

## **Impact of Antiretroviral Therapy Duration on Hematology Profile in HIV Patients at Buntok Health Center, Indonesia**

**Dwi Eka Wulandari, \*Leka Lutpiatina, Wahdah Norsiah, Aima Insana**

Medical Laboratory Technology Poltekkes Kemenkes Banjarmasin

Mistar Cokrokusumo Street 4A Banjarbaru Indonesia.

\*Email: leka.zns@gmail.com

**Abstract:** HIV/AIDS is a global health challenge that requires long-term therapy, one of which is the use of Antiretroviral (ARV). ARV therapy has a significant impact on the patient's hematological profile, such as hemoglobin, hematocrit, erythrocytes, leukocytes, and platelets. However, the long-term effects of ARV therapy on hematological profiles in Indonesia, especially in the Central Kalimantan region, have not been widely studied. This study aims to analyze the relationship between the length of ARV therapy and hematological profile in HIV patients at Buntok health center. This study used an analytic survey design with a cross-sectional approach. The study sample involved 29 HIV patients undergoing ARV therapy, taken by total sampling. Data were obtained from medical records and laboratory examinations and then analyzed using the Spearman correlation test to test the relationship between variables. The results showed a significant association between the duration of ARV therapy and the levels of hemoglobin ( $p = 0.005$ ), hematocrit ( $p = 0.001$ ), erythrocytes ( $p = 0.000$ ), and platelets ( $p = 0.023$ ). However, no significant relationship was found between the duration of ARV therapy and the number of leukocytes ( $p = 0.063$ ). The correlation found was negative, indicating that the longer the ARV therapy, the more certain hematological parameters decreased. It is concluded that the duration of ARV therapy is associated with changes in the hematological profile of HIV patients. These findings suggest the importance of routine monitoring of hematologic profiles to detect adverse effects of ARV therapy, especially in patients on long-term therapy.

**Keywords:** Antiretrovirals; hematologic profile; HIV patients.

## **INTRODUCTION**

HIV is one of the world's most serious public health problems. Since the beginning of the epidemic, the virus has infected more than 79 million people, and more than 36 million have died<sup>1</sup>. Globally, at the end of 2020, approximately 37.7 million people were living with HIV. An estimated 0.8% of adults aged 15–49 years worldwide have HIV<sup>1</sup>. In 2021, 74% of adults living with HIV had access to antiretroviral therapy<sup>2</sup>. In Indonesia, according to data from the Ministry of Health from the 2022 HIV AIDS Information System, 10,423 people with HIV/AIDS received ARV treatment in the period July–September 2022. In Central Kalimantan, according to data from the Central Kalimantan Provincial Health Office, in 2023, 967 people with HIV/AIDS received ARV treatment. Meanwhile, based on data from the HIV AIDS Information System (SIHA) of the Buntok Health Center UPT in 2023, 28 people received ARV therapy.

**Corresponding Author:** Leka Lutpiatina

Medical Laboratory Technology Poltekkes Kemenkes Banjarmasin.

Mistar Cokrokusumo Street 4A Banjarbaru Indonesia..

Email: leka.zns@gmail.com

HIV infection is a multisystem disease with various pathological manifestations, including hematological disorders that often occur in HIV patients. Anemia, leukopenia, and thrombocytopenia are the most common hematological disorders found in HIV patients<sup>3</sup>. These disorders are the second leading cause of morbidity and mortality in HIV patients<sup>4</sup>. Recent studies have shown that HIV can affect almost all blood cell lineages, with 63% of HIV patients experiencing one or more types of cytopenia. Anemia is the most commonly reported disorder, but leukopenia, neutropenia, lymphopenia, and thrombocytopenia are also common<sup>5,6</sup>.

The mechanism of these hematological disorders is complex and multifactorial. HIV infects multipotent hematopoietic progenitor cells, forming a latent cellular reservoir, disrupting the bone marrow environment, and causing immune deregulation<sup>7,8</sup>. Recent reports indicate that thrombocytopenia is the second most common hematological complication in HIV patients, with a prevalence of around 3% to 40%, and can occur at various stages of infection<sup>9</sup>. In addition, leukopenia is also common, especially in patients with advanced stages, where neutropenia is the most common finding in 10–30% of patients<sup>10</sup>.

