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Anemia and Fatigue in Patients with Chronic Kidney Failure

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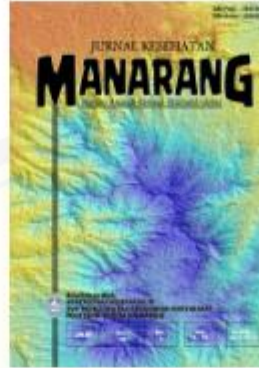
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Abstract

Chronic renal failure results in impaired kidney function, effectively eliminating metabolic waste and regulating fluid and electrolyte balance. The accumulation of waste metabolites is thought to impact the occurrence of anemia and fatigue. However, no research has shown a correlation between the incidence of anemia and fatigue in sufferers of chronic kidney failure. This study aimed to evaluate the relationship between hemoglobin levels and the degree of fatigue experienced by individuals diagnosed with chronic kidney disease. This research uses a cross-sectional study approach. The study population consisted of patients with chronic kidney failure at one of the hospitals in Lumajang Regency who were identified by the indicator of high BUN values. The sample size for this research was 50 people selected through purposive sampling. The data type used is primary data, with the independent variable being the Hb value, while the dependent variable is the level of fatigue in chronic kidney failure patients. The results of the Pearson correlation test in this study showed that there was a significant relationship between the percentage of hemoglobin levels in the blood and the level of fatigue in chronic kidney failure patients (p -value = $<0,000$; $\alpha = 0,05$), with a strength of relationship 0,6092 which means the level Hemoglobin in the blood and the level of fatigue have a perfect degree of correlation. In patients with chronic renal failure and low hemoglobin levels, their fatigue levels will become more severe. Insufficient hemoglobin levels lead to a reduced count of red blood cells, causing a decline in the body's capacity to transport oxygen. This inadequate oxygen supply hampers the oxidation process and energy production in the form of ATP within the body's cells. Consequently, patients with chronic renal failure may undergo a substantial decrease in energy levels and experience significant tiredness.



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ANEMIA AND FATIGUE IN PATIENTS WITH CHRONIC KIDNEY FAILURE

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ABSTRACT

Chronic renal failure results in impaired kidney function, effectively eliminating metabolic waste and regulating fluid and electrolyte balance. The accumulation of waste metabolites is thought to impact the occurrence of anemia and fatigue. However, no research has shown a correlation between the incidence of anemia and fatigue in sufferers of chronic kidney failure. This study aimed to evaluate the relationship between hemoglobin levels and the degree of fatigue experienced by individuals diagnosed with chronic kidney disease. This research uses a cross-sectional study approach. The study population consisted of patients with chronic kidney failure at one of the hospitals in Lumajang Regency who were identified by the indicator of high BUN values. The sample size for this research was 50 people selected through purposive sampling. The data type used is primary data, with the independent variable being the Hb value, while the dependent variable is the level of fatigue in chronic kidney failure patients. The results of the Pearson correlation test in this study showed that there was a significant relationship between the percentage of hemoglobin levels in the blood and the level of fatigue in chronic kidney failure patients ($p\text{-value} = <0,000$; $\alpha = 0.05$), with a strength of relationship 0,6092 which means the level Hemoglobin in the blood and the level of fatigue have a perfect degree of correlation. In patients with chronic renal failure and low hemoglobin levels, their fatigue levels will become more severe. Insufficient hemoglobin levels lead to a reduced count of red blood cells, causing a decline in the body's capacity to transport oxygen. This inadequate oxygen supply hampers the oxidation process and energy production in the form of ATP within the body's cells. Consequently, patients with chronic renal failure may undergo a substantial decrease in energy levels and experience significant tiredness.

