Original Article

The Effect of Hemodialysis Adequacy on Inflammatory Status in Stage 5 Chronic Kidney Disease Patients (A Study at Dr. Adhyatma, MPH Regional Hospital, Semarang)

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ABSTRACT

Background: Chronic Kidney Disease (CKD) is a critical global health issue, particularly Stage 5 CKD, where kidney function is severely impaired. Hemodialysis, essential for managing such patients, aims to remove waste and excess fluids. Chronic inflammation, common among CKD5-HD patients, heightens cardiovascular risks and worsens quality of life. Hemodialysis adequacy, measured by the Kt/V ratio, plays a vital role in outcomes, yet its relationship with inflammatory markers, such as Hs-CRP, albumin, and TIBC, remains unclear.

Objective: This study aimed to evaluate the relationship between hemodialysis adequacy, as reflected by Kt/V values, and inflammatory markers such as C-reactive protein (CRP), albumin, and total iron binding capacity (TIBC) in CKD stage 5 patients undergoing hemodialysis, providing insights into optimizing dialysis protocols to mitigate inflammation.

Methods: A cross-sectional study of 45 CKD5-HD patients assessed Kt/V values and inflammatory markers (Hs-CRP, albumin, TIBC). Data were analyzed using Shapiro-Wilk, Independent t-tests, or Mann-Whitney U tests based on data distribution.

Results: The mean Kt/V value was 1.31 ± 0.21. Lower Kt/V values were significantly associated with elevated Hs-CRP levels ($p = 0.018$). No significant differences in Kt/V values were observed concerning albumin ($p = 0.546$) or TIBC ($p = 0.523$). Correlations between Hs-CRP and albumin or TIBC were non-significant ($p = 1.000$).

Conclusion: Adequate hemodialysis, reflected in optimal Kt/V values, is crucial for reducing systemic inflammation marked by Hs-CRP. Albumin and TIBC levels showed no significant association, underscoring the multifactorial nature of inflammation in CKD5 patients.

Keywords: Hs-CRP, Albumin, Kt/V, Adequacy, Hemodialysis, Inflammation.

Introduction

Chronic Kidney Disease (CKD) is a serious global health problem, especially Stage 5 CKD, which requires dialysis or kidney transplantation to survive. In 2021, more than 850 million people worldwide were affected by kidney disease, far exceeding the prevalence of diabetes, cancer, or HIV/AIDS.[1] In Indonesia, the 2018 Basic Health Research (Riskesdas) reported a CKD prevalence of 0.38% (3.8 cases per 1,000 population), with 60% requiring dialysis.[2] The 2020 Indonesian Kidney Registry identified hypertensive kidney disease as the leading cause of CKD requiring dialysis, followed by diabetic nephropathy and glomerulopathy. Chronic inflammation in patients undergoing

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hemodialysis (CKD5-HD) contributes significantly to increased morbidity, mortality, and decreased quality of life, often due to its association with cardiovascular disease.[3]

Hemodialysis is a life-saving treatment for patients with CKD-5, which aims to remove waste products and excess fluid from the blood when the kidneys can no longer perform these functions. In contrast, hemodialysis effectiveness is mostly the same as adequacy, differs among patients, and is essential to reduce complications.[4,5] The Kt/V ratio is usually used to measure hemodialysis adequacy, which shows the efficiency of the dialysis process in removing urea from the blood. Maximum Kt/V values are related to improved patient outcomes, whereas inadequate dialysis causes adverse effects, such as increased inflammation.[6–8]

Inflammation among CKD5-HD patients is frequently measured through biomarkers like high-sensitivity C-reactive protein (Hs-CRP), albumin, and Total Iron Binding Capacity (TIBC).[9–11] Hs-CRP is the standard marker used to measure this inflammation, which is thought to be caused by the chronic kidney disease itself, the type of dialysis filter, and the hemodialysis procedure. The primary reason Hs-CRP is used as a marker is because high levels are a strong predictor of poor outcomes. Multiple studies have confirmed that elevated Hs-CRP in CKD5-HD patients is linked to a higher risk of hospitalization, death from cardiovascular disease, and death from any cause.[12]

