

Factors Related to the Occurrence of Anemia in Pre-Dialysis Chronic Kidney Disease Patients at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital, 2020-2022

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DOI: <https://doi.org/10.52403/ijrr.20231283>

ABSTRACT

Background: Patients with chronic kidney disease (CKD) are most commonly found to develop complications such as anemia. This complication is caused by deficiencies of erythropoietin, iron, folic acid, and vitamin B12. The prevalence of anemia is associated with patient's glomerular filtration rate (GFR), age, gender, and erythrocyte index.

Aims: The aim of this study is to report prevalence of anemia in CKD pre-dialysis patients and factors related to the incidence of anemia in CKD pre-dialysis patients at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital in 2020-2022.

Methods: This research is descriptive analytical with a cross-sectional approach by using medical record data of pre-dialysis CKD patients from the Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital which obtained a sample of 712 patients.

Results: It was found that cases of anemia in pre-dialysis CKD patients were mostly found in women (75%), age group ≥ 65 years (73.6%), and stage IV (88.2%) and V (94.1%). Pre-dialysis CKD patients stage $\geq III$ (stage III-V) were 1.6 times more likely to develop anemia compared to patients with stages I and II (OR 1.641, 95% CI: 1.175-2.293; $p=0.004$), as well as female gender 1,6 times more likely to suffer from anemia compared to male patients (OR 1.610, 95% CI: 1.138-2.277; $p=0.007$).

Conclusion: The overview of anemia cases in CKD pre-dialysis patients were dominated by men, age group ≥ 65 years, and stage V. Prevalence of anemia increases when the patient is stage $\geq III$ (stage III-V) and female.

Keywords: Chronic Kidney Disease, anemia, pre-dialysis, age, gender, stage

INTRODUCTION

An estimated 10% of adults worldwide suffer from chronic kidney disease (CKD), which causes 1.2 million deaths annually^(1,2). Erythropoietin deficiency, along with iron, folic acid, and vitamin B12 deficiencies, is the most prevalent cause of anemia, a common complication in people with CKD⁽³⁾. In addition, the group of patients with complications of anemia has a risk of increased mortality and morbidity⁽⁴⁾. Based on previous studies, of 933,463 CKD patients, 20.6% developed anemia and this was associated with a higher risk of hospitalization due to cardiovascular disease⁽⁵⁾. Anemia has a poor prognosis, several conditions can occur including cognitive impairment, angina, and cardiorenal anemia syndrome, and worsen the condition of CKD patients. Anemia in CKD patients causes a significant increase in health care costs. Early diagnosis and monitoring of anemia is needed in CKD

patients. Ensuring patients have optimal hemoglobin and hematocrit values before starting dialysis can reduce mortality⁽⁶⁾.

Anemia in CKD is primarily caused by a decrease in erythropoietin production, which is frequently made more severe by iron deficiency conditions. Anemia in CKD can also be caused by a decrease in erythrocyte age, inflammation, infection, hyperparathyroidism, uremic inhibitors, and nutritional deficits⁽⁷⁾. Previous studies discovered a significant positive correlation between erythropoietin levels, glomerular filtration rate (GFR), and hemoglobin (Hb) levels⁽⁸⁾.

There are several risk factors that can cause anemia complications in CKD patients. Older age and female gender were identified as risk factors involved in the development of anemia in CKD patients. Older patient age was associated with a greater incidence of inflammation as well as more age-related comorbidities. Although the Hb threshold for diagnosing anemia in female is lower than in male, female patients with CKD tend to have a higher risk of developing anemia than male patients⁽⁹⁾. In a systematic review study, it was reported that anemia relatively occurs in CKD patients with increasing disease severity, with up to 90% of cases found in stage V patients⁽¹⁰⁾. According to the above description, with the high incidence of CKD as a risk factor for anemia, this study aims to assess the prevalence of anemia and to investigate the factors influencing the occurrence of anemia in pre-dialysis CKD.

MATERIALS & METHODS

This study was designed cross-sectional with the type of analytical observational and

conducted at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital. This analysis included data from male and female patients aged ≥ 18 years with CKD diagnosis ((GFR) < 90 mL/min/1.73 m²) who were not on dialysis. Exclusion criteria included dialysis in the previous 12 months, a lack of documented medical record, diagnosis of anemia caused by malignancy and bleeding. Pregnant women were also excluded from the analysis. The criteria from WHO defined anemia as serum Hb < 12 g/dL in women and < 13 g/dL in men. Sampling in this study used total sampling method. Final sample for this study were 712 patients who met the inclusion criteria. We observed hemoglobin from blood samples that were recorded in the medical record. Patient characteristic data including gender, age, and stage of CKD were obtained from the medical record. There are two types of variables observed in this study. Gender, age, and the stage of CKD, the independent variables in this study, while the incidence of anemia is the dependent variable.