ABSTRAK

Gagal ginjal kronis mengakibatkan gangguan fungsi ginjal dalam menghilangkan sisa metabolisme dan mengatur keseimbangan cairan dan elektrolit secara efektif. Penumpukan limbah metabolit diduga berdampak pada terjadinya anemia dan kelelahan. Namun, belum ada penelitian yang menunjukkan adanya korelasi antara kejadian anemia dan kelelahan pada penderita gagal ginjal kronik. Penelitian ini bertujuan untuk mengevaluasi hubungan antara kadar hemoglobin dan derajat kelelahan yang dialami individu yang didiagnosis menderita penyakit ginjal kronis. Penelitian ini menggunakan pendekatan studi cross-sectional. Populasi penelitian terdiri dari pasien gagal ginjal kronik di salah satu rumah sakit di Kabupaten Lumajang yang diidentifikasi dengan indikator nilai BUN yang tinggi. Besar sampel pada penelitian ini adalah 50 orang yang dipilih melalui purposive sampling. Jenis data yang digunakan adalah data primer, dengan variabel bebasnya adalah nilai Hb, sedangkan variabel terikatnya adalah tingkat kelelahan pada pasien gagal ginjal kronik. Hasil uji korelasi pearson pada penelitian ini menunjukkan adanya hubungan yang signifikan antara persentase kadar hemoglobin dalam darah dengan tingkat kelelahan pada pasien gagal ginjal kronik ($p\text{-value} = <0,00$; $\alpha = 0,05$), dengan kekuatan hubungan 0,6092, yang berarti kadar hemoglobin dalam darah dengan tingkat kelelahan mempunyai derajat korelasi yang sempurna. Pada penderita gagal ginjal kronik dan kadar hemoglobin rendah, tingkat kelelahannya akan semakin parah. Kadar hemoglobin yang tidak mencukupi menyebabkan berkurangnya jumlah sel darah merah, sehingga menyebabkan penurunan kapasitas tubuh untuk mengangkut oksigen. Pasokan oksigen yang tidak mencukupi ini menghambat proses oksidasi dan produksi energi dalam bentuk ATP di dalam sel-sel tubuh. Akibatnya, pasien dengan gagal ginjal kronis mungkin mengalami penurunan tingkat energi yang signifikan dan mengalami kelelahan yang signifikan.

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INTRODUCTION

Kidney failure is a condition where the kidneys can no longer maintain the balance of composition and volume of fluids in the body due to damage to the structure of the kidney organs (Garini, 2019). The damage occurs gradually and continuously, resulting in permanent harm to the organ (Garini, 2019 and Arhamawati, Saryono and Awaludin, 2019). Individuals with kidney failure can experience a range of symptoms, including a decrease in hemoglobin levels, which is known as anemia.

Anemia begins to appear when serum creatinine levels reach 2.0 mg/dL in patients with Chronic Kidney Disease (CKD). However, more pronounced symptoms occur when the Glomerular Filtration Rate (GFR) decreases to 20–35 ml/min (Rosnety et al., 2018). In general, anemia is caused by a deficiency of erythropoietin, leading to a decrease in the production of red blood cells (Hapzah dan Putri, 2018). Erythropoietin serves as a hematopoietic growth factor that stimulates the production of red blood cells. When erythropoietin levels decrease, hemoglobin levels also drop, resulting in symptoms like weakness, fatigue, pallor, and changes in heart rate due to a reduced supply of oxygen (Arhamawati et al., 2019; Faridz et al., 2021). Anemia worsens as kidney function declines (Rosnety dkk., 2018). Additionally, anemia raises the risk of disease and death, reduces the quality of life, and expedites the progression to the end stage of kidney failure (Senduk, Palar and Rotty, 2016).

The measurement of urea and creatinine levels in the serum can be utilized to diagnose kidney failure. Creatinine results from the breakdown of creatine, a nitrogen-containing compound found in muscles. Muscle mass estimation can be derived from the amount of creatinine that has been generated and excreted (Heriansyah, Humaedi dan Widada, 2019).

According to the CDC (2021) More than 1 in 7 adults in the United States, approximately 15% of the adult population, are estimated to be affected by kidney failure, which equates to about 37 million people. Kidney failure is more prevalent among individuals aged 65 years and older, with approximately 38% of those affected falling within that age group. Additionally the CDC (2021), It is noted that women have a higher risk of kidney failure compared to men, with a ratio of about 14% for women and 12% for men. In Indonesia, the prevalence of kidney failure in 2018 was 3.8%. There has been a 2.0% increase in the incidence of kidney failure since 2013. The provinces of North Kalimantan and North Maluku have the highest percentages at 6.4% and 5.6%, respectively. In the East Java Province, the prevalence of kidney failure is 2.9% (Riskesdas, 2018).