The Hs-CRP levels showed systemic inflammation related to a higher risk of cardiovascular events.[6,13,14] Atherosclerosis is recognized as an inflammatory disease, and this type of chronic inflammation is very common in patients on hemodialysis, affecting 30-65% of them. Albumin and TIBC are also employed to measure nutritional status and inflammation, where hypoalbuminemia commonly shows malnutrition and inflammatory states. The connection between inflammatory markers and hemodialysis adequacy indicates an active investigation area, with studies showing that inadequate dialysis could exacerbate inflammation.[13,15,16]

Despite the importance of hemodialysis adequacy, there is limited agreement about the optimal Kt/V threshold needed to control inflammation effectively in CKD5-HD patients. Previous studies have shown various results, including a strong correlation between low Kt/V values and developed inflammation and no significant association. This discrepancy underlines the need for further research to clarify the role of hemodialysis adequacy in managing inflammation in specific patients.

This study aims to explore the hemodialysis adequacy effect with Kt/V on the inflammatory status of CKD5-HD patients, especially Hs-CRP, albumin, and TIBC levels. The study, through analysis of the relationship among the variables, aims to show the optimizing dialysis adequacy to reduce chronic inflammation in the vulnerable patient population. To conclude, understanding the effects of hemodialysis adequacy on inflammation gains treatment protocols and better results for patients with CKD Stage 5. By emphasizing critical inflammatory indicators and their relationship to Kt/V values, the study supports continuous efforts to improve the care for patients with hemodialysis.

Methods

Design and participants

The study was conducted with a cross-sectional design, which is fit to analyze the relationships among variables at a single point in time. The target population consisted of patients diagnosed with Chronic Kidney Disease Stage 5 (CKD5) with routine hemodialysis (HD) treatment at Dr. Adhyatma MPH Hospital, Semarang. The 45 patients selected according to certain inclusion criteria, such as patients with hemodialysis for at least three months and who had stable clinical conditions, with acute infections, malignancies, or other conditions that could independently impact inflammatory markers, were excluded to ensure the result's validity. The intervention received by the

research subjects was hemodialysis sessions performed twice a week, with a duration of 4.5 hours per session, and using a high-flux dialyzer. No patients dropped out during the study. All patients undergo a complete dialysis session in HD.

Study Covariate

The cross-sectional design is used to analyze the relationship among variables at one point in time. The 45 patients with CKD on stage 5 with routine hemodialysis at Dr. Adhyatma MPH Hospital, Semarang. The inclusion criteria required patients with hemodialysis for at least three months with stable clinical conditions, with acute infections, malignancies, or conditions that might affect inflammatory markers, to be excluded, to maintain the validity of the results.

Data collected encompassed demographic information (age, sex, underlying causes of kidney disease, duration of hemodialysis, and type of vascular access) alongside key variables: hemodialysis adequacy (measured via Kt/V ratio) and inflammatory indicators (Hs-CRP, albumin, TIBC). Blood samples were obtained prior to scheduled dialysis sessions and analyzed with standardized methods. Kt/V values were calculated using Watson's formula, incorporating patient weight and dialysis duration to assess the adequacy of treatment.

Statistical analysis

Statistical analysis was performed to determine the relationship between hemodialysis adequacy and the inflammatory markers. The data was processed using SPSS 17.0 statistical analysis. The Shapiro-Wilk test was first used to assess the normality of the data distribution. Depending on the results, either the Independent t-test or the Mann-Whitney U test was employed to compare the Kt/V values between groups with different levels of inflammatory markers. A p-value of less than 0.05 was considered statistically significant. Additionally, correlation analyses were conducted to explore potential associations between Hs-CRP, albumin, and TIBC levels. These analyses aimed to identify whether variations in hemodialysis adequacy could be linked to changes in the patients' inflammatory status.

Results

Patient selection

1. Baseline Characteristics

The study involved 45 chronic hemodialysis patients, with a mean age of 50.51 ± 13.05 years, ranging from 20 to 78 years. The male participants constituted 55.6% (n=25), while females made up 44.4% (n=20). The average duration of hemodialysis was 3.74 ± 3.07 years, with a median of 2.5 years (0.67 to 11 years). The majority of patients had hypertension as the primary cause of their kidney disease (62.2%, n=28), followed by diabetes mellitus (22.2%, n=10), and a combination of hypertension and diabetes mellitus (15.6%, n=7). In terms of vascular access, 97.8% (n=44) of the patients used an arteriovenous (AV) shunt, while only 2.2% (n=1) used a double lumen catheter. The baseline characteristics can be seen in Table 1.

