Section: Biochemistry

Original Research Article

STUDY THE RELATIONSHIP OF SERUM CYSTATIN C AND C - REACTIVE PROTEIN IN PATIENTS ON PRE AND POST HEMODIALYSIS

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Abstract

Background: CKD poses a significant global health burden, necessitating enhanced efforts in early detection, prevention, and management strategies. The interplay between serum cystatin C, inflammatory markers like C-reactive protein, and thyroid profile parameters in CKD patients undergoing haemodialysis represents a crucial area of research to improve clinical understanding and therapeutic interventions. **Materials and Methods:** The present Observational Cross-sectional study was conducted on 300 subjects and it was divided into 2 groups. Group A consists of 150 chronic kidney disease with end-stage renal disease patients and Group B consists of healthy subjects. (n=150) from both genders, who aged more than 18 years. The marker dialysis adequacy measurement in a single HD treatment at pre-dialysis and post-dialysis on consecutive. Detailed personal and clinical history of all the subjects was taken and recorded in the Proforma. Basic anthropometric measurements were recorded on all the subjects. Biochemical investigations like Cystatin C, CRP, creatinine, Urea, and Uric acid were performed on all participant's Blood samples and analysed statistically. **Result:** The mean Cystatin C of the case group was 6.52 mg/l and that of the control group was 0.66 mg/l with p-value < 0.001, showing that it is statistically significant. The average value for post-dialysis case cystatin C is 5.70 mg/l. The p-value is less than 0.001 which indicates that there is a significant difference among them. The mean CRP of the case group was 29.37 mg/L and that of the control group was 1.87 mg/L. The average value for post-dialysis CRP was 21.48 mg/l. The p-value was less than 0.001 which shows that there is a significant difference between control CRP and case CRP post dialysis. The mean Creatinine from the case group was 7.16 mg/dL and that of the control group was 0.74 mg/dL. Post dialysis creatinine mean value 3.02 mg/dl. The p-value of less than 0.05 shows a significant difference. **Conclusion:** Overall, this study underscores the critical role of biomarker monitoring in CKD management. The observed changes in Cystatin C and CRP in pre- and post-dialysis provide valuable insights into the physiological impacts of CKD and dialysis. These findings can inform personalized treatment strategies aimed at optimizing dialysis efficacy, managing systemic inflammation, and addressing endocrine dysfunction. Future research should explore the longitudinal effects of these biomarkers on patient outcomes and investigate novel interventions to mitigate CKD-related complications.

INTRODUCTION

Chronic Kidney Disease (CKD) is becoming more widely acknowledged as a global public health concern as a result of its rising prevalence. CKD is increasing at an annual growth rate of 8% worldwide since there are no valid surrogate measures of renal function to identify pre-existing illness, especially in its early stages.[1,2] Strengthening efforts for CKD detection and prevention is urgently needed, as the majority of patients often appear in the late stages of renal impairment.

It is estimated that 13.4% of people worldwide suffer from CKD, and between 4.9 and 7.8 million have end-stage kidney disease (ESKD), which requires

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treatment with renal substitutes.[3] In India alone, 4–20% of people have CKD, with incidence rates greater in rural areas. As an illustration of the substantial burden in particular areas, Rajasthan, a state in India, is home to almost 90,000 people with CKD. The prevalence of CKD is rising, and many patients in this setting find the cost of managing the illness to be prohibitive. Therefore, in order to take action to prevent progressive and end-stage renal illness, it will be necessary to search for a better method of diagnosing early renal disease.[4]

The widespread use of serum Cys-C as a therapeutically relevant GFR marker has been made possible by the advent of automated and quick particle-enhanced immunoturbidimetric and immunonephelometric techniques.[5] CRP, also known as C-reactive protein, is comprised of five identical subunits and acts as the prototypical acute-phase protein in reaction to infection and inflammation. As with many acute-phase reactants, the liver is responsible for producing CRP, and it serves as a dependable biochemical indicator of systemic inflammation in clinical settings. As a result, increased CRP is thought to be a biomarker for tissue damage, inflammatory response, and the long-term progression of illnesses.[6]

MATERIALS AND METHODS

The present Observational Cross sectional study was conducted in the Department of Biochemistry in collaboration with Department of Nephrology of RNT Medical College & associated hospitals, Udaipur, Rajasthan.