STATISTICAL ANALYSIS

Data was entered into *Microsoft excel* and exported to SPSS version 24 for analysis. Descriptive statistics, counted with percentage for categorical variables to look for prevalence. Bivariate analysis in this study will use the chi-square method. Regression logistic analysis was used to examine the association between incidence of anemia and patient's characteristic data (gender, age, CKD stage).

RESULT

Table 1. Prevalence of Pre-Dialysis CKD Patients with Anemia at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital in 2020-2022

Variables	Anemia n (%)	Non-anemia n (%)
Gender		
Male	302 (65,1)	162 (34,9)
Female	186 (75,0)	62 (25,0)
Age		
17 – 25	8 (80,0)	2 (20,0)
26 – 35	16 (66,7)	8 (33,3)
36 – 45	37 (62,7)	22 (37,3)
46 – 55	84 (65,1)	45 (34,9)

56-65	148 (65,8)	77 (34,2)
≥ 65	195 (73,6)	70 (26,4)
CKD Stage		
Stage I	81 (61,4)	51 (38,6)
Stage II	57 (60,6)	37 (39,4)
Stage III	180 (60,0)	120 (40,0)
Stage IV	75 (88,2)	10 (11,8)
Stage V	95 (94,1)	6 (5,9)
Total	488 (68,54)	224 (31,46)

The total number of pre-dialysis CKD patients with anemia was 488 patients and the total number of CKD patients without anemia was 224 patients, therefore it was found that the prevalence of anemia in pre-dialysis CKD patients in 2020-2022 was 68.54%. **Table 1** shows the prevalence of anemia in pre-dialysis CKD patients based on gender, age, and CKD stage. Based on findings in research data, 186 (75%) of pre-

dialysis CKD patients in women were found to have anemia, and 302 (65.1%) of men with anemia. The age group with the highest prevalence of anemia was found in 17-25 years (80%) and ≥ 65 years (73.6%). The CKD stage most commonly found in patients with anemia is stage IV with a total of 75 patients (88.2%) and stage V with a total of 95 patients (94.1%).

Table 2. Chi Square Test Results of Factors Associated with Anemia in Pre-dialysis CKD patients at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital in 2020-2022

Profile	Anemia N (%)	Non-anemia N (%)	p-value
Gender			
Male	302 (65,1)	162 (34,9)	0,007
Female	186 (75,0)	62 (25,0)	
Age			
≥50	402 (69,1)	180 (30,9)	0,517
<50	86 (66,2)	44 (33,8)	
CKD Stage			
≥III	350 (72,0)	136 (28,0)	0,003
<III	138 (61,1)	88 (38,9)	

Table 2 shows the Chi Square result of factor associated with anemia in pre-dialysis CKD patients. Gender was found to have a significant relationship with the occurrence

of anemia (p=0.007). A significant relationship was found between CKD stage and the incidence of anemia (p=0.003).

Table 3. Correlation of Age and CKD Stage with the Occurrence of Anemia in Pre-Dialysis CKD Patients

	p-value	OR	95% C.I. for EXP(B)	
			Lower	Upper
Stage (≥III)	0,004	1,641	1,175	2,293
Gender (Female)	0,007	1,610	1,138	2,277

Table 3 shows the correlation between anemia and gender and CKD stage of pre-dialysis CKD patients in 2020-2021. The correlation of these two variables was analyzed using the binary logistic regression method. Based on the data above, CKD stage has a significant relationship with the incidence of anemia (p=0.004). The correlation between gender and the incidence of anemia was also found to be

significant (p=0.007). Logistic regression analysis with odds ratio (OR) and 95% confidence interval showed an increased prevalence of anemia in patients with stage ≥III (OR 1.641, 95% CI: 1.175-2.293) and female gender (OR 1.610, 95% CI: 1.138-2.277).

