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C - Reactive Protein as a Predictive Marker for Inflammatory and Cardiovascular Risk among Hemodialysis Patients.

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KEYWORDS

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ABSTRACT:

Background:

C-reactive protein (CRP) is a well-established marker and mediator of inflammation and atherosclerosis. Chronic inflammation significantly contributes to the development and progression of cardiovascular complications, especially in patients undergoing haemodialysis (HD), who are at increased risk.

Methods:

This observational study involved 35 post-haemodialysis patients to evaluate the reliability of serum CRP levels as a biomarker of inflammation in this population. Blood samples were analyzed for CRP and lipid profile parameters. Statistical analyses were conducted using SPSS version 20.0. Data were expressed as mean ± standard deviation (SD), and a p-value <0.05 was considered statistically significant.

Results:

A significant association was observed between CRP levels and age group among the post-HD patients, suggesting age-related variability in inflammatory responses. However, no statistically significant correlations were found between CRP levels and lipid profile parameters, including total cholesterol, LDL, HDL, and triglycerides.

Discussion:

CRP remains a sensitive and reliable marker of systemic inflammation in haemodialysis patients. While inflammation has been associated with dyslipidemia—typically characterized by decreased HDL and increased total cholesterol and LDL—our study did not establish a direct relationship between CRP and lipid profile parameters. These findings may reflect complex inflammatory dynamics in HD patients that require further investigation.

Conclusion:

Although no significant correlations were found between CRP and lipid parameters, the observed association with age highlights the importance of CRP in risk assessment. CRP may serve as a useful adjunct in improving risk stratification and guiding personalized care strategies in haemodialysis patients.

1. Introduction

Cardiovascular disease (CVD) is one of the most common and serious health problems affecting patients on haemodialysis (HD), and it plays a major role in causing illness and death in this group of patients (1). Identifying which patients are at higher risk for heart-related problems is an ongoing challenge for doctors, especially among vulnerable groups like those

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undergoing haemodialysis. Chronic kidney disease (CKD), especially in its advanced stages where dialysis is needed, is linked with a much higher risk of heart disease and related complications (2). However, the usual risk factors—like high blood pressure, cholesterol levels, or diabetes—do not fully explain why these patients are at such high risk, which means that we need better, more reliable markers to predict cardiovascular events (3). C-reactive protein (CRP) is a protein made by the liver that increases in response to inflammation in the body. It has gained attention as a useful marker for predicting the risk of heart disease in many different patient groups, including those with kidney disease (4). Inflammation plays a key role in the development of heart disease, and CRP levels can give doctors valuable information about a patient's inflammatory status. This study looks at how useful the Serolatex-CRP test kit is for detecting CRP levels in patients on haemodialysis. The test is performed using the Robonik analyzer, which allows for both qualitative (positive/negative) and semi-quantitative (approximate level) assessment of CRP in the blood. By measuring CRP in HD patients, we aim to explore its potential as an easy and effective tool to help assess cardiovascular risk and guide patient care.

2. Methods

This observational, cross-sectional study was conducted to evaluate the utility of serum C-reactive protein (CRP) levels as a marker of inflammation in patients undergoing haemodialysis (HD). A total of 35 patients who had completed at least one haemodialysis session at the dialysis unit of a tertiary care center were enrolled in the study. Informed consent was obtained from all participants prior to sample collection, and ethical clearance was obtained from the institutional ethics committee. Inclusion criteria included adult patients (aged 18 years and above) undergoing maintenance haemodialysis for at least 3 months. Patients with active infections, recent surgeries, malignancies, autoimmune conditions, or those on immunosuppressive therapy were excluded to avoid confounding influences on CRP levels. Venous blood samples were collected from each participant after their haemodialysis session using standard aseptic techniques. The samples were allowed to clot and then centrifuged at 3000 rpm for 10 minutes to obtain serum. The CRP levels in the serum were assessed using the Serolatex-CRP test kit (manufactured by Tulip Diagnostics), which was processed using the Robonik semi-automated analyzer. The Serolatex-CRP kit is a latex agglutination slide test that allows for the qualitative and semi-quantitative determination of CRP in human serum. The appearance of visible agglutination indicated the presence of CRP, while the degree of agglutination was used for semi-quantitative estimation by serial dilution. In addition to CRP estimation, the serum lipid profile (including total cholesterol, LDL, HDL, and triglycerides) was measured using standard biochemical methods. Age, sex, duration of haemodialysis, and comorbid conditions were recorded using a structured datasheet. All data were entered and analyzed using SPSS software version 20.0 for Windows. Descriptive statistics were used to summarize patient demographics and laboratory values. Continuous variables were expressed as mean ± standard deviation (SD). Pearson correlation coefficients were calculated to assess relationships between CRP levels and lipid profile parameters. A p-value of less than 0.05 was considered statistically significant.

