

## ORIGINAL ARTICLE

# Levels of Hemoglobin, Leukocytes, and Platelets of Chronic Kidney Disease Patients Undergoing Hemodialysis in Surabaya

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## ARTICLE INFO

### Article history:

Received 4 April 2018

Received in revised form 18 April 2018

Accepted 20 April 2018

Available online 30 April 2018

### Keywords:

Chronic Kidney Disease,  
Hemodialysis,  
Hemoglobin,  
Leukocytes.

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## ABSTRACT

**Introduction:** Chronic kidney disease (CKD) is increasing in Indonesia, furthermore, it requires high treatment cost such as conservative therapy and kidney transplantation or dialysis. There are two types of dialysis; hemodialysis (HD) and peritoneal dialysis. The patient who undergoes HD needs periodical laboratories evaluation due to its impact on hemoglobin (Hb), leukocyte and platelets. The purpose of this study was to obtain the levels of Hb, leukocyte and platelets regularly in stage 5 CKD patients undergoing HD.

**Methods:** Data were collected from patients' medical record from October to December 2014 and it was characterized based on age, sex, HD frequency, HD period, hemoglobin, iron saturation, ESA (erythropoiesis-stimulating agent), leukocyte level and platelets level. 60 samples were included with the same ratio.

**Results:** The average of age was 45 years old and the average of HD period was 40 months. All patients suffered anemia, however, only 51 patients could be evaluated the iron saturation. From it, 37 patients had the iron saturation of  $\geq 20\%$  which 14 (38%) of them received ESA. There were 14 patients who suffered zinc deficiency anemia with the iron saturation of  $< 20\%$  which 4 (29%) of them received ESA.

**Conclusion:** Most of patients' leukocyte and platelets levels were normal. Patients who received ESA had higher Hb levels. Platelets levels had a reverse correlation with the longer period of hemodialysis.

## 1. Introduction

Chronic kidney disease (CKD) is one of the world's health problems with high treatment costs(1). Data from 249 units of hemodialysis in Indonesia, showing an increasing trend in the number of new patients undergoing HD from year to year. In succession from 2013, 2014 and 2015 the number of new patients undergoing hemodialysis as much as 5128, 17193 and 21050. This data though not showing data throughout Indonesia but can be used as a representation of the current conditions(2). CKD is a condition in which both kidneys are damaged for a long time and irreversible(3).

CKD is often asymptomatic and rarely acknowledged, thus many patients know its disease when it has reached an advanced stage(4).

Kidney damage and/or glomerular filtration rate (GFR) of  $< 60$  ml/men/1.73 m<sup>2</sup> for more than three months were classified as CKD(1). Based on the size of GFR, CKD is divided into 6 stages(5). If the GFR decreases then the complications increase(1). The complications of CKD include cardiovascular disease, susceptibility to infection, anemia, malnutrition, and bone damage(5).



CKD therapy is divided into conservative therapy and renal replacement therapy such as transplantation and dialysis to survive(1). CKD patients undergoing hemodialysis (CKD-HD) require heparin to prevent blood clots in the extracorporeal circuit during the process(6).

Anemia is the most common complication in patients with CKD. There are many factors that can cause anemia in patients with CKD, but erythropoietin hormone deficiency is the most common cause. Anemia may arise in the early stages of renal impairment and will progressively worsen in accordance with impaired renal function(1).

The number of leukocytes was generally normal in CKD patients but there was a function change(7). It causes CKD patients tend to decrease the body's defenses which can increase the risk of bacterial infection up to four times than the healthy population(5).

Not only leukocytes but also platelet counts in CKD patients are normal but there is a function change(7) that causes CKD patients have a tendency to bleeding(5). However, the use of heparin in CKD-HD patients have side effects such as pruritus, allergies, osteoporosis, hyperlipidemia, bleeding, and it can also induce the occurrence of Heparin-Induced Thrombocytopeni(8).

CKD-HD patients require periodic laboratory tests for long-term evaluation such as a complete blood count (CBC) (9). The complete blood count is easily performed, inexpensive, and provides a lot of information(10). Information that can be given from the CBC are hemoglobin (Hb) to determine anemia, leukocytes to determine the presence of infection, as well as the platelet counts that can be normal or decreased and increased(11). Therefore, this study aims to determine the levels of Hb, leukocyte and platelets in CKD-HD patients in the hemodialysis installation of Dr. Soetomo General Hospital Surabaya from October to December 2014.

