The severity of anemia and type of erythrocyte index in patients with chronic kidney disease undergoing regular hemodialysis in Prof. Dr. I.G.N.G Ngoerah General Hospital

Elionardo Enrique Pangkahila[1*], Shannen Callista[1], Gusti Ngurah Prana Jagannatha[1]

Introduction: Chronic kidney disease (CKD) is a clinical condition characterized by an irreversible decline in kidney function and requires renal function replacement therapy in the form of dialysis or kidney transplantation. Anemia is a complication that occurs in 80-90% of CKD patients. This study aimed to observe the severity of anemia and type of erythrocyte index in patients with CKD undergoing regular hemodialysis.

Methods: This is a descriptive observational study with retrospective method to analyze data by describing the data that has been analyzed as it is. This study was performed in Prof. Dr. I.G.N.G Ngoerah General Hospital, Bali within the month of May 2022. The population of this study was 100 CKD patients who underwent routine hemodialysis according to inclusion and exclusion criteria using medical record data. The sample collection technique was purposive sampling method and this study design has been approved by the institutional ethical board.

Results: Out of 100 CKD patients who underwent regular hemodialysis that were observed, most of them are male patients (52%) and mostly at the age of 55-64 years old (31%). Anemia was found in 84 out of 100 CKD patients that were observed with the severity of anemia mostly is moderate anemia. Erythrocyte index was mostly in the normal range with the type of anemia generally is normocytic normochromic anemia.

Conclusion: The majority of MCV, MCHC, MCH values of CKD patients undergoing hemodialysis are normal.

Keywords: *chronic kidney disease, anemia, erythrocyte index, hemodialysis.*

INTRODUCTION

Anemia is a common finding in patients with CKD especially in patients with advanced CKD who undergoing the hemodialysis therapy.[1] Anemia in CKD will impact on the increasement of mortality and morbidity, lowering the quality of life, increase cost and length of hospitalization, and also a risk factor of cognitive function declinement.[2] Repeated hemodialysis and in a long term will cause the blood to be exposed to high concentrations of aluminum intoxication so that it effects on erythropoiesis and shortening of erythrocyte life span which will trigger the occurrence of anemia.[3] Research shows that by treating anemia with the aim of raising the hematocrit at least 36% can help to improve the quality of life, reduce the need for transfusion, improve cognitive function, and also reduce mortality and morbidity of patients with CKD undergoing hemodialysis.[4]

The mechanism of anemia is not well understood but the major factors to cause anemia in CKD patients involves inflammation which may result in impaired erythropoiesis, relative erythropoietin deficiency (EPO) and increasement of hepcidin.[5] Knowing the severity of anemia and the erythrocyte index is important because it can help to determine the best

therapy to treat anemia in CKD patients with the hope to improve the prognosis of CKD patients, increasing the quality of life, which later can reduce the morbidity and mortality rate. This study aimed to observe the severity of anemia and type of erythrocyte index in patients with CKD undergoing regular hemodialysis.

METHODS

This is descriptive observational with retrospective method to analyze data by describing the data that has been analyzed. Accessible population of the research were patients diagnosed with stage V CKD undergoing regular hemodialysis at the Hemodialysis Unit in Prof. Dr. I.G.N.G Ngoerah General Hospital. The inclusion criteria were patients with age above 18 years old and patients with stable condition, undergoing hemodialysis twice weekly. While the exclusion criteria were patients with emergency indication of hemodialysis, patients with malignancy, patients with sepsis and patients with active bleeding.

Anemia was considered as the Hb levels of $\leq$13 g/dl in men and $\leq$12 g/dl in women, using the data of Complete Blood Count testing hematology analyzer taken from Hospital

medical record. Patients with stage V CKD were considered with kidney failure of eGFR <15ml/minute/1.73m2 and undergoing regular hemodialysis at least 3 months. Erythrocyte index was consisted based on 1) MCV; calculated by formula 10 x hematocrit (mL/dL or %) / erythrocyte ($\times 10^{12}$/L) expressed in fL units, 2)MCH; calculated by formula 10 x hemoglobin (g/L) / erythrocyte ($\times 10^{12}$/L) expressed in pg/cell, and 3) MCHC; calculated by formula 10 x hemoglobin (g/L) / hematocrit (mL/dL or %) expressed in g/dl. Types of anemia were determined based on the results of the erythrocyte index, and categorized into: 1) Microcytic Hypochromic if MCV <80fL and MCHC <32 pg, 2) Normocytic Normochromic if MCV 80-100 and MCHC 32-36 pg and 3) Macrocytic if 100 fL or more.

The data used in this research was secondary data (medical record) to identify the Complete Blood Count test results specifically the Hb levels, erythrocyte index (MCV, MCH, MCHC). The collected data were then analyzed by using computer program. The processing of descriptive data consisted of editing, coding, scoring, tabulating, and data entry. The data were then presented in the form of table of frequency and percentage according to the research objectives.