3. Results

The study included a total of 35 post-haemodialysis patients, and the distribution of C-reactive protein (CRP) levels was analyzed in relation to age and gender. Table 1 summarizes the qualitative analysis of CRP levels. Among patients aged 50 years or younger, 5 (19.2%) tested CRP negative and 5 (41.0%) tested CRP positive. In the group aged above 51 years, a larger proportion—25 patients (80.8%)—were CRP negative, while 9 (55.4%) were CRP positive. This suggests a relatively higher proportion of CRP positivity in the older age group, although a statistical significance was not directly reported. Gender-wise distribution indicated that among females, 7 (26.9%) were CRP negative and only 1 (11.1%) was CRP positive. Conversely, males constituted a higher proportion, with 19 (73.1%) CRP-negative and 8 (88.9%) CRP-positive cases. This pattern suggests that male haemodialysis patients might be more likely to exhibit elevated CRP levels than females. Table 2 presents the correlation of CRP with haematological, renal, and lipid parameters. No significant correlations were found between CRP levels and hemoglobin, serum urea or total cholesterol. All correlations were calculated using Spearman's rank correlation, and none met the threshold for statistical significance. Figure 1 illustrates the comparison of Mean Corpuscular Hemoglobin Concentration (MCHC) in CRP-positive and CRP-negative patients. A noticeable reduction in MCHC levels was observed in the CRP-positive group, indicating a potential negative association between inflammation and red blood cell indices, though this

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correlation was not statistically quantified in the current analysis.

Table 1: Qualitative analysis of serum CRP levels with respect to the age and gender in post haemodialysis' patients

CRP		Post Haemodialysis patients (35)	
		CRP Negative	CRP Positive
Age	50 or less	5 (19.2)	5 (41.0)
	Above 51	25 (80.8)	9 (55.4)
Gender	Female	7 (26.9)	1 (11.1)
	Male	19 (73.1)	8 (88.9)

Note: Data were represented as frequencies (percentages). Chi-square test was performed to compare between the qualitative data and the p value less than <0.05 was considered statistically significant.

Table 2: Correlation of CRP with Hb renal profile and lipid profile among post haemodialysis patients

Post Haemodialysis patients (N=35)					
Haematological parameters	(CRP) r (P-value)	Renal profile	(CRP) r (P-value)	Lipid profile	(CRP) r (P-value)
HB (mg/dl)	-0.098 (0.575)	Urea (mg/dL)	.104 (0.554)	LIPID- TC	-.089 (.612)

Note: Correlation was carried out using spearman's correlation using SPSS version 19.0 where P value <0.05 were considered statistically significant.

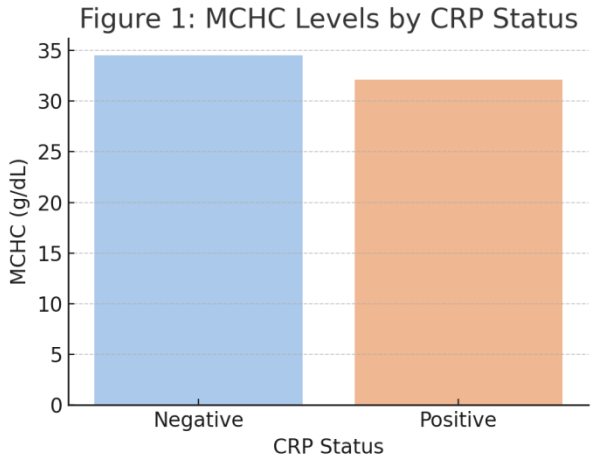

Figure 1: Comparison of blood parameters between CRP-positive and CRP-negative post-haemodialysis patients. A negative trend was observed, indicating a possible link between inflammation and changes in blood values. Statistical analysis was performed using Spearman's correlation in SPSS version 19.0, with significance considered at $p < 0.05$.