## 2. Methods

This was a descriptive study. The study population was CKD patients undergoing HD regularly at hemodialysis installation of Dr. Soetomo General Hospital Surabaya. The variables studied were Hb, leukocyte and platelet. Other supporting variables were HD frequency, HD duration, iron saturation, and ESA usage status (erythropoiesis-stimulating agent). We used medical record data of patients who had the complete blood test from October to December 2014. The collected data were processed and analyzed descriptively with quantitative approach.

## 3. Result

The total number of samples in this study were 72 patients with CKD undergoing outpatient treatment at Kidney-Hypertension Clinic, Dr. Soetomo Hospital, who met the inclusion and exclusion criteria, and divided into three groups consisting of 24 patients with stage 3, 24 patients with stage 4, and 24 patients with Sixty samples were included with similar ratio; 50% of male and 50% of female. The average age of samples was 45 years old and they have undergone HD in the 40th month. 82%, 5%, and 13% patients have undergone HD two times in a week, once in every five days, and once in a week, respectively.

### 3.1 Hemoglobin

All patients had anemia with the average levels of Hb was 8.17 g/dL. Nineteen (32%) patients had Hb levels of <7g/dL, 21 (35%) and 16 (27%) patients had Hb levels in the range of 7.1-9 g/dL and 9.1-11 g/dL respectively, and only 4 (7%) patients had Hb levels in >11 g/dL. Based on sex, the average levels of Hb male patients was higher than female patients. The number of female patients was highest at Hb of <7 g/dL. Meanwhile, its number was smaller at higher Hb levels. A high number of male patients was found at Hb levels of 7.1-9 g/dL (Figure 1).

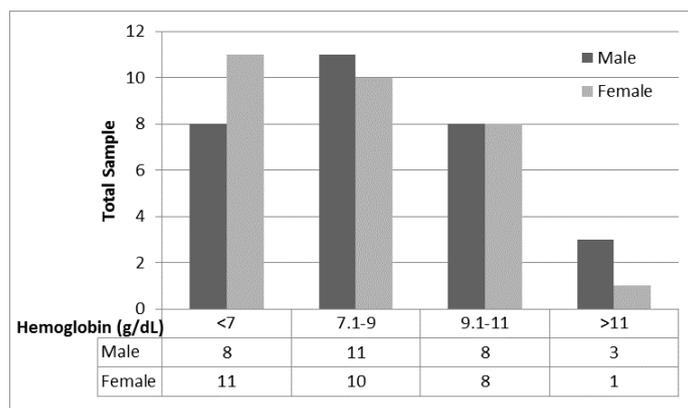


Figure 1. Frequency of Hemoglobin Distribution in CKD-HD patients at Hemodialysis Installation of Dr. Soetomo General Hospital from October to December 2014

Based on the frequency of HD, patients who undergo HD in every five days have a higher average level of Hb compared to the patients who undergo HD once or twice in a week (Table 1).

There were 51 patients whose iron saturation levels could be evaluated. There were 37 patients who had  $\geq 20\%$  iron saturation and 14 of them received ESA. There were 14 iron deficiency anemia patients with iron saturation levels of <20% and four of them received

ESA. Patients receiving ESA had a higher average of Hb levels (Table 2).

Table 1. Descriptive Statistics of Hemoglobin Levels in CKD-HD Patients at Hemodialysis Installation of Dr. Soetomo General Hospital Surabaya Based on the Frequency of HD from October to December 2014

The Frequency of HD	n	Minimum levels of Hb (g/dL)	Maximum levels of Hb (g/dL)	The average levels of Hb (g/dL)
Every five days	3	7.18	9.94	8.96
Once a week	8	5.84	12.9	8.74
Twice a week	49	4.93	12.5	8.03

Table 2. Descriptive Statistics of CKD-HD Patients' Percentage in Hemodialysis Installation of Dr. Soetomo General Hospital Surabaya who Received ESA Based on Iron Saturation Values from October to December 2014

Iron Saturation (%)	<20	≥20
Number of patients	14	37
Number of patients receiving ESA	4	14
Percentage of patients receiving ESA in each group	29%	38%

### 3.2 Leukocytes

There were two (3%) patients who had leukopenia, 54 (90%) patients had normal range, and 4 (7%) patients had leucocytosis. The average level of leukocyte was  $6.79 \times 10^3/\text{UL}$ . Based on leukocyte profile, 15% patients had normal neutrophil levels, 43% patients had normal lymphocyte levels, 22% had eosinophils higher than normal and 37% had basophils above normal.

