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The Influential Factors of Anemia on Patients with Chronic Kidney Failures Receiving Hemodialysis in Sultan Agung Islamic Hospital Semarang

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Abstract

Anemia suffered by patients with kidney failures can be prevented with erythropoietin administration (EPO). The chronic kidney disease (CKD) is the global epidemic with an estimated prevalence of 14% in the United States of America and 5% in the world. This research analyzes the influential factors of anemia via erythropoietin administration (EPO) for kidney failure patients who also receive hemodialysis in Sultan Agung Islamic hospital, Semarang. This research used analytical observation with Cross Sectional design. The population and sample were from 162 participants (total sampling). The statistical results with path analysis showed the direct influences with significant value on erythropoietin, comorbid, creatine, and ureum. The result showed insignificant results on family support, obedience levels, and cognition levels. The result found indirect and significant influences on family support, levels of obedience, levels of cognition. The insignificant values were on the comorbid, creatine, and ureum. The results showed the influential matters for the patients with anemia and chronic kidney failures that received hemodialysis were creatine with p=0.000, family support with p=0.00, levels of obedience with p=0.000, and levels of cognition with p=0.000.

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INTRODUCTION

Chronic kidney disease (CKD) is a global epidemic with a prevalence of 14% in the United States of America and 5% in the world (De Nicola & Zoccali, 2016). The disease also influences the health problems in the community for more than 10% of the whole world's population. Chronic kidney failure was ranked 16th in the world to cause a higher mortality rate. It can be higher and reaches rank 5 in 2040 (Id et al., 2020)

World Health Organization, 2016 reports that kidney disease contributes to the world disease with a mortality rate of 850.000 cases per year. According (Kemenkes RI, 2018), the prevalence of chronic kidney sufferers in Indonesia reaches 3.8%. The percentage showed the rate of patients that the doctors in all provinces already diagnosed.

The data from Central Java Province about chronic kidney disease patients showed an increase with a percentage of 0.06%. It was from 0.3% in 2013 to 0.37% in 2018 for Central Java citizens (Dinkes Jateng, 2017). The chronic kidney is progressive. It means the capability of an individual's body to keep the metabolism or the liquid and electrolyte balance fails. This causes uremia (Fishbane & Spinowitz, 2018).

The high prevalence of anemia is in patients with chronic kidney disease. The causes of anemia are decreasing erythropoietin production, zinc deficiency, red blood cell shortage, uremia toxication, inflammation, or hemorrhage. The inflammation process and the Cardiopulmonary resuscitation (CPR) increase were found in chronic kidney disease patients that received regular hemodialysis and suffered anemia. In this case, the prevalences for each chronic kidney are a percentage of 8.4% for the first stadium, 12.2% for the second stadium, 17.4% for stadium three, 50.3% for stadium four, and 53.4% for the fifth stadium.(Dwitarini et al., 2017)

Some previous studies found that patients with low hemoglobin levels (4.6g/dL) and normochromic normocytic mean corpuscular volume (MCV) 92.4 fl.ons and mean corpuscular hemoglobin (MCH) 30.5 pg). The kidney test for these patients showed azotemia with ureum 240 mg/dL and a creative level of 35.98 mg/dL. Those are the findings of (Payana. D, 2020; Sakaguchi et al. 2019).). The use of IV zinc therapy could increase 1 Hb 1 g/dL for patients with chronic kidney disease in China (Xu et al., 2016). The hemoglobin significantly increased from 8,34 ± 0,9 into 9,48 ± 0,9 g/dL p-value (0,000). (Rafiu et al., 2019).

According to Avdelidou., et al (2016) the highest prevalence of comorbidity for chronic kidney failure is diabetes mellitus (DM). The chronic patients could better undergo adequate hemodialysis medication with full family support (p-value < 0.001). (Winata et al., 2017) Some studies showed that the causal factors of anemia on chronic kidney disease were serum creatinine serum, family support, comorbid that were moderated by erythropoietin, folad acid, and zinc administrations.

In 2020, the highest case in 36 hospitals in Semarang was chronic kidney disease. One of the hospitals that encountered it was Sultan Agung Islamic hospital. The hospital received 11.342 cases with1.631 patients (BPJS Kota Semarang, 2020). The hospital is a B-type hospital in Semarang. It currently has 17 hemodialysis units, 17-bed units, and trained and professional nurses and doctors for hemodialysis treatment. The hospital is the referred hospital in Central Java. In 2017, the anemia patients with chronic kidney reached 265 patients that received hemodialysis (100%). In 2018, 227 anemia patients with chronic kidney disease received hemodialysis (100%). In 2019, 339 anemia patients with chronic hemodialysis received hemodialysis (100%). In 2020, 162 anemia patients with chronic kidney disease received hemodialysis (100%) (The Hemodialysis Unit of Sultan Agung Islamic Hospital, 2020).