Study Population

The study population was comprised of chronic kidney disease with end-stage renal disease patients on regular twice or three-weekly 4-hour sessions haemodialysis for at least 3 months, from both genders, aged more than 18 years attending kidney dialysis unit at RNT Medical College & associated hospitals, Udaipur, Rajasthan.

Study groups

The target subjects were divided into 2 groups:

Group A

A total of 150 chronic kidney disease with end-stage renal disease patients, from both genders, aged more than 18 years. All patients were recruited from kidney dialysis unit at RNT Medical College & associated hospitals, in Udaipur, Rajasthan. The marker dialysis adequacy measurement in a single HD treatment at pre-dialysis and post-dialysis on consecutive.

Group B

This group was consisting of healthy subjects. (n=150)

Exclusion criteria

CKD Patients aged below 18 years old and do not need dialysis. Patients who take hormone replacement therapy or corticosteroid therapy. Patient with liver cirrhosis, thyroid dysfunction, hematologic disorder or malignant disease and pregnant women and smokers, was excluded from the study.

Inclusion criteria

CKD with ESRD patients, who are aged more than 18 years old, attending kidney dialysis unit at RNT Medical College & associated hospitals, Udaipur, Rajasthan.

Patients on regular twice or three-weekly 4-hour sessions HD for at least three months. Include all consecutive patients of renal failure including (interstitial nephritis, glomerular nephritis, Diabetic Nephropathy, chronic kidney disease, and polycystic kidney disease), functionally anephric with residual urine volume of 0 to 100 ml/day, which is on dialysis.

Physical Examination and Anthropometry

Detailed personal and clinical history of all the subjects were taken and recorded in the Proforma. Basic anthropometric measurements were recorded on all the subjects.

Sample Technique

Convenient sampling**.**

Sample collection

5ml of venous blood sample was collected from all the subjects from antecubital vein by using aseptic techniques before and after dialysis into Plain tube.

Samples were allowed to incubate for 30 min at 37ºC, centrifuge at 3000 rpm for 15 min for the separation of serum and subjected for various biochemical investigations by standard protocol using commercially available reagents and kits on fully automatic chemistry analyzer and Chemiluminescence analyzer. Following biochemical investigations were performed by commercially available kits like Serum Cystatin C, Serum C-Reactive Protein (CRP), Serum Creatinine, Serum Urea and Serum Uric acid. Statistical analysis was done by using online student t test calculator and p value was Calculated. p value less than 0.001 considered as significant.

RESULTS

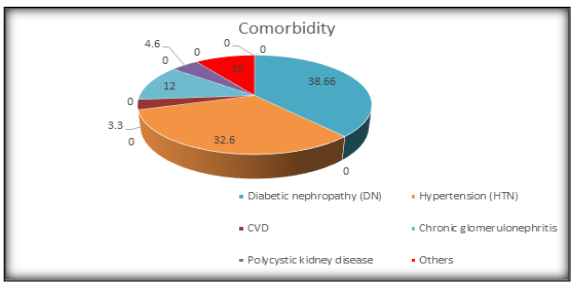

Figure 1: Comorbidity associated with CKD

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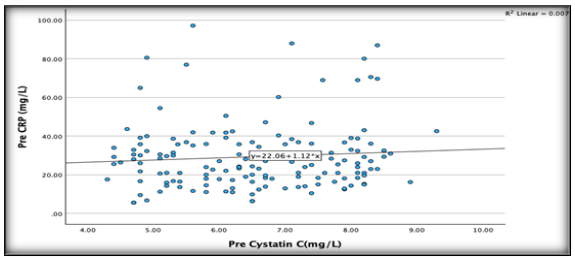

Figure 2: Correlation between pre dialysis Cystatin C and Pre dialysis CRP

The average age of the individuals in the case group was 50.01±11.33years, while in the control group, it was 37.26 ±11.33 years with a standard deviation of 11.83. The p value was less than 0.001, indicating a statistically significant difference.