On the other hand, the use of antiretroviral drugs can also cause continued hematopoietic suppression and trigger various hematological disorders<sup>11</sup>. HAART therapy is known to be associated with a number of serious hematological side effects that can limit the benefits of this treatment<sup>12</sup>. Research conducted by Lestari (2016) showed a relationship between the duration of ARV use and hemoglobin levels in HIV/AIDS patients. The results of this study indicate that the longer the use of ARVs, the greater the effect on hemoglobin levels, which can cause a decrease in hemoglobin levels<sup>13</sup>.

HIV patients undergoing ARV therapy need to undergo routine hematological profile examinations at least every three or six months to monitor side effects and ensure the safety and effectiveness of therapy<sup>14</sup>. In contrast to Lestari's (2016) study, which only examined the relationship between the duration of ARV use and hemoglobin levels, this study analyzed five hematological parameters, namely hemoglobin, hematocrit, erythrocytes, leukocytes, and platelets. In addition, this study was conducted at the Buntok Health Center UPT, Central Kalimantan, which previously had not received much attention in similar studies. Therefore, this study aims to determine the relationship between the duration of antiretroviral (ARV) therapy and hematological profiles in HIV patients at the Buntok Health Center UPT. The results of this study are expected to provide empirical evidence regarding the pattern of hematological changes in patients with long-term therapy and highlight the importance of regular hematological monitoring, especially for patients with a duration of therapy of more than 24 months.

## **MATERIALS AND METHODS**

This research is a type of analytic survey with a cross-sectional design. It was conducted at the Voluntary Counselling and Testing (VCT) Poly and Laboratory of Buntok health center from July to August 2024. The sample was comprised of 29 HIV patients undergoing Antiretroviral (ARV) therapy at Buntok health center. The sampling technique used was total sampling.

The independent variable was the duration of ARV therapy, which was categorized into three categories: less than 12 months, 12 to 24 months, and more than 24 months. The dependent variable was the hematological profile of HIV patients, including hemoglobin,

hematocrit, erythrocyte count, leukocyte count, and platelet count.

This study used instruments in the form of medical records that included patient data, such as initial name, age, gender, and duration of ARV therapy. In addition, tools such as a tourniquet, alcohol swab, 22G flashback needle, K2 EDTA vacutainer tube (3 ml), and hematology analyzer (ZENIX-144) were used. Venous blood samples of as much as 3 ml were taken from HIV patients who met the study criteria, which were then analyzed to obtain hematological profile data. The data used in the study consisted of primary data and secondary data. Primary data were obtained from the results of hematological profile examinations and questionnaires. In contrast, secondary data came from the HIV/AIDS Information System (SIHA) and medical records to determine the number of patients and duration of ARV therapy.

The hematology profile examination procedure was performed using a hematology analyzer (ZENIX-144). The steps included setting the device to whole blood mode, homogenizing the blood sample, and aspirating the sample using the device. Results included hemoglobin, hematocrit, erythrocyte, leukocyte, and platelet counts. The normal value for hemoglobin in men is 13.0 g/dl and in women 12.0 g/dl. Normal hematocrit in men is in the range of 40-54% and in women 36-46%. The normal erythrocyte count in men is 4.6-6.0 million/ $\mu$ l, while in women it is 4.0-5.0 million/ $\mu$ l. The normal leukocyte count in men and women is 4,500-10,000 cells/ $\text{mm}^3$ , while the normal platelet count for both ranges from 150,000-400,000/ $\text{mm}^3$ .

The data collected in this study were analyzed using computer applications and the Spearman correlation test. This analysis aims to determine the relationship between the duration of ARV therapy and the hematological profile of HIV patients Buntok health center. The research ethics commission of the Poltekkes Kemenkes Banjarmasin approved this research with certificate number 729/KEPK-PKB/2024.

## RESULTS AND DISCUSSION

In this study, 29 patients, namely HIV patients undergoing Antiretroviral (ARV) therapy at Buntok health center, were included. Blood samples of HIV patients were taken for Hematology Profile examination, and HIV patients were also asked to fill out questionnaires that researchers provided as additional data. The following research results are presented in Table 1.

Table 2. The results of the analysis of the characteristics of HIV patients at Buntok health center based on gender, the majority of HIV patients in this study were 20 men (69.0%), adult age as many as 27 people (93.1%). The majority of the last education in this study was SMA 17 people (58.6%). Based on the length of therapy in this study, patients more than 24 months of treatment, as many as 12 people (41.0%), and the type of ARV consumed by HIV patients in this study who consumed TLE as many as 15 people (52.0%).