DISCUSSION

Hemoglobin (Hb) levels ≤ 12 g/dL in women and ≤ 13 g/dL in men are considered anemia. Although complications of anemia can be treated, its frequency continues to increase in later stages of CKD⁽¹¹⁾. In this study, analysis and data collection on characteristics of CKD patients with anemia and without anemia were carried out. Based on the data, 75% of women were found to have anemia, and gender was found to have a significant relationship ($p=0.007$) to the incidence of anemia in pre-dialysis CKD patients. Logistic regression analysis on gender showed that female patients were 1.6 times more likely of developing anemia compared to male patients. This result is consistent with previous research that discovered female gender increases the risk of anemia in chronic kidney disease⁽¹²⁾. A meta-analysis study reported that female CKD patients were 36% more likely to experience anemia. Female patients tend to have lower Hb concentrations compared to male patients, this may explain why women have a greater risk of developing anemia⁽⁹⁾. Sociodemographic research conducted at Banaras Hindu University found different result, where 95.8% of men with CKD were diagnosed with anemia⁽¹³⁾. Based on the findings of this research, it was discovered that the age group with the highest prevalence of diagnosed anemia is ≥ 65 years old. The high incidence of chronic kidney disease (CKD) in the elderly age group may be caused by several comorbid diseases associated with age, as well as changes in kidney function and anatomy⁽¹⁴⁾. This is in line with previous research which stated that the age of CKD patients with anemia was most commonly found in the range of 65-74 years (32.7%)⁽¹⁵⁾. Age-related reductions in kidney function occur in both men and women. According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative guidelines, more than half of the elderly population has CKD stages III-V⁽¹⁶⁾. The pathogenesis of anemia in the elderly can include clonal hematopoiesis,

dietary inadequacies, and anemia brought on by inflammation or other unknown causes. Nutritional deficiencies that can be experienced include iron, vitamin B12 and folate deficiencies. According to a study that used data from the US National Health and Nutrition Examination Survey, around one-third of those over 65 had anemia for unknown reasons⁽¹⁷⁾.

Data from the National Health and Nutrition Examination found that anemia prevalence rates based on CKD stage showed stage I (8.4%), stage II (12.2%), stage III (17.4%), stage IV (50.3%), and stage V (53.4%)⁽¹¹⁾. This study also found a similar result, with patients diagnosed with anemia being most prevalent in stages IV and V, and a significant relationship ($p=0.003$) was found between the stages of chronic kidney disease and the occurrence of anemia in pre-dialysis chronic kidney disease patients. According to the study's logistic regression analysis, patients in stage $\geq III$ (stages III-V) are 1.6 times more likely to develop anemia in comparison to patients in stages I and II. This decrease in hemoglobin levels could be due to a decrease in erythropoietin secretion in CKD patients, can cause CKD patients to be more susceptible to anemia. Decreased oxygen flow to kidney tissue as a result of decreased GFR in CKD patients causes dysregulation of erythropoietin production by increasing oxygen pressure in the tissue. This condition causes a decrease in HIF stability and transcriptional activity, resulting in damage to cells that produce erythropoietin⁽¹⁸⁾.

CONCLUSION

In conclusion, the text discusses the prevalence and factors associated with anemia in chronic kidney disease (CKD) patients. The study reveals a significant association between gender and anemia in pre-dialysis CKD patients, with 75% of women found to have anemia and indicates that female gender as a risk factor for anemia in CKD. The age group with the highest prevalence of diagnosed anemia is ≥ 65 years old, aligning with the broader

trend of CKD incidence in the elderly. The decrease in GFR makes patients more susceptible to anemia, where patients with stage \geq III (stages III-V) are at a higher risk of developing anemia compared to stages I and II. The findings underscore the complexity of anemia in CKD, involving gender, age, and CKD stage as key factors influencing its occurrence. The study contributes to the understanding of anemia in CKD patients, offering insights that may inform future research and clinical interventions.

Declaration by Authors

Ethical Approval: This research was approved by the Ethics Committee of Faculty of Medicine Udayana University Approved (No:

237/UN14.2.2.VII.14/LT/2023)

Acknowledgement: None

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

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How to cite this article: Ni Komang Ayu Amanda Setiari Jaya, I Gusti Ayu Widiyanti, Muliani, I Nyoman Gede Wardana. Factors related to the occurrence of anemia in pre-dialysis chronic kidney disease patients at Prof. Dr. I Goesti Ngoerah Gede Ngoerah Hospital, 2020-2022. *International Journal of Research and Review*. 2023; 10(12): 834-839. DOI: <https://doi.org/10.52403/ijrr.20231283>