RESULTS

This study was conducted at RSUP Prof. Dr. I.G.N.G Ngoerah Bali in May 2022. There were 100 eligible subjects involved in the study. Based on Table 1 the proportion of male patients was higher than female patients. Male patients were as many as 52 people (52%) and women patients as many as 48 people (48%). Based on table 2, the highest proportion of CKD patients undergoing hemodialysis was in age group 55-64 years with the frequency 31% at the average age of 58.96 years old. Other CKD patients were at the age of <35 with the frequency of 12%, 35-44 years with the frequency of 23%, 45-54 years old with the frequency of 23%, and age >= 65 are 11%.

From the total of 100 patients there were 84 patients experiencing anemia and 16 patients who did not. From 84 CKD patients with anemia there were 36.9% patients with mild anemia. Meanwhile, 53.6% of them experienced moderate anemia, and 9.5% had severe anemia. Table 3 also shows the average Hb proportion of CKD patients undergoing hemodialysis had low Hb values (<12 g/dl). Based on table 4 shows that from 84 CKDat patients who had anemia and undergoing hemodialysis, 11.9% had an MCV value below normal and 88.1% had normal MCV value. On the other hand, 45.2% had MCHC value below normal and 54.8% had normal MCHC value. In addition to that, 22.6% had MCH value below normal, 75% had normal MCH value and 2.4% had higher MCH value than normal. Based on the types of anemia, 43% of CKD patients had normocytic normochromic anemia, 31% normocytic hypochromic anemia and 10% microcytic hypochromic anemia (Table 5).

DISCUSSION

The majority of CKD patients undergoing regular hemodialysis in Prof. Dr. I.G.N.G Ngoerah General Hospital are male patients with the frequency of 52% rather than women 45%. This is in accordance with the description of the data in Indonesia where 56% are male; 44% are female.[6] There are several things that affect this, including in terms of kidney anatomy, renal response to hemodynamic stress, effects of sex hormones, diet, fat metabolism, and blood pressure.[4,6] The male kidney is larger in size and has more glomerulus which causes men to be more tolerant of increased blood pressure under hemodynamic stress compared to women.[7] Estrogen has an antifibrotic effect and antiapoptotic, whereas

Table 1. Gender Distribution of CKD Patients Undergoing Hemodialysis

Characteristics	Frequency (f)	Percentage (%)
Gender		
Male	52	52
Female	48	48
Total	100	100

Table 2. Age Distribution of CKD Patients Undergoing Hemodialysis

Characteristics	Frequency (f)	Percentage (%)
Age (year)		
<35	12	12
35-44	23	23
45-54	23	23
55-64	31	31
>=65	11	11
Total	100	100

Table 3. Anemia Severity Distribution of CKD Patients Undergoing Hemodialysis

Characteristics	Frequency (f)	Percentage (%)
Hemoglobin Value		
Normal	16	16
Mild (11.0 – 12.9 g/dl)	31	31
Moderate (8.0 – 10.9 g/dl)	45	45
Severe (<8.0 g/dl)	8	8
Total	84	100

Table 4. Erythrocyte Index Distribution of CKD Patients Undergoing Hemodialysis (84 patients)

Characteristics	Frequency (f)	Percentage (%)
MCV Value		
Low (<80 fL)	10	11.9
Normal (80-100 fL)	74	88.1
High (>100 fL)	0	0
MCHC Value		
Low (<31 g/dl)	38	45.2
Normal (31-36 g/dl)	46	54.8
High (>36 g/dl)	0	0
MCH Value		
Low (<26 g/dl)	19	22.6
Normal (26-34 g/dl)	63	75.0
High (>34 g/dl)	2	2.4

Table 5. Type of Anemia Distribution of CKD Patients Undergoing Hemodialysis (84 patients)

Characteristics	Frequency (f)	Percentage (%)
Microcytic Hypochromic	10	11.9
Normocytic Normochromic	43	51.1
Normocytic Hypochromic	31	36.9
Macrocytic	0	0
Total	84	84

testosterone has profibrotic and proapoptotic effects in the kidney which increases renal impairment in men.[8] Men also tend to consume tobacco products more frequently, have uncontrolled hypertension, and consume calories, protein, phosphorus, and more salt.[9]

The highest proportion of CKD patients undergoing hemodialysis was in age group 55-64 years with the frequency 31% with the average age of 58,96 years old. This situation is in line with research conducted at Dr. Hospital. M. Djamil Padang found the age range of patients most are 50-59 years old that is equal to 50.86%.[10] Another study in Nigeria shows the prevalence of CKD patients was more at the age > 50 years, which was 58%.[11] Kidney function tend to decrease with the increasing of age. The increment of age will case an increase in the in the kidney's response to vasodilator and vasoconstrictor which will increase the filtration fraction and lead to a decrease in GFR. The decline in the value of GFR also usually starts at age 30 years and will experience a rapid decline

if there are disease comorbidities, such as arteriosclerosis with hypertension.[12]