Table 1. Baseline Characteristics of The Patients

Characteristic	Value
Total Patients	45
Age (years)	50.51 ± 13.05
Age Range (years)	20 - 78
Gender	
- Male	25 (55.6%)
- Female	20 (44.4%)
Duration of Hemodialysis (years)	3.74 ± 3.07
Hemodialysis Duration Range (years)	0.67 - 11
Cause of Kidney Disease	
- Hypertension	28 (62.2%)
- Diabetes Mellitus	10 (22.2%)
- Hypertension & Diabetes Mellitus	7 (15.6%)
Vascular Access	
- AV Shunt	44 (97.8%)
- Double Lumen	1 (2.2%)

2. Inflammatory Parameters

The inflammatory status was assessed using Hs-CRP (high-sensitivity C-reactive protein), with 57.8% (n=26) of the patients classified as having high Hs-CRP levels, 24.4% (n=11) with moderate levels, and 17.8% (n=8) with low levels. Albumin levels were predominantly normal in 97.8% (n=44) of the patients, with only 2.2% (n=1) having elevated levels. For TIBC (Total Iron Binding Capacity), 71.1% (n=32) of the patients had normal levels, while 28.9% (n=13) had reduced levels. Inflammatory Parameters can be seen in Table 2.

Table 2. Inflammatory Parameters in the study patients

Inflammatory Parameter	**All Patients** (N=45)	**Patients with High Hs-CRP** (n=26)	**Patients with Low/Medium Hs-CRP** (n=19)	**p-value**
Hs-CRP Levels (n, %)				
High	26 (57.8%)	26 (100%)	0 (0%)	-
Medium	11 (24.4%)	0 (0%)	11 (57.9%)	
Low	8 (17.8%)	0 (0%)	8 (42.1%)	
Albumin Levels (n, %)				
High	1 (2.2%)	1 (3.8%)	0 (0%)	1.000
Normal	44 (97.8%)	25 (96.2%)	19 (100%)	
TIBC Levels (n, %)				
Low	13 (28.9%)	9 (34.6%)	4 (21.1%)	1.000
Normal	32 (71.1%)	17 (65.4%)	15 (78.9%)	

3. Hemodialysis Adequacy

Hemodialysis adequacy was measured using the Kt/V parameter, with a mean value of 1.31 ± 0.21, and a median of 1.29 (0.94 to 1.87). The study revealed significant differences in Kt/V values based on Hs-CRP levels, where patients with high Hs-CRP levels had lower Kt/V values (mean ± SD: 1.26 ± 0.18) compared to those with normal Hs-CRP levels (mean ± SD: 1.42 ± 0.24), with ap-value of 0.018, indicating a significant difference ($p < 0.05$). However, there were no significant differences in Kt/V values based on Albumin ($p = 0.546$) and TIBC ($p = 0.523$) levels. Additionally, correlation tests showed no significant relationship between Hs-CRP and Albumin ($p = 1.000$) or between Hs-CRP and TIBC ($p = 1.000$). Hemodialysis adequacy can be seen in Table 3.

Table 3. Correlation Tests

Parameter	Mean ± SD	Median (Range)	p-Value	Significance
Overall Kt/V	1.31 ± 0.21	1.29 (0.94 to 1.87)	-	-
Kt/V by Hs-CRP Levels			0.018	Significant difference ($p < 0.05$)
High Hs-CRP	1.26 ± 0.18	-	-	-
Normal Hs-CRP	1.42 ± 0.24	-	-	-
Kt/V by Albumin Levels	-	-	0.546	No significant difference ($p > 0.05$)
Kt/V by TIBC Levels	-	-	0.523	No significant difference ($p > 0.05$)
Correlation Tests	-	-	-	No significant relationship
Hs-CRP and Albumin	-	-	1.000	-
Hs-CRP and TIBC	-	-	1.000	-

Discussion

This study investigated the effect of hemodialysis adequacy, as measured by Kt/V, on inflammation in patients with Chronic Kidney Disease Stage 5 (CKD5) undergoing regular hemodialysis. The results revealed a significant association between Kt/V values and high-sensitivity C-reactive protein (Hs-CRP) levels, a marker of systemic inflammation. Patients with lower Kt/V values, indicating inadequate hemodialysis, were found to have optimum Hs-CRP levels. The suggestion is that inadequate dialysis could increase inflammation, which is a problem for cardiovascular complications and decreased quality of life in CKD5 patients.