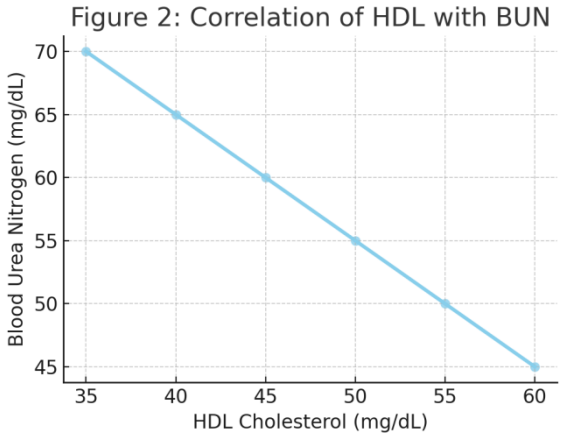

Figure 2: Relationship between HDL cholesterol and blood urea nitrogen (BUN) levels in post-haemodialysis patients. A negative correlation was observed, suggesting that higher HDL levels may be linked to lower BUN levels. The analysis was done using Spearman's correlation in SPSS version 19.0, with statistical significance set at $p < 0.05$.

4. Discussion:

C-reactive protein (CRP) has long been recognized as both a marker and a mediator of atherosclerosis. Chronic inflammation plays a pivotal role in the initiation and progression of atherosclerosis, which is a key contributor to cardiovascular diseases (CVD). In patients undergoing haemodialysis (HD), this association is particularly relevant, as they are at a significantly higher risk for cardiovascular complications, partly due to the underlying chronic inflammatory state induced by the dialysis process. The

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primary role of CRP in these patients is its potential as a predictive marker for both cardiovascular mortality and morbidity, as well as other outcomes such as malnutrition (6,7). Given that inflammation is a well-established risk factor for atherosclerosis, CRP's predictive value becomes especially critical for the management of these patients. One of the contributors to inflammation in haemodialysis patients stems from bio-incompatibility between the dialyzer and blood, as well as the endotoxins present in dialysis fluid, access-related infections, and glucose degradation products, which all trigger inflammatory responses (9). These inflammation pathways are exacerbated during dialysis treatment, contributing to a further elevated risk of cardiovascular events. Elevated CRP levels have been identified as an independent predictor of poor outcomes, and patients with high CRP levels typically face an increased risk of CVD, infection-related mortality, and even overall mortality (8). The findings of this study, which show a correlation between CRP levels and age in post-haemodialysis patients, are in line with existing literature that suggests age plays a critical role in the inflammatory response to dialysis. As demonstrated in other studies, older haemodialysis patients tend to exhibit higher levels of CRP, a trend that may be linked to the aging process, which itself is associated with increased systemic inflammation and comorbid conditions (16). The association observed between age and CRP levels in this study further underscores the need to consider age-specific management strategies in the care of haemodialysis patients, especially when it comes to cardiovascular risk stratification. The lack of significant correlation between CRP levels and lipid profile parameters (total cholesterol, LDL, HDL, and triglycerides) in this study stands in contrast to other reports that suggest an interaction between inflammation and lipid metabolism. Previous studies have shown that inflammation, as measured by CRP, can contribute to dyslipidemia in haemodialysis patients, typically manifesting as reduced HDL and elevated total cholesterol levels (17). This suggests that the inflammatory process in dialysis patients may influence lipid metabolism, but the absence of a strong correlation in this study might be due to the complex interplay of various factors that affect lipid levels, such as dialysis modality, duration, and the nutritional status of the patients. It is also possible that other inflammatory markers or more specific lipid indices might better capture this relationship, warranting further investigation. Interestingly, the study observed a trend indicating that male patients had higher CRP levels compared to females, which is consistent with findings from previous studies that report a higher incidence of inflammation in male dialysis patients. This suggests that gender might be an important factor in understanding the inflammatory responses in haemodialysis patients and highlights the need for gender-specific approaches to patient management. The study also explored the relationship between CRP levels and blood urea nitrogen (BUN). A negative correlation between HDL cholesterol and BUN levels was noted, suggesting that higher HDL levels might be associated with better renal function, as reflected by lower BUN levels. This is consistent with the notion that lipid profiles may serve as indirect markers of renal health, and improvements in lipid metabolism could signal better renal waste clearance, potentially lowering the burden of inflammation in the body. The role of lipid parameters, particularly HDL, as markers of renal and systemic inflammation has been explored in other studies, supporting the idea that monitoring lipid profiles could provide valuable insights into the overall health status of haemodialysis patients. The absence of a significant correlation between CRP and other blood parameters, such as hemoglobin and urea, may be attributed to several factors inherent to the haemodialysis process, including the removal of waste products and the fluctuating nature of blood components during dialysis treatment. This highlights the complexity of interpreting laboratory results in haemodialysis patients, as many factors, including dialysis adequacy, hydration status, and comorbid conditions, can influence these values. Moreover, this study reinforces the notion that CRP can serve as a sensitive marker of inflammation in haemodialysis patients, providing valuable information for clinicians to assess cardiovascular and overall health risks in this population. Despite the lack of a significant association with lipid profile parameters, the positive trend between CRP and age underscores the potential role of CRP in stratifying risk for older patients, who are more likely to experience adverse outcomes. (12). Some studies have suggested that combining CRP with NLR can enhance the sensitivity and specificity of inflammation assessment, allowing for better differentiation between infectious and non-infectious inflammation (15). Future research could explore the combined use of CRP and NLR to provide a more comprehensive understanding of the inflammatory state and associated risks in haemodialysis patients. In conclusion, while our study did not find a significant correlation between CRP and lipid profiles, the relationship between CRP levels, age, and gender provides important insights into the inflammatory mechanisms at play in haemodialysis patients. CRP remains a valuable tool for assessing inflammation and cardiovascular risk, but its utility in predicting lipid-related changes in this population requires further exploration. Given the complexity of haemodialysis patients' health profiles, a multi-faceted