The analyzed data show that there are still 16 patients who did not experience anemia. On the other hand, there are 84 patients out of 100 who experience anemia. This situation is in line with a study conducted on CKD patients undergoing hemodialysis at the Indonesian Christian University Hospital in 2011, which was found that the average Hb value was in the range of 7.0-10.4 g/dl. CKD patients have decreased in Hb caused by decreased levels of erythropoietin which plays a role in erythrocyte maturation.[13] Immature erythrocytes will have less Hb and shorter life span (120 days). Other contributing factors are iron deficiency, bleeding, inflammation, hemolysis, and nutritional deficiencies.[14]

Based on the data that has been analyzed, shows that out of 84 CKD patients with anemia which undergoing hemodialysis has an MCV value below normal is 11.9%, normal MCV value is 88.1%, and none of MCV value is above

normal. On the other hand, MCHC value below normal is 45.2%, normal MCHC value is 54.8%, and none of the MCHC value is higher than normal. In addition, MCH value below normal is 22.6%, normal MCH value is 75%, and 2.4% of the MCH value is higher than normal. Quite different from the another study that found erythrocyte index of CKD patients from 20 samples shows that MCV value below normal is 40%, normal MCV value is 60%, and 0% of MCV value is above normal. MCHC value below normal is 0%, normal MCHC value is 75%, and 25% of MCHC value is above normal. In addition, MCH value below normal is 15%, normal MCH value is 80%, and 5% are above the normal value.[6]

However, results above are known that the majority of MCV, MCHC, MCH values of CKD patients undergoing hemodialysis are normal. Similar research done by Suyatno in 2016, the erythrocyte index in patients with CKD is generally normocytic normochromic, this is because in patients with CKD there is a deficiency of erythropoietin which serves to stimulate adequate erythropoiesis production.[15] Normochromic normocytic results were obtained, because this has been overcome by administering erythropoietin therapy and taking tablets iron (Fe) and other vitamins such as B12 so that patients do not experience deficiency of Fe and vitamin B12 so that the results of this study obtained normochromic normocytic.

Based on the type of anemia on from total of 84 CKD patients with anemia, there are 43% normocytic normochromic anemia, 31% are normocytic hypochromic anemia, 10% are microcytic hypochromic anemia, and none of them is macrocytic anemia. Supported from research conducted by health survey in Indonesia.[16] Based on the type of anemia in CKD patients undergoing hemodialysis, 50% are normochromic normocytic anemia, 15% are hypochromic microcytic, and 35% are hypochromic normocytic. In addition, according to the 2009 Paul Draw theory which states that anemia found in patients with CKD varies widely, consisting of: normocytic normochromic anemia, iron deficiency anemia with microcytic hypochromic, folic acid and vitamin B12 deficiency anemia with macrocytic - hypochromic morphology.[5] The erythrocyte index in patients with CKD is generally normocytic normochromic because in patients with chronic renal failure there is a deficiency of erythropoietin which serves to stimulate adequate erythropoiesis production. In this study, normochromic normocytic results were obtained, because patient has administered with erythropoietin therapy and taking tablets of iron (Fe) and other vitamins such as B12 so that patients do not experience deficiency of Fe and vitamin B12. This will cause the results of this study obtained normochromic normocytic.[5,17]

Chronic renal failure patients with chronic and acute inflammatory conditions that affect the inflammatory cytokine agents that decrease erythropoietin production and induce apoptosis in CFU-E.[5] Inflammatory cytokine agents may also indicate the production of hepcidin, a liver-derived peptide, which inhibits erythrocyte production by reduces the availability of iron to become erythroblasts.[5,9] This can reduce the production of erythrocytes, therefore there are some patients who have iron deficiency anemia. Iron deficiency anemia often produces red blood cells that are hypochromic microcytic, with MCV <80fL and MCHC <32 pg fl.[5,9,11] There are indications of hypochromic microcytic type anemia which is the size erythrocytes smaller than normal however have normal amount of hemoglobin suspicion this due iron deficiency.

This study is not without limitation. This study still lacks consideration of the anemia treatment received by the patients, as well as factors that could affect the erythrocyte index in patients with chronic kidney disease. Future research would have to consider this, such as the duration of illness, vitamin consumption, history of blood transfusions and the use of erythropoietin therapy.

CONCLUSION

The distribution of gender in CKD patients undergoing hemodialysis was equivalent with variable distribution of age. The severity of anemia found in CKD patients undergoing hemodialysis was mostly with moderate anemia 53.6%. The majority of MCV, MCHC, MCH values of CKD patients undergoing hemodialysis are normal. The type of anemia found in CKD patients undergoing hemodialysis is mostly normocytic normochromic anemia. This research did not pay attention to the anemia treatment that received by the patients, so for further research need to add other variable that can affect the erythrocyte index in patients with chronic kidney disease such as duration of illness, vitamin consumption, history of transfusion blood and use of erythropoietin therapy.

CONFLICT OF INTEREST

None to declare.

ETHICAL STATEMENT

This study had been approved by the Research Ethics Commission of the Faculty of Medicine, Udayana University / Prof. Dr. I.G.N.G Ngoerah General Hospital.

FUNDING

AUTHORS' CONTRIBUTION

All authors each contributed equally from drafting, conducting the research until the finalization of this article.

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