Table 1: Showing Distribution of Participants according to BMI.

Parameter	Group	Mean BMI	Std. Deviation	P-value
BMI (Kg/m²)	Case	20.6079±	3.54548	< 0.001
	Control	22.6690±	3.30308	

The mean BMI of case group was 20.60 Kg/m² (SD = 3.54) (Kg/m²) and that of control group was 22.66 Kg/m² (SD = 3.30) (Kg/m²) with p value < 0.001, showing that there is statistically significant difference in mean BMI between the groups. Mean BMI of control group is significant higher as compared to case group.

Table 2: Diastolic blood pressure mm/Hg (DBP).

	Group	Mean CRP	P-value
DBP (mm/Hg)	Case	87.69±5.76	< 0.001
	Control	78.12±3.84	

The mean DBP of case group was 87.69 mm/Hg (SD = 5.76) and that of control group was 78.12 (SD = 3.84) with p< 0.001, showing that there is statistically significant difference in mean DBP (mm/Hg) between the groups. Mean DBP (mm/Hg) of control group is significant lower as compared to case group.

Table 3: Comparing Systolic blood pressure mm/Hg (SBP) between Case and Control.

	Group	N	Mean CRP	Std. Deviation	P-value
SBP (mm/Hg)	Case	150	141.09	9.52	< 0.001
	Control	150	120.18	3.75	

The mean SBP of case group was 141.09 mm/Hg (SD = 9.52) and that of control group was 120.18 mm/Hg (SD = 3.75) with p value < 0.001, showing that there is statistically significant difference in mean SBP (mm/Hg) between the groups. Mean SBP (mm/Hg) of control group is significant lower as compared to case group.

Table 4: Comparison of Cystatin C level between Pre dialysis, Post dialysis and Control Group.

	Group	N	Mean	P-value
Cystatin C (mg/l)	Pre dialysis	150	6.52±1.26	< 0.001
	Control	150	0.66±0.10	
	Post dialysis	150	5.701±1.29	

The mean Cystatin C of case group was 6.52 mg/l (SD = 1.26) and that of control group was 0.66 mg/l (SD = 0.10) with p value < 0.001, showing that there is statistically significant difference in mean Cystatin C (mg/l) between the groups. Mean Cystatin C (mg/l) of control group is significant lower as compared to case group. The average value for post dialysis case cystatin C is 5.70 mg/l (SD = 1.29). The p value is less than 0.001 which indicate that there is significant difference among them.

Table 5: Comparison of CRP level between Pre dialysis, Post dialysis and Control Group.

CRP (mg/L)	Group	N	Mean CRP	P-value
	Pre dialysis	150	29.37±17.38	< 0.001
	Control	150	1.87±0.49	
	Post dialysis	150	21.4825±13.70	

The mean CRP of case group was 29.37 mg/L and that of control group was 1.87 mg/L with p value < 0.001, showing that there is statistically significant difference in mean CRP (mg/L) between the groups. average value for post dialysis CRP was 21.48 mg/l .The p value was less than 0.001 which shows that there is significant difference between control CRP and case CRP post dialysis. It was higher for cases.

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Table 6: Comparison of S. Urea level between Pre dialysis, Post dialysis and Control Group.

UREA (mg/dl)	Group	N	Mean Urea	P-value
	Pre dialysis	150	133.94±45.50	< 0.001
	Control	150	24.59±7.7	
	Post dialysis	150	41.96±12.19	

The mean UREA of case group was 133.94 mg/dl and that of control group was 24.59 mg/dl with p value < 0.001, showing that there is statistically significant difference in mean UREA mg/dl between the groups. Mean UREA (mg/dl) of control group is significant lower as compared to case group. post dialysis urea average was 41.96 mg/dl. It was also observed that p value for control urea and post urea is <0.001 which shows that there is significant difference between both. It was higher for cases.

Table 7: Comparison of Serum Creatinine level between Pre dialysis, Post dialysis and Control Group.