Table 2. shows the results of the research questionnaire of HIV patients at Buntok health center who had side effects from taking ARVs as much as 62.0%, routinely took medicine 93.0%, took medicine at the same time 69.0%, did not have a history of comorbid diseases 93.0%, smoking habits 66.0%, never had a complete blood test 96.5%, did not often consume foods containing iron 76.0%, felt that the condition improved after ARV therapy 83.0%, rarely exercised 97.0%, sleep duration at night 4-5 hours 44.83% and HIV patients never felt excessive anxiety 93.0%.

Table 1. Characteristics of HIV Patients at Buntok Health Center

Variables	Frequency	Percentage
<b>Gender</b>		
Male	20	69,0
Female	9	31,0
<b>Age</b>		
Adults	27	93,1
Children	2	6,9
<b>Education</b>		
Elementary school	5	17,0
High school	17	58,6
Diploma	1	3,4
Bachelor	6	21,0
<b>Duration of Therapy</b>		
< 12 Months	6	21,0
12-24 Months	11	38,0
>24 Months	12	41,0
<b>ARV Type</b>		
TLE (Tenofovir, Lamivudine, Efavirenz).	15	52,0
TLD (Tenofovir, Lamivudine, Dolutegravir).	12	41,0
Zidovudin, Lamivudin, Evafirenz.	2	7,0

Table 3 shows the mean length of ARV therapy for HIV patients at Buntok health center is 2.24 years with a standard deviation of 0.739 and a range of 1-3 years. The mean hemoglobin was 12.317 gr/dl with a standard deviation of 1.6454 and a range of 9.5-15.7 gr/dl. The mean hematocrit was 34.903%, with a standard deviation of 7.8017 and a range of 24.7-50.8%. The mean erythrocyte count was 4.3697 million/ $\mu$ l with a standard deviation of 0.85116 and a range of 2.81-6.41 million/ $\mu$ l. The mean leukocyte count was 5.74862 thousand/ $\text{mm}^3$  with a standard deviation of 1.633176 and a range of 2,760-8,240/ $\text{mm}^3$ . Meanwhile, the mean platelet count reached 228,931.03/ $\text{mm}^3$  with a standard deviation of 58,730.578 and a range of 145,000-383,000/ $\text{mm}^3$ .

The results of the hematological profile of HIV patients based on the length of ARV therapy in Table 4 show that on therapy <12 months, all patients (100%) have normal hemoglobin, hematocrit, erythrocyte, leukocyte, and platelet levels. At 12-24 months of therapy, decreased hemoglobin, hematocrit, and erythrocyte levels were found in 7 people (58%), while 5 people (42%) remained normal. For leukocyte count, 9 people (75%) were normal, while 3 people (25%) were abnormal.

Table 2. Research Questionnaire Results

Variables	Frequency	Percentage
<b>Side effects of ARVs</b>		
Yes	18	62,0
No	11	38,0
<b>Routinely take medicine</b>		
Yes	27	93,0
No	2	7,0
<b>Take medicine at the same time</b>		
Yes	20	69,0
No	9	31,0
<b>History of other diseases (comorbidities)</b>		
Diabetes mellitus	1	3,5
Hypertension	0	0,0
Hepatitis B or C	1	3,5
No disease	27	93,0
<b>Smoking habit</b>		
smoking	19	66,0
No smoking	10	34,0
<b>Complete blood test</b>		
Ever	1	3,5
No	28	96,5
<b>Eat foods that contain iron</b>		
Often	7	24,0
Not often	22	76,0
<b>Condition improves after ARV therapy</b>		
Yes, very good	3	10,0
Yes, improving	24	83,0
No change	2	7,0
Worsening	0	0,0
<b>Exercise routine</b>		
Every day	0	0,0
4-6 times a week	0	0,0
1-3 times a week	1	3,0
Rarely	28	97,0
<b>Night sleep duration</b>		
8 hours	1	3,45
6-8 hours	12	41,38
4-5 hours	13	44,83
< 4 hours	3	10,34
<b>Ever felt overly anxious</b>		
Ever	2	7,0
No	27	93,0

Decreased platelet count was found in 7 people (58%), while 5 people (42%) were normal. At >24 months of therapy, all patients had decreased hemoglobin, hematocrit, and erythrocyte levels (100%). Decreased leukocyte counts were found in 7 people (58%), while 5 people (42%) remained normal. Decreased platelet counts were found in 8 people (67%), while 4 people (33%) were normal. This data shows a decrease in hematological profile as the length of ARV therapy increases.

