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The Relationship Between Serum Ferritin Levels and Left Ventricular Function in Patients Undergoing Hemodialysis

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ABSTRACT

Introduction: Left ventricular hypertrophy (LVH) is a common condition that often occurs in patients undergoing regular hemodialysis, and it is associated with a poor prognosis in these patients. The worsening of LVH symptoms in patients undergoing hemodialysis is the strongest predictor of sudden cardiac death in such individuals. The aim of this study was to determine the relationship between serum ferritin levels and left ventricular function in patients undergoing hemodialysis at RSUP Haji Adam Malik, Medan.

Method: The design of this study is a cross-sectional study with consecutive sampling. The study population consists of patients undergoing regular hemodialysis, and the population includes patients who undergo regular hemodialysis in RSUP H. Adam Malik.

Results: There was a significant relationship between hemoglobin, albumin, and serum ferritin levels with left ventricular function ($p < 0.005$). Hemoglobin showed a moderate positive correlation with LVEF ($r = 0.477$). The relationship between albumin and LVEF had a stronger correlation ($r = 0.681$). There was a strong and significant negative correlation between serum ferritin and LVEF ($r = -0.961$).

Conclusion: A significant relationship was found between hemoglobin levels, albumin levels, mean serum ferritin level, and left ventricular function in hemodialysis patients. Hemoglobin and albumin showed a positive correlation with left ventricular function, while serum ferritin level had a significant and strong negative correlation with left ventricular function.

Keywords

Serum ferritin level, Left ventricular function, Hemodialysis

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INTRODUCTION

Chronic Kidney Disease (CKD) is a condition affecting the structure or function of the kidneys that lasts for more than 3 months.[1] Prolonged hemodialysis in CKD patients carries a risk of cardiovascular problems. Left ventricular hypertrophy (LVH), or enlargement of the left ventricle, is a common cardiovascular issue in patients undergoing regular hemodialysis and is associated with a poor prognosis in these individuals. The worsening of pre-existing LVH in hemodialysis patients is the strongest predictor of sudden cardiac death. The prevalence of LVH is estimated to be between 16-31% in individuals with a GFR > 30ml/min, which increases to 60-75% before starting kidney replacement therapy and further increases to 90% after dialysis initiation. After 18 months of dialysis, it has been reported that 62% of patients experience an increase in the left ventricular mass index, with 49% of them progressing to left ventricular failure.[2]

Iron metabolism disorders, including both iron deficiency and excess, have been linked to increased morbidity and mortality in cardiovascular diseases. Serum ferritin is widely recognized as an acute-phase reactant, which non-specifically increases in systemic inflammatory conditions such as chronic kidney disease, liver disease, and cancer. Higher serum ferritin levels can induce macrophage accumulation and increase the production of reactive oxygen species (ROS) during inflammation. Previous studies have reported that serum ferritin levels are not only an important risk factor for rapid kidney damage but also appear to increase morbidity and mortality in patients with CKD and those undergoing hemodialysis.[3,4]

Inflammation in hemodialysis patients can lead to an elevation in serum ferritin levels. Serum ferritin levels have been independently associated with an increased risk of cardiovascular death and can predict patient mortality regardless of inflammation or nutritional status in dialysis patients.[5] Increased serum ferritin levels (≥ 800 μg/L) are positively associated with the occurrence of LVH in patients undergoing regular hemodialysis. Serum ferritin levels ≥ 100 μg/L carry a higher risk of cardiovascular-related death compared to levels < 100 μg/L.[1,3,6] This study aims to analyze the relationship between serum ferritin levels and left ventricular function in patients undergoing hemodialysis at RSUP Haji Adam Malik, Medan.

METHOD

This study is an analytical study with a sample size of 30 respondents. The inclusion criteria for this study were age >18 years, undergoing hemodialysis for >3 months, and being cooperative. The exclusion criteria for this study were patients undergoing irregular hemodialysis, having a history of malignancy, severe infection, chronic liver disorders, and coronary artery disease.

This study used primary data obtained directly from patient examinations or medical records, including measurements of serum ferritin levels, hemoglobin, albumin, EKG, chest X-ray, and the body mass index of the patients.

Univariate analysis was used to describe the descriptive data by presenting frequency distribution and percentages for categorical data. Numerical data were presented as mean and standard deviation. Bivariate analysis was used to evaluate the relationship and correlation between the research variables. The normality of data was tested using the Shapiro-Wilk test. If the data were normally distributed, the Pearson correlation test was used, while the Spearman correlation test was used for non-normally distributed data. Statistical analysis was performed using SPSS 26 (Statistical Product and for Social Sciences) software with a confidence level of 95%. Statistical significance was indicated if the p-value was <0.05.