From the explanation, the researchers would find the influence of comorbid, family support, level of knowledge, level of obedience, creatinine serum, ureum, and erythropoietin administration toward anemia patients with chronic kidney failure that received hemodialysis in Sultan Agung Islamic hospital, Semarang.

METHODS

The study was an analytical *cross-sectional* observation with a 4-week duration. It was a one-time measurement on informative, dependent and independent, variables which was done at the time of study using questionnaires and medical records (Sugiyono, 2017) The sampling included a total of 162 respondents, with being alive as the inclusive criteria. The instruments used in this study were records and questionnaires, and the data was analyzed using Stata 13 software path analysis.

RESULTS AND DISCUSSION

Table 1 describes the effects of X values family support, knowledge and compliance on Y1 value EPO consumption.

Table 1. The effects of family support, compliance and knowledge on EPO consumption

Variables	Beta	Z	p-*value*
(X2) Family support	0.281	4.74	0.000
(X3) Compliance	0.414	3.61	0.000
(X4) Knowledge	0.307	3.25	0.000

Source: Primary Data 2021

Family support (the X2 variable) was found to have a positive and significant effect on EPO consumption (the Y1 variable), with the p-value being smaller than α (0.000 < 0.050). The positive coefficient indicated that an increase in the Family support significantly increases EPO consumption.

Family support is effective for patient's compliance with hypertension medications. Subsequently, a normal blood pressure is prerequisite to a patient's consumption of EPO after taking a hemodialysis for his/her chronic kidney disease (Desitasari, 2014; Rustandi et al., 2018; Siti Ihwatun, 2020)

In our calculation, compliance (the X3 variable) showed a positive and significant effect on EPO consumption (the Y1 variable), with the *p-value* being smaller than α (0.000 < 0.050). The positive coefficient signifies that increasing compliance significantly boosts EPO consumption.

This finding was in line with a previous research (Beta, 2013) that found a significant effect of patients' compliance on consumption of the prescribed medications, of which *p-value* was similarly low (0.02). In addition, Knowledge (the X4 variable) has a positive and significant effect on EPO consumption (the Y1 variable), again with *p-value* smaller than α (0.000 < 0.050). This positive coefficient also means that the patients' knowledge significantly counts for the Y1 increase. There has been an understanding that, in case of CKD, patients whose education is well-given tend to make better acceptances to EPO administrations to raise hemoglobin level (Gapira et al., 2020; Mathew et al., 2016)

Further calculations given in Table 2 below indicate direct effects of Xs and Y1 EPO consumption, comorbidities controls, creatinine and urea on Y2 chronic kidney disease (CKD) patient's anemia improvement after hemodialysis. Without a doubt, Y1 Erythropoietin (EPO) consumption has a positive and significant effect on Y2 (the anemia improvement), with *p-value* smaller than α (0.007 < 0.050). The positive coefficient indicates Y2 raise significantly with the increase of Y1.

Table 2. The effects of EPO consumption, comorbidities control, creatinine and urea on the anemia improvement

Variable	Beta	Z	p-*value*
Y1 (EPO Consumption)	0.242	2.71	0.007
X1 (Control of comorbidities)	0.483	3.25	0.001
X5 (Creatinine)	0.113	3.76	0.000
X6 (Urea)	0.005	2.31	0.021

Source: Primary Data 2021

Research has compared hemoglobin (Hb) levels of chronic kidney disease (CKD) patients before and after hemodialysis. In pre hemodialysis results, the mean, lowest and highest levels respectively were 8.4 g/dL, 7.0 g/dL and 10.3 g/dL. Meanwhile, in post hemodialysis these levels were raised significantly to 9.0 g/dL, 7.3 g/dL, and 10.6 g/dL respectively for the mean, lowest, and highest values. (Permana, 2019)

In terms of comorbidities, the X1 variable has positive and significant effects on Y2 (the anemia improvement), with *p-value* smaller than α (0.001 < 0.050). The category 2 of X1 variable (hypertension control) significantly matters in the increase of Y2, as marked by positive coefficient value.

Histories on DM, kidney stones and total cholesterol levels are the dominant variables for CKD in hypertensive patients. In addition, there has been a strong correlation between types of hypertensive therapies and CKD (Nauval & Hasanah, 2019). The main cause of CKD has been Hypertensive Nephrosclerosis (HN), where iron absorption becomes poor and may cause anemia, which further develops into chronical diseases (Arifa et al., 2017; Patambo et al., 2014; Yulistina et al., 2017)

On the other hand, creatinine (X5 variable) showed a significant, negative effect on the anemia improvement (Y2 variable)**,** with *p-value* lower than α (0.000 < 0.050). The negative value of the coefficient is indicative of the inverse proportional relationship, where X5 raise causes Y2 to decrease significantly. Research has revealed that the lab tests on stage-5, non-hemodialysis, CKD patients showed 100% increases in serum creatinine levels. There has also been a positive correlation (r = 0.82) between salivary and serum creatinine values, and creatinine has a significant effect in detecting CKD's patient. In addition, there has not been a correlation between serum creatinine level and TIBC in CKD patients (Loho et al., 2016; Temilola et al., 2019; Ulya et al., 2019)

