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Original Article

Multivariate Analysis of Factors Associated with Hemoglobin Levels among CKD Patients undergoing Hemodialysis

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ABSTRACT

Chronic Kidney Disease (CKD) is one of the silent killer diseases that often experience an increase in incidence every year. Common problem that often arises in someone with CKD is a decrease in hemoglobin levels. This study aims to identify and analyze factors related to hemoglobin levels among CKD patients undergoing hemodialysis. This was a correlational study with cross sectional approach. The study was conducted on March 21 – 31, 2022. The study population consisted of 90 CKD patients undergoing hemodialysis at Doctor Soedarso Regional General Hospital (as of January 2022). The samples involved 73 people who were selected using purposive sampling technique. The independent variables included age, gender, ethnicity, education, employment status, smoking history, creatinine and urea levels, while the dependent variable in this study was hemoglobin levels. Bivariate analysis in this study applied chi-square, Kendall's, and independent sample t tests, while the multivariate test applied logistic regression. The analysis results obtained p values for age, employment status, smoking history, creatinine levels, and urea levels of 0.069 (OR=8.4), 0.418 (OR=2.4), 0.286 (OR=4.3), 0.000, and 0.323, respectively. It can be concluded that there was an effect of creatinine levels on changes in hemoglobin levels among CKD patients undergoing hemodialysis. Patients undergoing hemodialysis are recommended to control the amount and source of protein intake, adjust physical activity according to age and ability, and pay attention to the regular dialysis schedule.

Keywords : Risk Factors, Hemoglobin, Kidney Failure, Hemodialysis.

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INTRODUCTION

The Global Burden of Disease (2017) explained that there were 9.1% or 697.5 million people who had CKD, even this study showed that the prevalence of women who had CKD was 9.5%, higher than men that was only 7,3 %. It is estimated that people with CKD in the world come from the People's Republic of China which ranked the first country with the number of cases of 132.3 million[1]. Such findings are even in line with the condition in Indonesia's neighboring country (Malaysia) which showed an increase in the number CKD cases in 2018 (15.48%) at the age of over 18 year[2]. This secondary clinical syndrome disease is one of the contributors to increased mortality as a silent killer due to persistent and irreversible changes in structure and function[3,4]. This disease is often found with a specific sign of an increase in blood urea levels[5].

Decreased hemoglobin is often found in patients with CKD with hemoglobin level of <13 g/dL for men and <12 g/dL for non-pregnant women[6]. Anemia complications are frequently found in ESRD status or earlier in grades 4 and 5 chronic kidney disease[7]. The result of previous case control study showed that there were more cases of anemia found in cases of death in patients with CKD[8]. Increased mortality in CKD patients was also found in other studies with marked increase in diastolic

volume and anemia[9]. Another impact also found was a decrease in lofe quality among patients with anemia[10].

There were limited studies regarding analysis of influential factors of hemoglobin changes among chronic kidney failure patients undergoing hemodialysis. A study conducted by Ani & Asni (2016) and Siti (2018) described factors that influenced anemia among patients with kidney failure including period of HD, age, gender, frequency of HD, nutritional status as well as economic status[11,12].

Results of a preliminary study towards 2019-2021 data at DR. Soedarso Regional General Hospital showed that 61% of patients who had a primary diagnosis of stage 5 chronic kidney failure (N18.5) had a secondary diagnosis of anemia. Through some of the facts that have been described, the researchers are interested to analyze the correlation between demographic characteristics and plasma creatinine and urea levels with hemoglobin levels among CKD patients undergoing hemodialysis.