RESULT

Characteristics of the study sample

This study included 30 respondents who met the inclusion and exclusion criteria and were willing to participate in the research process. Blood tests were conducted to assess serum ferritin levels in the sample, followed by echocardiography to assess LVEF. The data on the characteristics of the study sample are presented in Table 1.

Correlation between BMI and LVEF

After conducting the Shapiro-Wilk test, it was found that the distribution of EF values was not normal. Therefore, the Spearman correlation test was performed to evaluate the correlation between EF and BMI. The data analysis of the correlation between BMI and LVEF is presented in Table 2.

Correlation between Hemoglobin, Serum Ferritin, and Albumin with LVEF

Table 3 presents the results of the correlation analysis using the Spearman method between hemoglobin levels and LVEF, serum ferritin levels and LVEF, and albumin levels and LVEF.

Table 1. Characteristics of study sample

Characteristics	Mean ± SD (total)
Age (Year)	49.80 ± 13.94
Gender, n (%)	
Male	17 (56.67)
Female	13 (43,33)
Weight (kg)	58.60 ± 5.817
Height (cm)	160.87 ± 5.494
Body Mass Index	22.59 ± 1.305
Hemoglobin (g/dL)	8.84 ± 1.50
Albumin (g/dL)	3.61 ± 0.51
Ferritin Serum (µg/L)	131.43 ± 50.25
Ferritin <100 ng/dl (%)	9 (30%)
LVEF	0.48 (48%)
History of transfusion (%)	10 (34%)
Duration of HD (%)	
<1 year	10 (33,4)
>1 year	20 (66,6)
Number of HD sessions (%)	
≤3 times per week	21 (70)
>3 times per week	9 (30)
IDWG	3,07 ± 6.24
History of EPO use	7 (23%)
Iron Substitution (%)	6 (20%)
Etiology of HD (%)	
Diabetic nephropathy	17 (56,7)
Chronic glomerulonephritis	8 (26,7)
Nephrosclerosis	1 (3,3)
Polycystic Kidney Disease	1 (3,3)
Others	3 (10)
Ferritin levels in DM patients (n = 17)	128,35 ± 5.494

This research involved a sample of 30 respondents. The analysis results showed that the average age of the respondents was 49.80 ± 13.94 years, with the majority of respondents being male, totaling 17 individuals (56.67%). The respondents had an average body mass index (BMI) value of 22.59 ± 1.305. The research also found that the hemoglobin level in the entire sample had an average value of 8.84 ± 1.50 g/dL, while the albumin level had an average value of 3.61 ± 0.51 g/dL. The average serum ferritin level in the sample was found to be 93.12 ± 42.87. The majority of the sample had good left ventricular ejection fraction (LVEF) (>50%), which was observed in 16 samples.

Table 2 presents the results of the Spearman correlation test between body mass index (BMI) and left ventricular function (LVEF). In the analysis, it was found that the correlation value between BMI and LVEF was 0.246, with a p-value of 0.191. These results indicate that there is no significant relationship between body mass index and left ventricular function, as measured by LVEF, with a p-value >0.05.

Table 2. Correlation between BMI and LVEF

		LVEF		Total (%)	Correlation coefficient (r)	p-value
		<50%	≥50%			
BMI	Normal	12	17	29 (96.67%)	0.246	0.191
	Overweight	0	1	1 (3.33%)		

The correlation analysis between hemoglobin and LVEF is presented in Table 3. Based on the Spearman correlation analysis, a correlation coefficient (r) of 0.477 with a p-value of 0.008 was found. These results indicate a significant relationship between hemoglobin and LVEF. The correlation between albumin and LVEF is shown in Table 4. The Spearman correlation analysis revealed a significant relationship between albumin and LVEF, with a p-value of 0.00 (<0.05). Additionally, a positive correlation was also found between

the two variables. Table 5 displays the correlation between serum ferritin level and LVEF. The Spearman correlation analysis revealed a significant relationship between serum ferritin level and left ventricular function, as seen through the EF value, with a p-value <0.05. The correlation coefficient found was -0.961, indicating a strong and meaningful negative correlation.