Creatinine (mg/dL)	Group	N	Mean Creatinine	P-value
	Pre dialysis	150	7.1659±2.04	< 0.001
	Control	150	0.7488±.15	
	Post dialysis	150	3.0248±1.09	

The mean Creatinine from case group was 7.16 mg/dL and that of control group was 0.74 mg/dL with p value < 0.001, showing that there is statistically significant difference in mean CREATININE (mg/dL) between the groups. post dialysis creatinine mean value 3.02 mg/dl (SD = 1.09) A p value of lesser than 0.05 shows significant difference. It was higher for case.

Table 8: Comparison of S. Uric acid level between Pre dialysis, Post dialysis and Control Group

Uric Acid (mg/dL)	Group	N	Mean Uric Acid	P-value
	Pre dialysis	150	7.2040±0.92	< 0.001
	Control	150	4.9109±1.04	
	Post dialysis	150	5.211±0.80	

The mean Uric Acid from case group was 7.20 mg/dL and that of control group was 4.91 mg/dL with p value < 0.001, showing that there is statistically significant difference in mean Uric Acid (mg/dL) between the groups. Post dialysis uric acid study group mean was 5.21 mg/dl.

Table 9: Comorbidity associated with CKD.

Comorbidity	Total patients (n=150)	Percentage %
Diabetic nephropathy (DN)	58	38.66
Hypertension (HTN)	49	32.6
CVD	05	3.3
Chronic glomerulonephritis	18	12
Polycystic kidney disease	07	4.6
Others	15	10
Total	150	100

Table 10: Correlation between Pre dialysis CRP and pre dialysis Cystatin C

		Pre CRP (mg/L)
Pre dialysis Cystatin C(mg/L)	Pearson Correlation	0.082
	Sig. (2-tailed)	0.321
	N	150

It is found that for Pre CRP and Pre-Cystatin C, Pearson Correlation was 0.08 and p value = 0.32, showing positive association.

Table 11: Correlation between Post dialysis Cystatin C and post dialysis CRP

		Post dialysis CRP (mg/L)
Post dialysis Cystatin C (mg/L)	Pearson Correlation	-0.013
	Sig. (2-tailed)	0.876
	N	150

For the post dialysis CRP and post dialysis Cystatin C, value of Pearson Correlation was found to be – 0.013. It also does not have any significant association.

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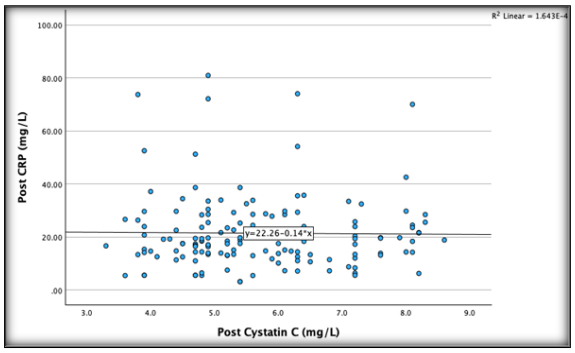

Figure 3: Correlation between Post dialysis CRP and Post Dialysis Cystatin C

DISCUSSION

The present study was conducted on 150 chronic kidney disease with end-stage renal disease patients, from both genders, aged more than 18 years. The marker dialysis adequacy measurement in a single HD treatment at pre-dialysis and post-dialysis on consecutive. Include all consecutive patients of renal failure including (interstitial nephritis, glomerular nephritis, Diabetic Nephropathy, chronic kidney disease, and polycystic kidney disease), functionally anephric with residual urine volume of 0 to 100 ml/day, which are on dialysis and 150 Healthy adults between the age of 18 - 80 years with No history of any severe illness.

Cystatin C is a sensitive marker of kidney function, particularly in assessing glomerular filtration rate (GFR). Elevated levels of cystatin C indicate reduced kidney function and are especially relevant in the context of CKD. The average Cystatin C level in healthy controls is 0.66 mg/L, which reflects normal kidney function. Cystatin C levels are significantly elevated in pre-dialysis patients, with an average of 6.52 mg/L. This sharp increase is indicative of severe kidney dysfunction, as reduced renal function impairs the clearance of cystatin C from the blood. After dialysis, Cystatin C levels decrease slightly to 5.70 mg/L but remain elevated compared to both healthy controls and the pre-dialysis group. This suggests that while dialysis helps remove some waste products from the bloodstream, it does not fully restore kidney function. Elevated cystatin C levels post-dialysis reflect ongoing kidney impairment and decreased filtration capacity.