METHOD

This was a correlational study with cross sectional approach. The study population consisted of 90 CKD patients undergoing hemodialysis at Doctor Soedarso Regional General Hospital (as of January 2022). The sample calculation applied the Lameshow formula which obtained 73 respondents who were selected using purposive sampling technique that was quota sampling. The inclusion criteria for this study were CKD patients undergoing hemodialysis, were able to communicate and had complete medical records. Exclusion criteria in this study included having a history of Systemic Lupus Erythematosis (SLE) and psychiatric disorder. The independent variables included age, gender, ethnicity, education, employment status, smoking history, creatinine and urea levels, while the dependent variable in this study was hemoglobin levels. Hemoglobin levels in this study were grouped based on empirical cut-off point. Kuzma (1984) explains that the cut-off point with the mean can be used for normally distributed data, while the cut-off point with the median is used for data that were not normally distributed [13].

This study used a list of questions that contained demographic data and laboratory results derived from the medical records of respondents. This study was approved by the Health Research Ethics Committee Board of DR. Soedarso Regional General Hospital through Ethics Approval Registration Number No. 28/RSUD/KEPK/II/2022 which was stipulated on February 26, 2022. Data collection was carried out on March 21 – 31, 2022.

The analysis technique in this study was divided into 2 types of data on the dependent variables. Categorical independent variable, namely demographic data were tested using Chi-Square test. On the other hand, Kendall's test was applied on categorical variables that had more than 2 degrees. If the expected count value was not met, then the Fisher test was applied. Numerical independent variables such as creatinine and urea levels were tested using the independent sample t test. If the data were not normally distributed, Mann Whitney was applied as an alternative test. Multivariate analysis in this study applied a binary logistic regression test by including all independent variables that had a bivariate p value of <0.250.

RESULTS

The results of this study were taken through direct interviews related to demographic data and direct observation of medical record data related to laboratory examination results. The calculation results (See Table 2) revealed that the characteristics of respondents with hemoglobin (Hb) levels of <8.48 g/dL were found among respondents aged ≥55 years (57%), male respondents (55%), Malay respondents (33%), had higher education (43%), and had no smoking history (71%). The group with Hb levels of <8.48 g/dL had a mean creatinine and urea levels of 8.73 and 178.29, respectively. Such mean levels were higher than the creatinine and urea values in the group with Hb levels of >8.48 g/dL.

The results of the Kolmogrov-Smirnov test obtained p values for the numerical data in this study included creatinine levels (0.200), urea levels (0.200) and haemoglobin levels (0.098), which indicated that the data were normally distributed.

Table 1. Laboratory Results of Respondents

Result	Mean	SD
Creatinine	6.44	3.855
Urea	149.0	65.141
Hemoglobin	8.48	1.593

Source: Secondary data, 2022

Table 1 showed that the mean creatinine, urea and hemoglobin levels of CKD patients undergoing hemodialysis were 6.44 mg/dL, 149 mg/dL and 8.48 g/dL, respectively. Such findings also indicated that the hemoglobin levels of 8.48 as the mean could be used as a reference for the cut-off value.

Table 2. Bivariate Test Results for Demographic Characteristics with Hemoglobin Levels.

Variable	Hemoglobin Levels			p-Value	Unadjusted OR	Statistical Test
	< 8.48 g/dL (n=42)	≥ 8.48 g/dL (n=51)				
	n (%)	n (%)	N (%)			
Age				0.187	0.474	Chi-square
< 55 years	18 (49%)	19 (51%)	37 (100)			
≥ 55 years	24 (67%)	12 (33%)	36 (100)			
Gender				0.977	1.135	Chi-square
Man	23 (59%)	16 (41%)	39 (100)			
Woman	19 (56%)	15 (44%)	34 (100)			
Ethnicity				0.558		Kendall's
Malay	14 (50%)	14 (50%)	28 (100)			
Dayak	9 (75%)	3 (25%)	12 (100)			
Tionghoa	6 (60%)	4 (40%)	10 (100)			
Javanese	8 (50%)	8 (50%)	16 (100)			
Other	5 (71%)	2 (29%)	7 (100)			
Education				0.990		Kendall's
Elementary School	9 (60%)	6 (40%)	15 (100)			
JHS-SHS	15 (58%)	11 (42%)	26 (100)			
Higher Education	18 (56%)	14 (44%)	32 (100)			
Employment Status				0.038*	3.089	Chi-square
Unemployed	29 (69%)	13 (31%)	42 (100)			
Employed	13 (42%)	18 (58%)	31 (100)			
Smoking History				0.214	0.481	Chi-square
No	30 (54%)	26 (46%)	56 (100)			
Yes	12 (70%)	5 (30%)	17 (100)			

*p-value of < 0.05

Table 2 presents the results of the bivariate test with the chi square test, as well as Kendall's Test for Demographic characteristics and Hemoglobin Levels.

