competing interest.

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