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Original Research

The Association Between Protein, Iron, Folate, and Vitamin C Intakes with Hemoglobin Level among Chronic Kidney Disease Patients Undergoing Hemodialysis at Haji Regional Public Hospital, East Java Province

Hubungan Asupan Protein, Zat Besi, Asam Folat dan Vitamin C dengan Kadar Hemoglobin Pasien Gagal Ginjal Kronik dengan Hemodialisis di RSUD Haji, Provinsi Jawa Timur

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Abstract: *Anemia is a common complication in patients with chronic kidney disease (CKD) undergoing hemodialysis. Anemia in CKD is multifactorial, including impaired erythropoiesis, iron deficiency, and chronic inflammation. Adequate nutrient intake plays an essential role in hemoglobin synthesis, anemia management, and improving patients quality of life. This study aimed to determine the association between protein, iron, folate, and vitamin C intakes with hemoglobin levels in CKD patients undergoing hemodialysis at Haji Regional Public Hospital, East Java Province. This study used quantitative with cross-sectional design. Purposive sampling was applied, involving 54 respondents who met the inclusion criteria. Data on protein, iron, folate, and vitamin C intakes were collected through direct interviews using a semi-quantitative food frequency questionnaire on previous month, while hemoglobin data were obtained from the most recent laboratory recods. Bivariate analysis used the Pearson Corelation test for protein intake and Hb level, while the Spearman test was used for iron, folate, and vitamin C intakes and Hb level. The results showed that protein intake was significantly associated with hemoglobin level (p<0.001), with a moderate positive correlation (r=0.45). In contrast, iron, folate, and vitamin C intake were not significantly associated with hemoglobin level (p>0.05). Adequate protein intake, particularly high biological value animal protein, is required to compensate for protein losses following dialysis. Personalized protein management based on urea burden, metabolic acidosis, phosphorus status, and comorbidities may support improvements in hemoglobin level without exacerbating renal metabolic burden.*

Keywords: *chronic kidney disease (CKD), folate, homodialysis, hemoglobin, protein, vitamin C*

1. INTRODUCTION

Chronic kidney disease (CKD) is a progressive renal disorder characterized by a glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 for at least three months (1). CKD has become a major global health problem and is currently the third fastest-growing cause of death worldwide. It is projected to rank fifth among the leading causes of years of life lost (YLL) by 2040 (2). In Indonesia, the prevalence of CKD based on the Indonesia Health Survey (SKI) 2023 is approximately twice the global prevalence reported by the Global Burden of Disease (GBD) 2021, indicating a substantial national burden. One of the main treatments used to maintain the health status of CKD patients is hemodialysis (HD), a renal replacement therapy that removes metabolic waste and toxins from the blood through a semi-permeable membrane (3). Controlling CKD prevalence is essential to reduce healthcare costs, decrease mortality, and improve the quality of life and productivity of the population (4).

Anemia is one of the most common complications in CKD patients. In Indonesia, approximately 81% of hemodialysis patients experience anemia (5). In CKD, anemia is primarily caused by erythropoietin deficiency resulting from damage to renal peritubular cells, which leads to reduced red blood cell production in the bone marrow and decreased hemoglobin levels (6). Nutritional deficiencies are also frequently observed in CKD patients due to the hemodialysis process. Adequate intake of protein, iron, folate, and vitamin C plays a crucial role in hemoglobin synthesis and anemia management. Protein is essential for globin synthesis, ferric ion transport, and iron delivery to the bone marrow (7), while protein deficiency may impair globin synthesis and reduce hemoglobin production (8).

In addition, iron is a key component of heme, the non-protein structure of hemoglobin responsible for oxygen binding (9). Erythropoiesis strongly depends on iron availability for hemoglobin synthesis during the final stage of erythropoietin activity (7). Iron supplementation in hemodialysis patients has been shown to improve hemoglobin production efficiency and reduce the need for high doses of erythropoiesis-stimulating agents (ESA) (10). Folate also plays an important role in one-carbon metabolism, supporting purine and thymidylate synthesis required for DNA replication and cell division (11). Folate deficiency may trigger erythroblast apoptosis due to impaired DNA synthesis, thereby reducing erythropoiesis efficiency (12). Another nutrient that enhances iron utilization is vitamin C, which promotes non-heme iron absorption by reducing ferric iron (Fe^{3+}) to ferrous iron (Fe^{2+}), making it more readily absorbed by enterocytes. Vitamin C also facilitates iron mobilization from storage proteins such as ferritin for hemoglobin synthesis (13). Therefore, adequate intake of protein, iron, folate, and vitamin C may contribute to the management of anemia in CKD patients undergoing hemodialysis. Optimal monitoring and management of hemoglobin levels are essential to support treatment outcomes and improve the quality of life of patients with CKD (14). This study aims to analyze the relationship between dietary protein and micronutrient intake such as iron, folate, and vitamin C and hemoglobin levels among patients with CKD undergoing hemodialysis.