Table 3. Correlation between Creatinine and Urea Levels with Hemoglobin Levels.

	Hemoglobin	n (%)	Mean ± SD	p-Value	Statistical Test
Creatinine	≥ 8.48 g/dL	31 (42%)	3.33 ± 1.77	0.000*	Independent sample t Test
	< 8.48 g/dL	42 (58%)	8.73 ± 3.34		
Urea	≥ 8.48 g/dL	31 (42%)	109.34 ± 39.09	0.000*	
	< 8.48 g/dL	42 (58%)	178.29 ± 65.30		

Table 3 revealed that there was a correlation between employment status, creatinine and urea levels on hemoglobin levels among CKD patients undergoing hemodialysis.

Table 4. Multivariate Test Results.

Predictor	Sig.	B	Adjusted OR	95% CI
Constant	0.001	3.894		
Age (x1)				
< 55 Years	0.069	-2.128	8.4	0.8 – 83.3
≥ 55 Years (Ref)				
Employment Status (x2)				
Unemployed (Ref)	0.418	0.850	2.4	0.3 – 18.3
Employed				
Smoking History (x3)				
Yes	0.286	1.454	4.3	0.3 – 61.8
No (Ref)				
Creatinine (mg/dL) (x4)	0.000	-1.116		
Urea (mg/dL) (x5)	0.323	-0.009		

Table 4 revealed that age and smoking history had p-values of <0.250, so that these two variables could be candidates in logistic regression modelling. The final accumulation confirmed that there were 5 predictors to be applied in follow-up test.

Table 5. Logistic Regression Basic Test Results.

Test	Sig.
Hosmer & Lameshow test	0.377
Omnibus test of model	0.000

The results of the modelling obtained the Hosmer & Lameshow test scores of >0.05. Thus, it can be concluded that the model involving 5 predictors of the dependent variable met the fitness criteria (fit) for regression modelling. The omnimbus test obtained a sig value of < 0.05 which indicated that the addition of predictors would affect the dependent variable.

Table 6. Model Summary Results.

-2 LR	Cox & Snell R	Nagelkerke R Square
33.813	0.594	0.798

The model summary results showed a Nagelkerke R square value of 0.798 which indicated that the model involving age, employment status, smoking history, creatinine and urea levels had an impact of 79.8%, while 23.3% could be due to other factors that had not been studied.

DISCUSSION

In general, anemia occurs due to decreased EPO and impaired iron metabolism associated with increased hepcidin, circulating urea in the blood can also induce EPO inhibitors which are thought to also play a role in CKD cases[39]. Several triggers for biomarker instability in the elderly (>55 years) can be affected by decreased body function. This phenomenon can be found in cases of decreased hemoglobin in old age which can occur with a 25-hydroxyvitamin D deficiency mechanism which results in erythropoietin resistance in the hematopoietic stem cell pathway[14]. Psychological problem can also be another indirect cause of changes in hemoglobin levels in the elderly, for example the presence of additional stressors resulting in depression[15]. Previous studies have demonstrated poor sleep quality and insomnia in nearly half the population with advanced CKD[16]. This is indirectly related to the increase in cases of anemia due to disturbed sleep duration[17]. The results of this study indicated a difference in finding from previous study which showed that the prevalence of CKD among women was 9.5%, higher than men, that was only 7.3%[3].