Fatigue is a common complication experienced by kidney failure patients undergoing hemodialysis therapy. Persistent physical fatigue, resulting from hemoglobin deficiency, can disrupt daily activities and diminish productivity. At least half of the patients report enduring fatigue, and about 86% of them experience fatigue after dialysis (Jesmi et al., 2022; Kurnianto et al., 2022). Between 78% and 83.8% of individuals ranked fatigue as a significant issue in hemodialysis patients. In general, the prevalence of fatigue in chronic kidney disease patients undergoing hemodialysis therapy is very high, ranging from 44.7% to 97%, spanning from mild to severe (Prastiwi et al., 2022).

Fatigue is an uncomfortable sensation characterized by weakness and decreased energy. Patients dealing with chronic kidney failure often encounter a buildup of metabolic waste, which can contribute to fatigue, along with irregular energy expenditure (Supriyadi et al., 2021). In patients undergoing hemodialysis, fatigue is linked to the primary cause of death from heart issues and the occurrence of cardiovascular disease (Gregg et al., 2019). As a consequence of the fatigue that occurs, it not only impacts daily activities but also hinders the psychological well-being of the patients (Arhamawati et al., 2019). Psychological factors such as anxiety, depression, panic attacks, or psychotic symptoms also contribute to fatigue (Rizkia et al., 2022). Understanding the factors associated with fatigue is important for nurses in optimizing interventions and improving patients'

quality of life (Prastiwi et al., 2022). The psychological quality of life of patients includes the problems face and the way they deal with these problems (Widianto et al., 2020; Maisyaroh et al., 2021). Knowing the relationship between anemia and the level of fatigue in chronic kidney failure patients can help nurses organize activity schedules that suit the patient's physical condition.

METODE

Types of Research

The research conducted is a quantitative study using a cross-sectional approach, and has received approval from the research ethics committee of the Faculty of Nursing, The University of Jember with Number 158 / UN25.1.14 / KEPK / 2021.

Location and Time of Research

The study was conducted on patients at Lumajang District Hospital in February 2022.

Population and Sample

The population in this study were all patients who experienced chronic kidney failure with BUN examination results > 50 mg/dL and serum creatinine > 1.5 mg/dL at one of the regional hospitals in Lumajang district, with a total of 63 patients. The sample involved in this study was 50 patients whom the researchers selected using a purposive sampling technique through the inclusion criteria determined by the researchers, including:

1. patients experiencing pale conjunctiva,
2. have hemoglobin levels < 12 grams/dL for women and < 13.5 grams/dL for men,
3. have never been involved in similar research,
4. willing to become a research respondent by signing informed consent.

The exclusion criteria that researchers set include:

1. The patient is unconscious
2. Patients who are required to have bed rest
3. The patient refuses to participate in the study

Data Collection

At this stage, researchers measured data on hemoglobin levels to identify the incidence of anemia in respondents. Researchers at the Surabaya Health Laboratory Center, Ministry of Health of the Republic of Indonesia, measured hemoglobin levels using venous blood samples. Apart from that, researchers also measured the respondents' level of fatigue using the Fatigue Assessment Scale (FAS) instrument, which has been tested for reliability and validation internationally. FAS was developed by Michielsen et al. (2003), who analyzed the scale's psychometric properties and found an internal consistency of 0.90, thus ensuring the validity and reliability of the FAS (Michielsen et al., 2003).

Data Processing and Analysis

The data obtained was collected and analyzed using software, namely STATA version 17, the researcher carried out an inferential test using the Pearson correlation test to assess the relationship between the variables studied. The results of the Pearson correlation test show a relationship if the p-value is <0.05.

RESEARCH RESULTS

Table 1. Respondents of CKD Patients in Lumajang

Variables	Summary
n (%)	50 (100.0)
Sex of Respondent, n (%)	
Female	29 (58.0)
Male	21 (42.0)
Age Group of Respondent, n (%)	
<30	3 (6.0)
31-60	28 (56.0)
>=61	19 (38.0)
Hb level of Respondent, n (%)	
8-10.9 (Moderate anemia)	28 (56.0)
<7.9 (Severe Anemia)	22 (44.0)

Table 1. Illustrates the distribution of the female respondents' population with chronic kidney failure treated at Lumajang Hospital, which is greater than the male respondents. Specifically, the proportion of women is 58%. The average ages of those involved in the study were as follows 31- 60 years old (56%), and respondent had moderate anemia in 56% of participants. This increase in age can lead to various age-related deteriorations in the body's organs (Maisyaroh *et al.* , 2021).