Table 3. Correlation between hemoglobin, serum ferritin, and albumin with LVEF

		LVEF		Total (%)	Correlation coefficient (r)	p-value
		<50%	≥50%			
Hb	Normal	1	1	2 (6.67%)	0.477	0.008
	Low	11	17	28 (93.33%)		
Ferritin	<100 µg/L	0	9	9 (30.0%)	-0.961	0.000
	≥100 µg/L	12	9	21 (70.0%)		
Albumin	≥3.5 g/dL	2	15	17 (56.67%)	0.681	0.000
	<3.5 g/dL	3	10	13 (43.33%)		

DISCUSSION

This research involved 30 patients undergoing hemodialysis who met the study criteria. Based on the subjects' characteristics, the average age of the patients undergoing hemodialysis was 49.8 years. Male subjects accounted for the largest percentage, with a total of 17 individuals (56.67%). This study is similar to Moreira et al.'s study on self-assessment of hemodialysis patients, where the majority of the sample consisted of males (914 individuals or 56.4%).[7] Adult males often tend to neglect healthcare, possibly influenced by beliefs and values associated with masculinity. However, chronic kidney disease can be prevented through lifestyle modifications such as reducing sodium, fat, and tobacco consumption, increasing water intake, regular exercise, reducing alcohol consumption, and following healthy habits regularly.[8]

In this study, the average weight and height of the sample were 58.6 kg and 160.87 cm, respectively. Consequently, the average body mass index (BMI) in the study sample was 22.59. This study aligns with Al Husna et al.'s study on the relationship between BMI and hemodialysis adequacy in Indonesia, which reported an average BMI of 22.67 in the sample [9]. Higher BMI levels up to 45 kg/m2 have been associated with better survival and lower cardiovascular-related deaths. Low body weight in patients undergoing hemodialysis is strongly associated with increased cardiovascular risk and overall mortality. Inflammation in hemodialysis patients can be caused by various factors such as kidney failure, dialysis, oxidative damage, impaired immune function, malnutrition, dialysate, accumulation of advanced glycation end products, dialysate back-leak, vascular access issues, and advanced age. A higher BMI plays a protective role in dialysis patients with inflammation.[10]

The average hemoglobin level found in hemodialysis patients in this study was 8.86 g/dL, which is not significantly different from the finding reported by Kahdina et al., where the average hemoglobin level in CKD patients undergoing hemodialysis was 8.17 g/dL. Anemia is the most common complication in CKD patients and can occur at the early stages of kidney disease, worsening as kidney function declines. Anemia in hemodialysis patients can also be caused by iron deficiency. Anemia significantly contributes to reduced quality of life, increased morbidity, and mortality related to cardiovascular health, leading to unfavorable cardiovascular outcomes.[11]

The average albumin level in this study was 3.61 ± 0.51 g/dL, and a positive correlation was found between albumin and left ventricular ejection fraction (LVEF). Several studies have shown that low serum albumin is an independent predictor of heart failure development. Low serum albumin is considered a predictive factor for the development and prognosis of cardiovascular disease.[12]

The average serum ferritin level in this study was 131.43 µg/L. There was a significant correlation between serum ferritin level and left ventricular function with a p-value < 0.05. Serum ferritin levels increase as EF values decrease, and conversely, serum ferritin levels decrease when EF values are high. This finding is

higher than the study by Son et al., which evaluated the relationship between serum ferritin levels and clinical outcomes in hemodialysis patients, reporting an average serum ferritin level of 50.7 ng/mL.[13]

Increased ferritin levels can reflect an excess of exogenous iron due to iron treatment and conditions related to inflammation, including acute or chronic inflammation, malignancies, and liver disease. In dialysis patients, increased serum ferritin is associated with erythropoietin resistance, malnutrition, or inflammation status.[14] Serum ferritin levels >100 ng/mL are associated with poor long-term survival in patients, even after adjusting for age, gender, hemodialysis vintage, CRP levels, and cardiovascular event history. High serum ferritin levels (>800 µg/L) are positively associated with left ventricular hypertrophy in patients undergoing hemodialysis.[13,15]

CONCLUSION

There is a significant relationship between hemoglobin, albumin, and serum ferritin levels with left ventricular function ($p < 0.005$). Hemoglobin shows a moderate positive correlation with LVEF ($r = 0.477$). The relationship between albumin and LVEF has a stronger correlation ($r = 0.681$). There is a highly significant and meaningful negative correlation between serum ferritin and LVEF ($r = -0.961$).

DECLARATIONS

Ethics approval and consent to participate. Permission for this study was obtained from the Ethics Committee of Universitas Sumatera Utara and Haji Adam Malik General Hospital.

CONSENT FOR PUBLICATION

The Authors agree to publication in Journal of Society Medicine.

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AUTHORS' CONTRIBUTIONS

All authors significantly contribute to the work reported, whether in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas. Contribute to drafting, revising, or critically reviewing the article. Approved the final version to be published, agreed on the journal to be submitted, and agreed to be accountable for all aspects of the work.

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