Such difference could be due to differences in study site and data collection period. The results of previous study showed higher hemoglobin levels among postmenopausal men and women compared to premenopausal women[18]. Basically, there is similar physiological basis mechanism of anemia for both men and women, including in CKD cases. In fact, hemoglobin level of healthy women will be lower than that of men, and this phenomenon also occurs in populations with CKD[19]. Previous study identified that women started dialysis when their estimated kidney function was lower than men, and the mean age of women undergoing hemodialysis was older than men [20]. According to dialysis guidelines, the targeted Hb level of men and women is the same, namely 10 g/dL. Other study also showed that gender affected response to anemia, CKD and mineral disorders [21].

The result of this study indicated that there was no correlation between ethnicity and hemoglobin levels among CKD patients undergoing hemodialysis. Such finding is in line with previous study which found there was no significant difference in hemoglobin concentration among third trimester pregnant women between the Batak and Javanese ethnic groups[22]. Other previous study also showed a difference in hemoglobin levels related to Caucasoid, Hispanic, Asian, Oriental and African Races[23]. Such difference can be due to ethnicities recorded were still of the same race, namely Asian Race. Besides that, several respondents in this study were children born from mixed ethnicity. Other study further explained ethnicity which was generally classified based on a phenotype called race, e.g. Asian, Hispanic, Black, and White (Caucasoid) Races[24].

A person's level of education has not been able to describe a knowledge possessed and the use of such knowledge to improve the quality of life. This is in line with previous study which found that there was no correlation between education level and IDU's knowledge on HIV[25]. The right action of a nurse to ensure is by directly examining how basic knowledge is related to diseases and other conditions that are often encountered, one of which is anemia, as well as the level of knowledge of the patient's coping mechanisms. Providing self-management information is an effort to improve individual quality. Orem's theory explains that each individual has the ability to take care of himself. The nurse's main role is to identify individual abilities in carrying out such self-management. Knowledge considered important to be delivered are regarding activity modification and food patterns[26].

It is interesting to note that there was a correlation between employment status of CKD patients undergoing hemodialysis and their hemoglobin levels (p value=0.038), although this was a basic correlation value which required path analysis that showed how employment status can affect hemoglobin levels. The results of the researchers' assumptions indicated that employment status could affect hemoglobin levels indirectly through several mechanisms such as the income earned, coping mechanisms with the process of working as a daily activity, or socialization resulting from an occupation on patient psychology. Such opinion is supported by previous study which showed that there was a correlation between socioeconomic status and the incidence of anemia[27]. The result of other assumption was stated in a previous study regarding the correlation between physical activity and haemoglobin levels among workers with non-dialysis dependent CKD status. The study assessed the haemoglobin levels of CKD patients with Hb levels of >12 g/dL who had a high activity ratio, lower CKD progression and better survival[28]. Employment status contributes to quality improvement, either through nutritional intake, as well as mental health due to socialization during work. According to Camilia, et al (2015), individuals with CKD with an income of 5.1 times the Regional minimum wage had a better quality of life in terms of physical, pain, social, mental health aspects than unemployed individuals or those whose income was below the Regional minimum wage[29]. Current study further explained how poverty and the burden of disease had an impact on all aspects. Few resources for individuals with co-morbidities will result in "catastrophic spending" or costs beyond food needs exceeding 40%. This will further deplete remaining resources and even change the structure of the whole family which eventually affects medical treatment[30].

The result of the regression modelling test showed that patients with chronic kidney failure wit history no history of smoking had the potential to have a hemoglobin level of ≥8.48 g/dL 4 times, although there was no significant correlation in the regression test between the

two variables. Such finding is in line with a study conducted by Devina, et al. (2017), which found that there was no significant correlation between smoking status and hemoglobin levels. Conversely, the result of this study is not in accordance with previous study which showed that smoking women had higher hemoglobin levels compared to non-smoking women[31]. Another study also showed an increase in the Hb levels of smokers and non-smokers which even caused polycythemia[32]. The result of another study showed that the Kaplan-Meier test obtained a finding that smoking behavior among CKD patients reduced survival rates compared to non-smokers. The impact of smoking WAs more sensitive in someone with renal dysfunction due to the progress of immunoglobulin from IgA which causeD nephrotic. Further analysis also showed that there was a correlation between smoking and interstitial atrophy or fibrolysis due to oxidative stress from cigarette content[33].