2. METHODS

This research is a quantitative study with a cross-sectional design. The research was conducted in the hemodialysis unit of Haji Regional Public Hospital, East Java Province from August to September 2025. The study population included all outpatients with Chronic Kidney Disease undergoing hemodialysis at Haji Regional Public Hospital, East Java Province in 2024, totaling 96 patients (based on preliminary study data). A total sample of 51 patients was selected using purposive sampling technique. The inclusion criteria were patients aged ≥ 18 years who had undergone hemodialysis for ≥ months, received ESA therapy, had not received blood transfusion in the past month ot intravenous iron therapy in the past three months, and willing to sign an informed consent. Exclusion criteria included patients with hematological disorders, serve infections, or those who were pregnant or breastfeeding.

Independent variables included protein, iron, folate, and vitamin C intake, assessed using a semi-quantitative food frequency questionnaire (SQ-FFQ) covering the past month trough interviews. The study also recorded supplement intake. The dependent variable was hemoglobin level, obtained from secondary laboratory data in medical records. Hemoglobin was measured using a hematology analyzer once a month, and the study used the most recent measurement available during the study period (August 2025). A respondent characteristics questionnaire was also used to obtain data on age, sex, education level, occupation, duration of hemodialysis, and number of comorbidities. Post-hemodialysis body weight was measured directly to calculate the patient's protein requirements.

Protein, iron, folate, and vitamin C intakes were compared with each patient's nutritional requirements according to the Pernefri guidelines and expressed as precentages. Intake adequacy was cateforized as inadequate (<80%), adequate (80-120%), or excessive (>120%). According to Pernefri recommendations, the nutritional requirements for hemodialysis patients are 1.2 g/kg BB/day for protein, 15 mg/day for iron, 1000 mcg/day for folate, and 90 mg/day for vitamin C.

Univariate analysis was performed descriptively using a normlity test to determine data distribution and frequency, as well as to select the appropriate test for subsequent bivariate analysis. Pearson correlation was used to examine the relationship between protein intake and hemoglobin levels, while Spearman Rank Correlation was used to analyze the relationship between iron, folate, vitamin C intake and hemoglobin levels. This study was approved by the Research Ethics Committee of Haji Regional Public Hospital East Java Province (Approval Number: 445/155/KOM.ETIK/2025).

3. RESULTS

Table 1. Characteristic of Respondents

Characteristic	Total (n)	Percentage (%)
Usia		
18 – 44 years	18	(35.29)
45 – 59 years	29	(56.56)
≥ 60 years	4	(7.84)
Gender		
Male	30	(58.82)
Female	21	(41.18)
Occupation		
Unemployed	15	(29.41)
Civil servant	3	(5.88)
Private sector employee	7	(13.73)
Self-employed	10	(19.61)
Laborer	3	(5.88)
Homemaker	12	(23.53)
Student	1	(1.96)
Duration of Hemodialysis		
New patient (<12 months)	12	(23.53)
Long-term patient (>12 months)	39	(76.47)
Number of Comorbidities		
No comorbidity	4	(7.84)
One comorbidity	22	(43.14)
Two comorbidities	16	(31.37)
Three comorbidities	8	(15.69)
Four comorbidities	1	(1.96)

Table 1 shows that among the 51 respondents undergoing hemodialysis at Haji Regional Public Hospital of East Java Province, most were aged 45 – 59 years (pre-elderly) (56.86%), male (58.82%), had a senior high school education (41.18%), and were unemployed (29.41%). Most respondents had undergone hemodialysis for >12 months (76.47%) and had one cormobid disease (43.14%). Hypertension (88.24%) and heart disease (17.65%) were the most common comorbidities that may worsen CKD. All respondents received erythropoietin (EPO) therapy because they had hemoglobin levels <10 g/dL.