### 3.3 Platelets

There were 22 (37%) patients who had thrombocytopenia, 36 (60%) patients were in normal range and 2 (3%) patients had thrombocytosis. Platelet levels have an inverse correlation to the duration of HD. The average platelet level was  $185.93 \times 10^3/\text{UL}$ .

## 4. Discussion

We obtained all CKD-HD patients from the hemodialysis installation of Dr. Soetomo General Hospital from October to December 2014 who suffered anemia based on Indonesian Society of Nephrology criteria. Previous research at Prof. Dr. R.D Kandou Manado General Hospital(11) also obtained similar

results. Based on sex, the mean levels of Hb in male was higher than female. Fig. 1 showed that Hb level was highest at  $<7 \text{ g/dL}$  in female patients meanwhile, most of the male patients was in the range of  $7.1\text{-}9 \text{ g/dL}$ .

Low levels of Hb in female could be due to menstruation in every month. In addition, there were hormonal differences that dominate female and male. In males, the dominant sex hormone is testosterone, whereas the sex hormones in women are predominantly by estrogen. Testosterone can increase the speed of metabolism thus the speed of Hb formation also increases(12).

Based on Hb frequency, patients undergoing HD every 5 days had a higher mean of HD levels than those who undergone HD once or twice a week (Table 1). It ought that those who had HD twice a week had better Hb levels than patients who undergoing HD in once a week or every five days because of the sufficient HD dosage results in the smaller influence of uremia on erythropoiesis(9). However, this study obtained that the group who undergone HD every five days have a higher mean of Hb. This may be due to an unbalanced number of patients in each group where the majority of patients (82%) have HD twice a week thus, the results obtained in this study become less representative. In addition, the HD process itself also causes the blood volume to decrease because there is blood contained in the machine dialyzer.

Anemia is the most common complication in patients with CKD that may arise in the early stages of renal impairment and will worsen as kidney function impairment occurs(13). There are many factors that can cause anemia in patients with CKD, however, EPO hormone deficiency is the most common cause(1). EPO is a hormone that stimulates our body to make red blood cells (erythropoiesis). When our kidneys are damaged, the kidney can not form enough EPO resulting a decrease in the amount of Hb(7).

Moreover, anemia in CKD-HD patients can also be caused by iron deficiency(14). This study evaluated iron saturation levels in only 51 patients. Most of the patients (37 people) had iron saturation levels of  $\geq 20\%$  while the rest of patients (14 people) had iron saturation levels of  $< 20\%$  as a sign that they had iron deficiency anemia. Eighteen of 51 patients received ESA. Patients receiving ESA had a higher average level of Hb. ESA is a substitute for EPO which also serves to stimulate the formation of Hb. The requirement of ESA administration is when iron saturation levels reach  $\geq 20\%$  in order to obtain optimal results(14).

Table 2 showed that 37 patients had iron saturation level of  $\geq 20\%$  and only 14 patients received ESA. Despite having  $\geq 20\%$  iron saturation, the rest of patients did not receive ESA. This may be due to differences in the administration system of each patient. Administration of ESA in CKD-HD patients at the Dr. Soetomo General Hospital is purposed for ASKES patients. Meanwhile, patients with BPJS administration did not receive ESA

by its health insurance. Patients with BPJS can use ESA but they must purchase it personally.

Meanwhile, there were four patients who received ESA in the group whose iron saturation is not eligible (<20%). This is probably due to the fact that the patient was eligible for ESA. However, because of the old administration system and complete blood tests performed every 3 months, the iron saturation level has changed when the patient received ESA. It required the precision of the officer in the HD installation. Patients with iron saturation levels of <20% should receive intravenous iron therapy first. After that, the iron saturation level is evaluated again and can only receive ESA if the iron saturation level has reached  $\geq 20\%$ .