The result of this study indicated that there was a negative correlation between creatinine levels and haemoglobin levels. Such finding is in line with the finding of a case control study conducted by Ismatul, et al (2012) which showed that renal failure patients who died had high creatinine levels and low hemoglobin levels compared to living renal failure patients[34]. In addition, previous study also showed that there was a negative effect of creatinine levels on haemoglobin levels. Increased plasma creatinine levels indicated the process of hemodialysis to remove certain toxic substances[35]. Increased creatinine levels may indicate that the process of renal damage. Kidneys are the main producer of EPO which can decrease along with the degree of insufficiency of kidney function. Plasma EPO levels can be missed (detection), but elevated EPO levels can also be found due to the presence of reactive excrements of EPO which are biologically inactive[35].

The mean urea level among patients undergoing hemodialysis at Dr. Soedarso Regional General Hospital was 149 mg/dL. The result of this study indicated that there was a negative correlation between the urea (BUN) levels and hemoglobin levels among patients undergoing hemodialysis. Such finding is in line with a study conducted by Makiko, et al (2019) which showed that there was a decrease in hemoglobin levels along with an increase in BUN levels[36]. Furthermore, another study showed that increased protein consumption also had an impact on an increase in urea levels among patients with chronic kidney disease[37]. Urea concentration was closely related to chronic kidney failure among patients who reported an increase in reactive oxygen species (ROS) and oxidative stress in adipocytes, pancreatic beta cells which can reduce insulin sensitivity and aortic endothelium[36]. Consuming plant-based protein has the disadvantage of increasing potassium levels. However, other advantages are lowering blood pressure, increasing prevention of diabetes, delaying CKD progression and death[38]. Certain theory suggests that high circulating BUN levels may increase protein carbamylation and generate reactive oxygen species (ROS), increase oxidative stress, inflammation, endothelial dysfunction, and cardiovascular disease[40]. High consumption of protein can also have an impact on metabolic disorders which further become metabolic complications.

While there is currently no full elucidation of the underlying mechanism by which high protein intake may affect kidney function, especially in the context of CKD, the available data suggest that glomerular hyperfiltration induced by a high protein diet may lead to increased albuminuria or decreased GFR. Additionally, increasing evidence suggests that high-protein diets may be associated with a number of metabolic complications that can impair kidney health. Given the increasing popularity of high-protein diets and the high prevalence of CKD within the United States population, many individuals may be unaware of their CKD status[40].

The final step in the nursing process is assessing and evaluating the effectiveness of an intervention in chronic disease[41]. This action aims to observe comorbidities that have the potential to arise and can worsen the patient's condition[42]. Some nursing problems that can result from changes in hemoglobin among patients with CKD are the risk of gastrointestinal perfusion, myocardial perfusion, or ineffective renal function[43]. An important role of a nurse to decrease morbidity and mortality rates is definitely required, both for among patients with acute and chronic conditions. Nurses are responsible for nursing care and are present during treatment. Nurses are also required to observe and further assess the general condition of the patient by integrating multidisciplinary aspects such as the

physical, emotional or social condition of the patient[44].

CONCLUSION

The results of this study indicated significant correlations between employment status, creatinine and urea levels on the mean hemoglobin levels among CKD patients undergoing hemodialysis at RSUD DR. Soedarso, while there were no significant correlations between age, gender, ethnicity, education and smoking history on haemoglobin levels. In general, the regression test revealed age was the dominant predictor of changes in hemoglobin levels among CKD patients undergoing hemodialysis.

Some of the recommended activities to be implemented by CKD patients include controlling the amount and source of protein intake, adjusting physical activity according to age and ability, paying attention to the regular dialysis schedule.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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