Anemia has several causes, one of which is a reduction in erythrocyte production due to the lack of erythropoietin, a hormone normally produced by the kidneys. Additionally, anemia can also result from a shorter lifespan of erythrocytes in patients with chronic kidney failure, which is about half of that of normal red blood cells, approximately 120 days. This condition can become more severe due to a low intake of nutrients such as folic acid, vitamin B12, and iron, and may be associated with hindrances in iron absorption (ferros). Anemia leads to symptoms like weakness, pallor, fatigue, and changes in heart rate and performance, stemming from the reduced ability of the body to distribute oxygen from the lungs to all parts of the body (Guyton and Hall, 2012).

According to Nurko *et al.* in 2007, and as stated in the study conducted by Arhamawati *et al.* in 2019, chronic kidney failure patients frequently experience anemia. The study examined the correlation between anemia and chronic kidney failure. A decline in kidney function can lead to an increased incidence of anemia in patients. In individuals with stage 3 renal failure, the prevalence of anemia is approximately 5.2%. However, this figure rises to 44.1% in stage 4, and in stage 5, nearly all patients develop anemia. These findings align with the results of the National Health and Nutrition Examination Survey (NHANES) from a study by Radityamurti and Rodjani in 2013, which indicated that elevated urea and creatinine levels can reduce erythropoietin production, resulting in decreased red blood cell production and, consequently, decreased hemoglobin levels, as well as reduced oxygen supply to cells (Ma'shumah, Bintanah, and Handarsari, 2014). Chronic anemia, characterized by low levels of hemoglobin and hematocrit, is one of the factors that accelerate the progression of End-Stage Renal Disease (ESRD) in CKD patients. This is associated with increased creatinine levels and decreased glomerular filtration rate (GFR) in patients with or without diabetes (Pranawa 2015).

Table 2. Associate sex, age and Hemoglobin Levels with Fatigue Level

Variable	Total	Fatigue level of responden			P-value
		Normal/non fatigua	mild-to-moderate fatigua	severe fatigua	
B					
n (%)	50 (100.0)	7 (14.0)	25 (50.0)	18 (36.0)	
Sex of Respondent, n (%)					
Female	29 (58.0)	6 (85.7)	14 (56.0)	9 (50.0)	
Male	21 (42.0)	1 (14.3)	11 (44.0)	9 (50.0)	0.26
Age Group of Respondent, n (%)					
<30	3 (6.0)	0 (0.0)	0 (0.0)	3 (16.7)	
31-60	28 (56.0)	1 (14.3)	21 (84.0)	6 (33.3)	
>=61	19 (38.0)	6 (85.7)	4 (16.0)	9 (50.0)	<0.00
Hb level of Respondent, n (%)					
8-10.9 (moderate Anemia)	28 (56.0)	7 (100.0)	18 (72.0)	3 (16.7)	
<7.9 (severe Anemia)	22 (44.0)	0 (0.0)	7 (28.0)	15 (83.3)	<0.00

Table 2 explains that fatigue in CKD patients is influenced by the age and hemoglobin levels of patients, the older the age of the respondents and the lower the hemoglobin levels cause CKD patients to experience increasingly severe fatigue. Gender did not affect fatigue in CKD patients

Table 3. Correlation between Hemoglobin Levels with Fatigue Level

	Level of fatigue	level of anemia
Level of fatigue	1.0000	
level of anemia	0.6092	1.0000

Based on table 3 the strength of the relationship between hemoglobin levels and Fatigue Level is determined by the Pearson Correlation value of 0,6092, signifying that hemoglobin levels and fatigue levels exhibit a strong correlation. The correlation value above shows that the more severe the level of anemia patients with CKD then the level of fatigue is even severe.

DISCUSSION

The primary cause of fatigue in patients experiencing CRF is a decrease in Hb levels in the body. Low hemoglobin levels affect various physiological and metabolic aspects, creating an environment that does not support optimal health. One of the primary effects of low hemoglobin levels is a reduced capacity of erythrocytes to distribute oxygen throughout the body. Oxygen is an essential fuel for the human body, necessary for metabolic processes and energy production. The nerves required by body cells are generated through reactions between oxygen and glucose, resulting in ATP, or Adenosine Triphosphate (Gluba-brz et al., 2020). Conditions characterized by a lack of oxygen due to low hemoglobin levels diminish the body's energy reserves, leading to fatigue and overall weakness. Individuals with chronic renal failure are susceptible to fatigue, body aches, reduced activity levels, sleep disturbances, and difficulty concentrating. All of these symptoms result from decreased oxygen supply that impairs the functioning of body cells (Supriyadi et al., 2021).