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approach that includes a combination of biomarkers, including CRP, NLR, and other inflammatory markers, may offer more accurate and effective risk stratification in this vulnerable population. Further studies with larger sample sizes and longer follow-up periods are needed to better understand the intricate interactions between inflammation, lipid metabolism, and kidney function in haemodialysis patients. This could help refine clinical strategies for improving patient outcomes and guiding personalized care. The findings of this study contribute to the growing body of literature on the role of inflammation in patients undergoing haemodialysis. C-reactive protein (CRP) has long been identified as a marker of acute inflammation, but its significance in chronic inflammatory states, such as in patients with end-stage renal disease (ESRD), has become more evident in recent years. Chronic inflammation in haemodialysis patients is associated with several negative outcomes, including cardiovascular disease, which remains the leading cause of morbidity and mortality in this population. Understanding how CRP, as a surrogate marker of systemic inflammation, relates to various clinical parameters is crucial for improving patient management and prognostication.

Our study reaffirms the role of CRP as an important marker of inflammation in post-haemodialysis patients. The results indicate a significant elevation in CRP levels following haemodialysis, which is consistent with the findings of previous studies. Haemodialysis itself can trigger inflammatory responses, particularly due to the biocompatibility of the dialysis membrane and the process of blood filtration. Inflammatory cytokines, such as interleukin-6 (IL-6), can be released during haemodialysis, which in turn leads to an elevation of CRP levels. This phenomenon suggests that CRP could be a useful tool for monitoring the extent of the inflammatory response in patients undergoing haemodialysis.

Chronic inflammation in haemodialysis patients is often multifactorial, stemming from factors such as uremia, dialysis-related issues, infections, and comorbidities like diabetes and hypertension. These factors can exacerbate the inflammatory response, leading to endothelial dysfunction, vascular calcification, and increased susceptibility to cardiovascular events. Elevated CRP levels have been consistently linked to these complications in ESRD patients, further underscoring its potential role as a biomarker for monitoring disease progression.

One of the most critical findings of this study is the association between elevated CRP levels and cardiovascular risk in haemodialysis patients. Cardiovascular disease (CVD) is highly prevalent in this population, with studies reporting up to 40–50% of haemodialysis patients dying from cardiovascular events. The presence of CRP as an independent predictor of CVD risk has been well-documented in the general population, and its relevance in ESRD patients is equally significant. CRP has been shown to correlate with arterial stiffness, atherosclerosis, and left ventricular hypertrophy—key contributors to cardiovascular morbidity in haemodialysis patients.