CRP is a sensitive marker of systemic inflammation. Elevated levels are often observed in conditions like CKD, which are associated with chronic inflammation. The CRP level in healthy controls is relatively low at 1.87 mg/L, indicating the absence of systemic inflammation. This is consistent with a healthy immune system and the absence of kidney disease. CRP levels in pre-dialysis CKD patients rise sharply to an average of 29.37 mg/L. This is a clear indication of chronic inflammation, which is common in CKD due to factors like oxidative stress, uremic toxins, and vascular damage. The elevated CRP levels in this group reflect the systemic inflammatory response seen in CKD. After dialysis, CRP levels remain high at 29.37 mg/L, showing that dialysis does not resolve the underlying inflammation. Dialysis itself can induce an inflammatory response due to the procedure (e.g., blood-contacting materials, fluid shifts). Therefore, while dialysis may reduce some uremic toxins, it does not eliminate the chronic inflammatory state seen in CKD.

Similarly, Maheshwari et al. (2015)[7] studied that There was a statistically significant increase in the mean values of cystatin C from the pre-dialysis to the post-dialysis in the LF group. There was a statistically significant decrease in the mean values of cystatin C from the pre-dialysis to the post-dialysis in the HF group. The CysCRR was −9.7 ± 6.7% and 29.2 ± 11% in LF and HF hemodialysis, respectively. The statistically significant decrease in CysCRR in the HF group shows the effective clearance of MM by HF dialyzers. Hence, CysCRR could be applied to measure the MM clearance in HF hemodialysis.

Conversely, other studies have reported an increase in cystatin C levels post-dialysis. Krishnamurthy et al. (2010)[8] observed that despite a significant reduction in creatinine levels after dialysis, cystatin C levels paradoxically increased. Dharnidharka et al. (2016)[9] also found a post-dialysis rise in cystatin C levels, attributing this trend to its molecular size and slower clearance compared to creatinine. These contradictory results highlight the need for further investigation into factors affecting cystatin C removal, including dialysis modality, membrane permeability, and patient-specific characteristics.

The observed reduction in CRP levels post-dialysis in the current study aligns with findings from Stigant et al. (2005)[10] and Kaysen et al. (2000)[11], suggesting that hemodialysis can effectively decrease systemic inflammation. However, the contradictory results reported by Yeun et al. (2000)[11] highlight the complexity of the inflammatory response in haemodialysis patients.

Variations in CRP levels may be attributed to differences in patient populations, dialysis modalities, membrane types, and the presence of comorbid conditions. For instance, factors such as dialysis membrane biocompatibility and ultrafiltration rates can influence inflammatory markers. Additionally, underlying infections or vascular access issues may contribute to elevated CRP levels, independent of the dialysis procedure itself.

Further research is needed to elucidate the mechanisms underlying the variable effects of hemodialysis on CRP levels and to identify strategies to minimize inflammation in this patient population.

CONCLUSION

Overall, the present study demonstrated a significant reduction in both Cystatin C and C-reactive protein

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(CRP) levels following hemodialysis in the case group. Post-dialysis Cystatin C levels were significantly lower than pre-dialysis levels (5.70 mg/L vs. 6.52 mg/L, $p < 0.001$), suggesting effective clearance of this biomarker through dialysis. Similarly, CRP levels decreased significantly after dialysis (21.48 mg/L vs. 29.37 mg/L, $p < 0.001$), indicating a reduction in systemic inflammation.

These findings highlight the role of hemodialysis not only in improving renal function markers but also in modulating inflammatory responses. The comparison with the control group further emphasizes the altered baseline levels of these biomarkers in dialysis patients, reinforcing the need for routine monitoring and individualized treatment strategies.

Future studies with larger sample sizes and standardized protocols are needed to further elucidate these relationships and optimize hemodialysis strategies for better patient outcomes.

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