The mean of leukocyte in the patients was  $6.79 \times 10^3/\text{UL}$  with a median of  $9.10 \times 10^3/\text{UL}$ , mode of  $9.77 \times 10^3/\text{UL}$  and standard deviation of  $2.84 \times 10^3/\text{UL}$ . We obtained as much as 90% of patients who have normal levels of leukocytes. The remaining 3% patients had leukopenia and 7% patients had leukocytosis. This was in accordance with the theory that the number of leukocytes in CKD patients was usually normal(9). Previous research also conducted in Dr. Soetomo General Hospital Surabaya (15) on the index of leukocyte apoptosis in CKD-HD patients, it is another parameter that indirectly can be used to control the leukocyte count. There was no significant difference between CKD-HD patients and normal patients.

The leukocyte levels, especially neutrophils and lymphocytes, in CKD-HD patients may decrease below normal levels influenced by the type of dialyzer membrane(16). The use of unmodified cellulosic membranes in the HD process may cause the marginal type of granulocyte leukocytes (neutrophils, eosinophils and basophils) as they pass through the blood vessels in the lung thus the amount of circulating granulocytes decreases(7). The results obtained in the study were not suitable because the levels of neutrophils, eosinophil and basophils in patients tend to be above normal. This may be due to the difference in the membrane dialyzers used in the research. Although the number of leukocytes in CKD patients was usually normal, there was a change in function such as chemo taxis, adherence, and phagocytosis(7). CKD patients tend to decrease the body's defences which can increase the risk of bacterial infection up to four times than the healthy population. Infection is the second leading cause of death after cardiovascular in patients with CKD(5).

In addition to functional changes, decreased body defence in patients with CKD can be caused by uremia, vitamin D deficiency, excessive iron accumulation and induced hemodialysis action. Vitamin D plays a role in the development and function of macrophages. Excessive accumulation of iron will stimulate bacterial growth and increase the virulence of bacteria(16).

Most patients had normal platelet levels; however, there were 22 patients (37%) who had thrombocytopenia (Fig. 1). These results were higher than the previous study at the Prof. Dr. R.D.Kandou Manado General

Hospital (17) that found the incidence of thrombocytopenia by 25.45%.

The use of heparin when the hemodialysis process can cause complications of Heparin-Induced Thrombocytopenia (HIT) (8). There was a significant decrease in platelet levels before and after hemodialysis although sometimes the levels were still within the normal range(18). Thiagarajan mentioned that although the dosage was minimal if heparin was administered over a long period of time it can lead to a decrease in platelet levels(19).

Based on the theory, we assume that there is a relationship between the duration of HD with platelet value. Then we performed further analysis between platelet levels with the duration of HD after using the homogeneity test of Komogorov-Smirnov, the duration of HD with platelet value in subjects are homogeny. Based on correlation test of Pearson, we do find weak inversely proportional correlation between the duration of HD with platelet value, the longer patient undergone HD, then the thrombocyte level was lower ( $r = -0.317$ ;  $p = 0.014$ ) (table 3).

Table 3. Correlation between platelet levels with the duration of HD

	n	p	r
Platelet levels & the duration of HD	60	0,014	-0.317

All patients used standard heparin. There was an increase in the frequency of HIT occurrence in this study, according to the theory, there were only about 1-5% patients using standard heparin in the HD process(20). However, despite the amount of thrombocyte or normal coagulation factor, patients with advanced stage CKD usually show a tendency for bleeding. This is due to abnormalities in platelet function. Anemia also contributes to bleeding diathesis in uremia, because higher red blood cells will suppress platelets closer to blood vessel walls making them more effective(7).

### Conclusion

Platelet levels have an inverse correlation to the duration of HD. The results showed that only 51 patients with iron saturation levels could be evaluated. Thirty patients had iron saturation levels of  $\geq 20\%$  and 14 of them received ESA. Fourteen patients had iron saturation levels of <20% and 4 of them had ESA.

### Conflict of Interest

The author stated there is no conflict of interest

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