On calculation, the X6 variable, Urea, significantly has a negative effect on the anemia improvement after hemodialysis (the Y2 variable), with *p-value* smaller than α (0.021 < 0.050). This means the elevation of X6 level significantly hampers the patients' anemia improvements. Uremic toxins are most representative in CKD as results of molecular mechanisms underlying the anemia. Results have found a correlation between urea levels and decreases of renal functions in terms of anemic patients after hemodialysis (Rifnayeni et al., 2015 ; Rosari et al., 2017). There has been a correlation between urea level and the shrinkages of erythrocyte and hemoglobin counts in anemic patients after hemodialysis (Hamza et al., 2020 ; Kurniawan & Koesrini, 201 ; Nurkamila & Hidayati, 2013 ; Simarmata et al., 2017)

The overall research design includes 13 direct and 6 indirect effects, as seen in Table 3. The table shows results of direct and indirect testings on the effects.

Table 3. Results of hypothesys tests on Family support, Comorbidities control, Compliance, Knowledge, Urea, Erythropoietin (EPO)

Independent Variables	Mediating Variables	Dependent Variables	Coefficients	*p-values*
X1	Y1	Y2	0.025	0.443
X2	Y1	Y2	0.068	0.019
X3	Y1	Y2	0.074	0.022
X4	X1	Y2	0.100	0.030
X5	X1	Y2	0.004	0.577
X6	X1	Y2	0.0005	0.310

Source: Primary Data 2021

The indirect effect of X2 (Family support) on Y2 (Anemia improvement post-hemodialysis) through Y1 (EPO consumption) is significant, with *p-value* less than α (0.019 < 0.050). Thus Y1 is a mediator of X2 effect on Y2.

During hemodialysis therapies, patients with CKD demand family collaboration, which are proven to facilitate their medication and diet control processes. A complication mostly affecting CKD patients, anemia can be improved by focusing on controls of EPO and iron levels. Although relative deficiency of EPO is the main factor for anemia in CKD, iron scarcity has prominent contribution in the abnormality mechanism of erythropoiesis when kidneys

function decrease ((Batchelor et al., 2020; Khorsandi et al., 2020)

In view of compliance, the indirect effect of X3 (Compliance) on Y2 (Anemia improvement post-hemodialysis) through Y1 Erythropoietin (EPO) consumption is significant, with *p-value* less than α (0.022 < 0.050). Thus Y1 is a mediator of X3 effect on Y2.

There has been a result (Handayani et al., 2019) showing that drugs compliance is effective on DM patients. Poor, long-term, compliance and adherence to drug therapies are universally recognised as a main clinical issue in managing chronical diseases with drugs consumptions. One of these cases has been that of EPO administration (Burnier et al., 2015).

In terms of Knowledge, the indirect effect of X4 (Knowledge) on Y2 (Anemia improvement post-hemodialysis) through Y1 EPO consumption is significant, with *p-value* less than α (0.030 < 0.050). Thus Y1 is a mediator of X4 effect on Y2.

Epoetin alfa (Eprex®) is a subcutaneous injection formulation of recombinant human erythropoietin (rHuEPO) with a short half-life. EPO is a 30.4 kDa glycoprotein hormone produced mainly by the fetal livers and adult kidneys. EPO exerts its hematopoietic effect by stimulating erythrocyte proliferation and differentiation with increased tissue oxygenation. With receptor further expressed in non-hematopoietic tissues, EPO is known as a cytokine with many pleiotropic effects. Hydrodynamic gene therapy with erythropoietin (EPO) could restore hemoglobin (Hb) levels. Utilization of ESAs (Erythropoiesis-Stimulating Agents) in patients with stage-4 and stage-5 CKDs to increase hemoglobin (Hb) levels (Marsili et al., 2017 ; Pedersen et al., 2015 ; Sofue et al., 2020)

There has been a result (Li et al., 2016) have shown erythropoietin (EPO) medication capability in raising hemoglobin levels is more effective via IV, where it can be initiated when patients' Hb levels reach a minimum threshold of 7 g/dL and can be stopped when they reach 11-12 g/dL.

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CONCLUSION

In this research taking place in Sultan Agung Islamic Hospital in Semarang, it is concluded that comorbidities, knowledge, and compliance have significant, direct, effects on EPO consumptions, all of which with p-values of 0.000 (<0.05). In conclusion, the significant variables directly affecting Post-hemodialysis anemia improvement for chronic kidney disease (CKD) patients include EPO consumption (p=0.007, <0.05), comorbidities control (p<0.001), urea level (p=0.021, < 0.05) and creatinine level (p=0.000, <0.05). In addition, the significant variables indirectly affecting the post-hemodialysis anemia improvement include family support (p < 0.025), compliance (p=0.068, <0.05) dan knowledge (p=0.074, <0.05), all of which are mediated by EPO consumption.

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