Table 2. Distribusi of Protein, Iron, Folate, and Vitamin C Intake Categories and Hemoglobin Levels

Variable	Total (n)	Percentage (%)	Result
Protein Intake			
Inadequate	21	(41.18)	64.61 ± 15.15
Adequate	21	(41.18)	
Excessive	9	(17.65)	
Iron Intake			
Inadequate	34	(66.67)	9.73 (5.11 – 139.80)
Adequate	7	(13.73)	
Excessive	10	(19.61)	
Folate Intake			
Inadequate	43	(84.31)	213.22 (41.31- 1553.02)
Adequate	6	(11.76)	
Excessive	2	(3.92)	
Vitamin C Intake			
Inadequate	41	(80.39)	38.34 (2.69 – 162.23)
Adequate	5	(9.8)	
Excessive	5	(9.8)	
Hemoglobin Levels			
Anemia			
Male	30	(58.82)	8.27 ± 0.89
Female	21	(41.18)	

Table 2 shows that most respondents had adequate protein intake (41.18%), although the proportion with inadequate protein intake was also 41.18%. In addition, most respondents had inadequate inron intake (66.67%), inadequate folate intake (84.31%), inadequate vitamin C intake (80.39%). Most respondents with anemia in this study were male (58.82%).

The mean protein intake was 64.61 g/day. The mean dry body image was 61.31 kg. According to Pernefri guidelines, the recommended protein intake for hemodialysis patients is 1-1.2 g/kg BB/day. Based on the mean protein intake and dry body weight, average protein intake obtained 1.05 g/kg BB/day, which meets the Pernefri recommendation (1-1.2 g/kg BB/day). The mean hemoglobin level was 8.27 g/dL. Chronic Kidney Disease patients are considered anemic when hemoglobin levels are <12 g/dL in women and <13 g/dL in men, indicating that the respondents were generally anemic.

Table 3. Correlation Test Results of Protein, Iron, Folate, and Vitamin C Intake with Hemoglobin Levels

Variable	p-value	r
Protein intake (g)	<0.001*	0.45
Iron intake (mg)	0.084	0.24
Folate intake (μg)	0.26	0.16
Vitamin C intake (mg)	0.87	0.24

* significant (p>0.05)

Table 4 shows that protein intake was significantly associated with hemoglobin levels (p<0.001). A moderately positive correlation was observed between protein intake and hemoglobin levels (r=0.45). In contrast, iron, folate, and vitamin C intake were not sigficantly associated with hemoglobin levels (p>0.05). This finding indicates that higher protein intake was associated with higher hemoglobin levels.

4. DISCUSSION

The present study demonstrated a significant positive correlation between protein intake and hemoglobin levels among patients with chronic kidney disease (CKD) undergoing hemodialysis. This finding is consistent with the study by Hendardi et al. (2024), which also reported a significant association between protein intake and hemoglobin levels in hemodialysis patients. In this study, the mean protein intake was 1.05 g/kg body weight/day, which meets the recommendation of the Indonesian Society of Nephrology (Pernefri), and most respondents had adequate protein intake. This condition may be related to nutritional education provided by healthcare professionals in the hemodialysis clinic, as well as the relatively high educational background of the respondents, which may improve patients' understanding and adherence to dietary recommendations (15). The mean intake of animal protein was 36.40 g/day (56.33%), while plant protein intake averaged 28.21 g/day (43.67%). Animal protein provides essential amino acids with high biological value that are required for globin synthesis, a major component of hemoglobin (16). However, among hemodialysis patients, plant-based protein may serve as an alternative source when animal protein consumption needs to be limited due to its phosphorus and saturated fat content (17). Therefore, individualized protein intake management, taking into account uremic burden, metabolic acidosis, hemoglobin levels, phosphorus levels, and comorbidities, may help improve hemoglobin levels without increasing the metabolic burden on the kidneys.