Table 3. Descriptive Research Results

Inspection	Total	Minimal	Maximum	Average	Standard deviation
Length of therapy (months)	29	1	3	2.24	0.739
Hemoglobin (g/dl)	29	9.5	15.7	12.317	1.6454
Hematocrit (%)	29	24.7	50.8	34.903	7.8017
Erythrocyte count	29	2.81	6.41	4.3697	0.85116
Leukocyte count	29	2.760	8.240	5.74862	1.633176
Platelet count	29	145.000	383.000	228.93103	58.730578

Table 4. Hematology Profile Results with Length of Therapy

Hematology Profile	Value	Number of Respondents with Length of Therapy		
		<12 months	12-24 months	>24 months
Hemoglobin Level	Normal	5 (100%)	5 (42%)	0
	Decreased	0	7 (58%)	12 (100%)
	Total	5 (100%)	12 (100%)	12 (100%)
Hematocrit Level	Normal	5 (100%)	5 (42%)	0
	Decreased	0	7 (58%)	12 (100%)
	Total	5 (100%)	12 (100%)	12 (100%)
Erythrocyte Count	Normal	5 (100%)	5 (42%)	0
	Decreased	0	7 (58%)	12 (100%)
	Total	5 (100%)	12 (100%)	12 (100%)
Leukocyte Count	Normal	5 (100%)	9 (75%)	5 (42%)
	Decreased	0	3 (25%)	7 (58%)
	Total	5 (100%)	12 (100%)	12 (100%)
Platelet Count	Normal	5 (100%)	5 (42%)	4 (33%)
	Decreased	0	7 (58%)	8 (67%)
	Total	5 (100%)	12 (100%)	12 (100%)

Table 5. Correlation of ARV Therapy Duration with Various Blood Parameters

Spearman correlation test	Correlation coefficient	P value (sig. 2 tailed)
Duration of ARV therapy with hemoglobin	-0,510	0,005
Duration of ARV therapy with hematocrit	-0,569	0,001
Duration of ARV therapy with erythrocyte counts	-0,614	0,000
Duration of ARV therapy with leucocyte counts	-0,350	0,063
Duration of ARV therapy with platelet count	- 0,421	0,023

The data in Table 5 explains the results of the analysis of the relationship between the duration of ARV therapy and various blood parameters. The Spearman test shows that there is a significant relationship between the duration of ARV therapy and hemoglobin levels ( $p = 0.005$ ), with a correlation coefficient of -0.510 at a moderate level. This negative correlation indicates that the longer the ARV therapy, the lower the hemoglobin levels. A similar relationship was found in hematocrit levels, with a significance value of 0.001 and a correlation coefficient of -0.569 at a moderate level, which means that the longer the ARV therapy, the hematocrit levels also decrease. In addition, there is a significant relationship between the duration of ARV therapy and the number of erythrocytes, with a significance value of 0.000 and a correlation coefficient of -0.614 at a strong level, which indicates that the longer the therapy, the lower the number of erythrocytes. However, no significant relationship was found between the duration of ARV therapy and the number of leukocytes, with a significance value of 0.063 and a correlation coefficient of -0.350 at a weak level, although there was a tendency for a decrease in the number of leukocytes. Meanwhile, a significant relationship was found between the duration of ARV therapy and platelet count, with a significance value of 0.023 and a correlation coefficient of -0.421 at a moderate level, indicating that the longer the therapy, the platelet count tends to decrease.

Table 5. Correlation Strength (r. value)

Value of r	Interpretation
0,00-0,199	Very Weak
0,20-0,399	Weak
0,40-0,599	Medium
0,60-0,799	Strong
0,80-1,000	Very Strong

The results of this study indicate a significant relationship between the duration of ARV therapy and hemoglobin, hematocrit, erythrocyte, and platelet levels. However, no significant relationship was found between the duration of ARV therapy and the number

of leukocytes. The correlation found was negative, indicating that the longer the ARV therapy, the more certain hematological parameters decreased.

These results are in line with Duguma's findings, which showed that the prevalence of anemia, leukopenia, and thrombocytopenia was higher before the start of ARV treatment<sup>15</sup>. However, anemia and thrombocytopenia decreased after treatment began. This can be explained by the mechanism of action of ARV which suppresses HIV replication, thereby reducing the destructive effects of the virus on the hematopoietic system. However, the side effects of ARV therapy, especially from regimens containing Zidovudine (ZDV), are known to cause anemia due to myelotoxicity by inhibiting the differentiation of erythroid precursor cells in the bone marrow, which ultimately reduces red blood cell production<sup>16,17</sup>.