The kidneys play a significant role in maintaining the body's balance, particularly in the production of the hormone erythropoietin. Erythropoietin is a crucial hematopoietic growth factor involved in converting erythrocyte pronormoblasts into normoblasts, which then develop into reticulocytes and eventually erythrocytes (Putra and Rahman, 2022). High levels of erythropoietin promote the production of reticulocytes, subsequently favoring the premature release of reticulocytes from the bone marrow (Mutiawati, 2018). Nevertheless, it's important to note that patients with hemoglobin levels within the normal range can still be affected by high levels of urea in the blood. Specifically, when kidney function is impaired and unable to eliminate urea through urine, this can lead to uremic toxicity with associated side effects (Rahayu et al., 2019). It has been demonstrated that uremic toxicity can inhibit the function of erythropoietin or reduce the bone marrow's response to erythropoietin in the production of red blood cells (Guyton and Hall, 2012).

Anemia occurring in patients with chronic renal failure is a distinctive type of hypoproliferative normocytic anemia resulting from kidney damage. The kidneys play a crucial role in producing the hormone erythropoietin, which aids in the maturation of red blood cells in the bone marrow (Van Haalen et al., 2020; Supriyadi et al., 2021). In the context of chronic kidney damage, a reduction in EPO levels occurs because impaired kidney circulation affects the delivery of oxygen to the kidneys. EPO deficiency hampers erythropoiesis, leading to a decrease in the number of progenitor cells necessary for the formation of erythrocytes. This situation disrupts the processes of proliferation, differentiation, and hemoglobin formation (Putra and Rahman, 2022). Erythropoietin deficiency results in the bone marrow failing to release mature erythrocytes into the bloodstream, disrupting erythropoiesis, which is the maturation process of red blood cells in the bone marrow (Van Haalen et al., 2020; Supriyadi et al., 2021). The ultimate consequence of this disorder is that a reduction in hemoglobin levels in the peripheral blood circulation serves as a significant catalyst for the clinical symptoms of anemia. Furthermore, anemia that arises in the context of kidney failure can also induce hypoxia in kidney tissue, subsequently leading to a decline in kidney function or even kidney failure, which can adversely affect erythropoietin production (Supriyadi et al., 2021). Other factors that can precipitate anemia in CKD patients include reduced red blood cell lifespan, inflammation, and infection, hypothyroidism, severe hyperparathyroidism, excessive aluminum exposure, hemoglobin disorders, with the most common being iron and folate deficiencies (Yuniarti, 2021).

Understanding the connection between kidney failure, hemoglobin levels, and the overall health of patients is crucial (Maisyaroh dkk., 2023; Widiyanto dkk., 2023). Appropriate treatment can assist in managing fatigue symptoms and maintaining the well-being of patients (Widiyanto et al., 2022). Therapeutic efforts focused on raising hemoglobin levels and promoting erythropoietin production can be a crucial step in managing chronic renal failure (Maisyaroh et al., 2022; Kurnianto et al., 2023).

CONCLUSION AND ADVICE

This study revealed a significant correlation between Hb levels and fatigue in patients with chronic kidney failure. Patients in this condition experience permanent kidney dysfunction, disrupting the balance of fluids, electrolytes, and metabolism in the body, which leads to fatigue. The cross-sectional design of this study involved 50 respondents selected through the purposive sampling method at Lumajang Regency Hospital. Hemoglobin levels were measured using the cyanmethemoglobin method, and fatigue levels were assessed using the Fatigue Assessment Scale (FAS) questionnaire. The results of the Pearson correlation test analysis demonstrated a significant relationship between hemoglobin levels and fatigue levels in patients with chronic renal failure ($p = 0.001$), showing a strong correlation with a negative direction. These findings underscore the importance of monitoring and managing hemoglobin levels in individuals with chronic kidney failure since low hemoglobin levels contribute to higher levels of fatigue. Taking measures to maintain hemoglobin levels within an appropriate range may help reduce the fatigue experienced by patients with this condition.

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