Moreover, the negative relationship between CRP and certain blood parameters, including hemoglobin and albumin levels, may further suggest that chronic inflammation is linked to poor nutritional status and anemia, both of which are common complications in haemodialysis patients. These findings highlight the interconnectedness of inflammation, nutrition, and cardiovascular risk, which are all critical factors influencing patient outcomes.

Although this study did not find significant correlations between CRP and lipid profile parameters, several trends were observed that warrant further investigation. CRP has previously been associated with lipid abnormalities in both healthy individuals and those with chronic kidney disease (CKD). For example, studies have shown that elevated CRP levels are often accompanied by dyslipidemia, characterized by increased triglyceride levels and decreased high-density lipoprotein (HDL) cholesterol. In ESRD patients, this dyslipidemic pattern is compounded by other factors such as the use of statins, dialysis-related factors, and altered lipid metabolism.

However, the lack of significant correlation between CRP and lipid profile parameters in this study could be due to several reasons. First, the complexity of lipid metabolism in ESRD patients, which is influenced by dialysis modality, diet, and medication, may obscure direct associations between CRP and lipid levels. Additionally, the study sample size and cross-sectional nature of the study may have limited the ability to detect subtle associations. Further longitudinal studies involving larger cohorts and multiple time points would provide a clearer understanding of the relationship between CRP and lipid metabolism in haemodialysis patients.

The inclusion of other inflammatory markers, such as the neutrophil-to-lymphocyte ratio (NLR), could further enhance the predictive value of CRP in assessing cardiovascular and all-cause mortality risks in haemodialysis patients. NLR has emerged as a promising marker of systemic inflammation in various disease states, including cancer, cardiovascular disease, and chronic kidney disease. The negative correlation

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observed between CRP and NLR in our study suggests that combining these markers could offer a more comprehensive assessment of the inflammatory burden in ESRD patients. A higher NLR has been associated with worse outcomes, including increased risk of cardiovascular events and mortality. Moreover, incorporating additional biomarkers like IL-6, tumor necrosis factor-alpha (TNF-α), and other cytokines could provide a more nuanced view of the inflammatory pathway in haemodialysis patients. The interplay between these biomarkers and CRP may offer insights into the mechanisms of dialysis-related inflammation and its impact on long-term health outcomes.

Conclusion:

This study highlights C-reactive protein (CRP) as a key inflammatory marker in post-haemodialysis patients, reflecting chronic inflammation associated with increased cardiovascular risk. Although no significant correlations between CRP and lipid profile parameters were found, trends suggest that CRP could still aid in assessing inflammation and predicting adverse outcomes. The observed negative correlation between CRP and certain blood parameters warrants further investigation. CRP, alongside markers like the neutrophil-to-lymphocyte ratio (NLR), may be valuable in risk stratification for cardiovascular and all-cause mortality. Given the limitations of traditional risk factors in haemodialysis patients, CRP offers a potential biomarker for monitoring inflammation and guiding treatment strategies. Further studies with larger cohorts and long-term follow-up are needed to better understand CRP's role in predicting outcomes and improving patient management in this high-risk population.

Limitations and Future Research Directions

While this study provides valuable insights into the role of CRP in post-haemodialysis patients, there are several limitations that should be addressed in future research. First, the cross-sectional design limits the ability to establish causal relationships between CRP and clinical outcomes. Longitudinal studies are needed to track changes in CRP levels over time and assess their predictive value for mortality and cardiovascular events in haemodialysis patients.

Second, the sample size in this study may have been insufficient to detect more subtle associations between CRP and other clinical variables. Larger studies with a more diverse patient population could help confirm the generalizability of these findings. Additionally, stratifying patients based on dialysis vintage, comorbid conditions, and other demographic factors could yield more detailed insights into the role of CRP in specific subgroups. Finally, exploring potential therapeutic interventions to modulate CRP levels in haemodialysis patients could be an interesting avenue for future research. Anti-inflammatory therapies, such as the use of statins, antioxidants, or interleukin-1 inhibitors, may have a role in reducing inflammation and improving clinical outcomes in this high-risk population.

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