In addition to ARV therapy factors, other factors such as HIV enteropathy and intestinal bacterial or viral infections can also affect the hematological profile of patients. HIV enteropathy and other infections can interfere with nutrient absorption through malabsorption mechanisms, which ultimately lead to deficiencies of essential micronutrients for hematopoiesis (18). Intestinal parasite (IP) infestation can also activate this condition by damaging the intestinal mucosal membrane and causing gastrointestinal bleeding and malnutrition due to nutrient competition between the host and the parasite<sup>18</sup>.

Gudina et al. (2024) study also supports these findings, showing that Dolutegravir (DTG)-based therapy for three months can significantly increase the number of white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), CD4 count, and percentage of lymphocytes and neutrophils ( $P < 0.05$ ). However, several hematological parameters, such as red blood cell distribution width (RDW) and mean corpuscular hemoglobin (MCH), decreased after treatment ( $P < 0.05$ ). In addition, this study also revealed that anemia (12.1%) was the most common hematological disorder after the administration of new Highly Active Antiretroviral Therapy (HAART), followed by leukopenia (11.3%), neutropenia (6%), and thrombocytopenia (4%). Anemia in HIV patients undergoing ARV therapy was more common in women, with a significant odds ratio (AOR = 7.8, 95% CI: 1.9–32.2,  $P < 0.005$ )<sup>19</sup>.

Compared with this study, the results of a study at the Buntok Health Center UPT showed a decrease in hemoglobin, hematocrit, erythrocyte, and platelet levels in HIV patients with ARV therapy for more than 24 months. This may occur due to the cumulative effect of long-term treatment, in contrast to the study by Gudina et al. (2024), which began hematological changes in only three months of therapy. This finding is also supported by other studies showing a decrease in the number of erythrocytes after ARV therapy in HIV patients<sup>20,21</sup>.

This study also shows that respondents who were the study samples used an ARV regimen containing Zidovudine (ZDV) and Dolutegravir (DTG), similar to that used in previous studies. Therefore, the results of this study can be confirmed with the findings of previous studies showing that the use of Zidovudine can cause myelotoxicity and anemia due to suppression of erythrocyte production. At the same time, Dolutegravir is associated with changes in certain hematological parameters, including effects on the number of leukocytes and platelets.

In the context of this study, most patients who underwent therapy for more than 24 months experienced decreased hemoglobin, hematocrit, erythrocyte, and platelet levels. This indicates that regular hematological monitoring is very important to detect early side



effects of ARV therapy and prevent further complications. These findings support the recommendation that HIV patients undergoing ARV therapy require routine hematological profile examinations at least every three to six months to ensure the effectiveness of therapy and minimize adverse side effects<sup>14</sup>.

The advantage of this study is its approach that uses primary data from laboratory examinations so that the results obtained are more objective and accurate compared to studies that only use secondary data or interviews. In addition, this study includes several hematological parameters that provide a broader picture of the impact of ARV therapy on the condition of HIV patients. However, this study also has limitations, one of which is the relatively small number of samples, so the results may not be generalizable to a wider population. In addition, this study uses a cross-sectional design that only describes the relationship between variables at one point in time, so it cannot show changes longitudinally. Based on these findings, this study provides implicative suggestions that can be applied in clinical practice, namely the need for regular hematological monitoring for HIV patients undergoing long-term ARV therapy in order to detect early hematological changes that are at risk of causing complications. In addition, there needs to be better nutritional intervention for patients to reduce the risk of anemia and other hematological disorders, as well as education for patients about the importance of therapy compliance and a healthy lifestyle to minimize the side effects of ARVs.

## CONCLUSION

This study shows the relationship between the length of Antiretroviral (ARV) therapy with hematological profile in HIV patients at Buntok health center. Of the 29 patients, the length of therapy was divided into <12 months (21%), 12-24 months (38%), and >24 months (41%) with an average therapy of 2 years and 2 months. Most patients had abnormal hemoglobin, hematocrit, and erythrocyte levels (65.5%), while leukocyte counts were abnormal in 34.5% of patients, and platelet counts were almost balanced between normal (48%) and abnormal (52%). Spearman test showed a significant association between the duration of ARV therapy with hemoglobin, hematocrit, erythrocytes, and platelets, but no significant association was found with the number of leukocytes. We recommend a longer study to evaluate the long-term impact of ARV therapy on hematological profiles.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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