In contrast, this study found no significant associations between the intake of iron, folate, and vitamin C and hemoglobin levels. These findings are consistent with the results reported by Listrianah et al. (2019) but differ from those of Hendardi et al. (2024), who reported significant associations between iron and folate intake and hemoglobin levels in hemodialysis patients. The discrepancy may be attributed to methodological differences, such as the exclusion of patients receiving iron supplementation and the larger sample size in the previous study. In the present study, the median intakes of iron (9.82 mg/day), folate (225.24 μg/day), and vitamin C (38.61 mg/day) were generally below the Pernefri recommendations. The low intake of these micronutrients may be due to dietary restrictions on foods rich in iron, folate, and vitamin C that are also high in potassium, phosphorus, or oxalate, which are commonly restricted in hemodialysis patients. In addition, poor adherence to supplementation may also contribute to the inadequate intake of these micronutrients.

Physiologically, iron is a key component of the heme structure and plays a crucial role in erythropoiesis (9). However, anemia in CKD patients undergoing hemodialysis is multifactorial, involving reduced erythropoietin production, impaired iron metabolism, blood loss during dialysis, and chronic inflammation (18). Chronic inflammatory conditions may increase hepcidin levels, which inhibit intestinal iron absorption and the mobilization of iron stores from body tissues (19). The effectiveness of erythropoiesis-stimulating agents (ESA) depends on adequate iron status. In this study (20), respondents received ESA therapy at a dose of 3000 IU per week, which is below the Pernefri recommendation of 2000–5000 IU twice weekly. Furthermore, oral iron therapy may improve anemia relatively slowly and is often associated with gastrointestinal side effects, which may reduce patient adherence to treatment. Iron absorption can also be influenced by certain dietary components that may either inhibit or enhance its bioavailability (21).

Folate also plays an important role in one-carbon metabolism, which is required for purine and thymidylate synthesis during DNA replication and cell division (11). Folate deficiency may impair DNA synthesis, leading to asynchronous maturation of the nucleus and cytoplasm, cell cycle arrest in the S phase, DNA replication errors, and increased cellular apoptosis, ultimately reducing the effectiveness of erythropoiesis (12). In addition, elevated homocysteine levels in CKD patients may increase the production of reactive oxygen species (ROS), resulting in oxidative stress and reduced erythropoietic efficiency (18). In this context, folate contributes to the reduction of homocysteine levels through the remethylation pathway that converts homocysteine into methionine (22).

Vitamin C also plays an important role in iron metabolism by enhancing the absorption of non-heme iron through the reduction of ferric iron (Fe^{3+}) to the more readily absorbable ferrous form (Fe^{2+}) in the intestine (13). In hemodialysis patients, increased hepcidin production may occur due to chronic inflammation as well as reduced renal clearance of hepcidin (13). Vitamin C may facilitate the mobilization of iron from ferritin stores within reticuloendothelial cells, thereby increasing iron availability for erythropoiesis (23). Moreover, vitamin C has been reported to inhibit hepcidin expression in hepatocyte cells and may improve the downregulation of erythropoietin receptors (24). However, limited iron availability and inadequate vitamin C intake may reduce the effectiveness of these biological mechanisms. In addition, the hemodialysis procedure itself may lead to the loss of water-soluble vitamins, such as folate and vitamin C, through diffusion due to their low molecular weight (25).

5. CONCLUSION

Anemia remains a major health problem among patients with chronic kidney disease (CKD) undergoing hemodialysis in Indonesia. This study found that most hemodialysis patients at RSUD Haji, East Java Province, had inadequate intake of protein, iron, folate, and vitamin C. Such nutritional inadequacies may impair erythropoiesis and contribute to the persistence or worsening of anemia in this population. Therefore, strengthening nutrition education and counseling programs in healthcare facilities is essential to improve the adequacy of protein and micronutrient intake in accordance with the recommendations of the Indonesian Society of Nephrology (Pernefri). Nutritional education should emphasize appropriate food selection while considering patients clinical conditions, including uremic burden, metabolic acidosis, phosphorus levels, and comorbidities, in order to support improvements in hemoglobin levels without increasing the metabolic burden on the kidneys. Patients are also advised to avoid consuming iron absorption inhibitors, such as coffee and tea, simultaneously with main meals or iron supplementation, and to combine dietary sources of iron and folate with vitamin C to enhance iron absorption. Future studies are recommended to develop interventional approaches aimed at increasing protein intake to improve hemoglobin levels in hemodialysis patients. In addition, further research should consider measuring biomarkers of iron metabolism and inflammation, such as serum ferritin, transferrin saturation (TSAT), hepcidin, and C-reactive protein, in order to control for biological confounding factors that may influence the occurrence of anemia in hemodialysis patients.

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