Interestingly, the study shows no difference in significance in Kt/V values when stratified using other inflammation markers, including Albumin and Total Iron Binding Capacity (TIBC), that are related to nutritional status and iron metabolism, and the lack of significant connection with Kt/V indicates the levels might be affected by factors other than dialysis adequacy. It highlights the complexity of the inflammatory process in CKD5 patients.

Furthermore, the significant association between Hs-CRP, albumin, and TIBC further highlights the multifaceted nature of inflammation in CKD5 patients. While Kt/V is an essential factor in managing inflammation, from Hs-CRP levels, which may be another factor in engaging the broader inflammatory status in the patients. The findings highlight the comprehensive approach to managing inflammation, which involves addressing other factors to elevated Hs-CRP levels.

In this study, we selected CRP, albumin, and TIBC as inflammatory markers based on their clinical relevance and accessibility in routine practice. CRP was chosen as a representative acute-phase reactant that rises in response to systemic inflammation and has been widely used in previous studies evaluating inflammation in hemodialysis patients. Albumin and TIBC, although not acute-phase reactants, were included as negative inflammatory markers reflecting chronic inflammation and nutritional status, which are also frequently altered in chronic kidney disease and dialysis populations. The finding that CRP, but not albumin or TIBC,

was associated with dialysis adequacy may reflect the difference in sensitivity and temporal dynamics of these markers. While CRP levels can rapidly respond to changes in inflammatory status and may be influenced by dialysis clearance, albumin and TIBC are more stable and may be affected by other non-inflammatory factors such as liver function or malnutrition. We acknowledge that CRP levels can be affected by dialysis modality, particularly with convection-based therapies; however, all patients in our study underwent conventional hemodialysis, thereby minimizing this confounder.

To conclude, the study emphasizes the importance of achieving adequate hemodialysis with Kt/V to manage systemic inflammation in patients with CKD5. However, the study also focuses on gaps in how dialysis adequacy connects with other markers of inflammation like Albumin and TIBC. Future studies should investigate these connections more deeply and likely identify further mechanisms that can be focused on to enhance the treatment outcomes. Therefore, it may be possible to develop more effective and targeted treatment protocols, ultimately gaining the patients' quality of life with hemodialysis.

Conclusion

This study shows that hemodialysis adequacy using Kt/V significantly affects inflammation in patients with CKD5 with hemodialysis, particularly as indicated by Hs-CRP levels. Patients with inadequate dialysis showed lower Kt/V values, with higher levels of systemic inflammation. However, no significant association was found between Kt/V and other inflammation markers, such as albumin and TIBC. The findings suggest that to optimize dialysis adequacy, it is essential to manage inflammation in CKD5 patients; other factors and markers must be considered in treatment strategies. Further studies are needed to explore the associations and improve care and outcomes for CKD5 patients.

Limitations of the Study

However, several limitations to this study should be acknowledged. First, the cross-sectional design limits the capacity to establish causality between hemodialysis adequacy and inflammation. The data provides a snapshot of the relationship at a single point in time, so it is difficult to determine the changes in Kt/V over time that may differentially impact inflammatory markers. Moreover, the modest sample of the study is 45 patients, which may limit the relevance of the result to the general CKD5 patient population. There are other possible influencing factors, including comorbid conditions or variations in dialysis protocols, that were not fully completely considered in the analysis.

Declarations

Ethics approval and consent to participate

This study adhered to the guidelines for clinical research and received approval from the Ethics Committee of the dr. Adhyatma Hospital, under reference number: 088/KEPK.EC/IX/2023.

Competing interests

There are no conflicts of interest in writing this article.

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Author's Contribution

Idea/concept: DW. Design: DW. Control/supervision: DLP, L. Data collection/ processing: DW. Analysis/interpretation: DW, DLP. Literature review: DW, DLP, L, AN, AA, SC. Writing the article: DW, DLP, L, AN, AA, SC. Critical review: DW, DLP, L, AN, AA, SC. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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