



The Duration of Using ARV Therapy and the Incidence of Anemia in People Living with HIV/AIDS (PLWHA)

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Abstract. Background: Anemia is a hematological complication that occurs in people living with HIV/AIDS (PLWHA). Anemia is multifactorial and can cause a decrease in the clinical condition and quality of life of PLWHA. Anemia that occurs in PLWHA can be influenced by the side effects of using Antiretroviral (ARV) therapy because ARV can inhibit the proliferation of red blood cells based on the duration of therapy. Azidothymidine (AZT) combinations are often associated with anemia, but previous studies have found the incidence of anemia in the Tenofovir Disoproxil Fumarate (TDF) combination as well.

Aim: The aim of this study is to find out the correlation between the duration of using ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA.

Methods: The method of this study is a correlation analysis study with a retrospective method using secondary data, namely medical record data conducted at Public Health Center (Balai Kesehatan Masyarakat).

Results: This study found that 48% of PLWHA experienced anemia. Among them, 31.4% had mild anemia. The incidence of anemia was found to be higher (61.22%) in male. The incidence of anemia in this study was more common among AZT-combined ARV users as 54.4% of PLWHA using AZT experienced anemia. Further, this study found that 50% of PLWHA with ARV along with anti-TB treatment were anemic. All the PLWHA within 6–12 months of ARV therapy had anemia.

Conclusion: There was no significant correlation between duration of using ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA.

Keywords: ARV · Anemia · HIV/AIDS

1 Introduction

Human Immunodeficiency Virus (HIV) is a viral infection that attacks white blood cells, causing a decrease in the immune system and resulting in immunodeficiency [1, 2]. The

decline in the immune system and the development of HIV infection can trigger Acquired Immune Deficiency Syndrome (AIDS); AIDS is characterized by a reduced ability of the immune system to fight infection, causing sufferers to be susceptible to other diseases or infections [3].

In Indonesia there were 7,650 confirmed cases of HIV while 1677 cases had entered the AIDS stage as per data from January to March 2021. Out of all the PLWHA, 6,762 had accessed antiretroviral therapy (ARV) (4).

ARV is a drug therapy for PLWHA that functions to suppress viral growth and inhibit clinical deterioration, but in some conditions the use of Nucleoside Reverse Transcriptase Inhibitors (NRTI) ARVs can cause clinical deterioration due to the side effect of ARVs, namely suppressing the proliferation of red blood cells [4]. Side effects as anemia or decreased Hb levels are also influenced by the long duration of therapy [5]. The duration of ARV therapy at certain doses can cause slow drug decomposition in the blood, causing anemia [6].

Anemia or lack of red blood cells is a clinical manifestation that often occurs in people living with HIV/AIDS (PLWHA) [7]. Anemia that occurs in people living with HIV is a hematological complication that is multifactorial, as HIV infection itself can suppress the process of hematopoiesis [8]. Anemia that occurs in people living with HIV is influenced by several factors such as age, female chlamydia, clinical stages III and IV, AZT type ARV, duration of ARV therapy, use of anti-TB drugs, opportunistic infections, chronic disease, low CD4 cell count, high viral load, and Body Mass Index (BMI) < 18.5 [4, 9, 10].

Previous research in Kendari City found that 6 out of 20 PLWHA adults had low Hb levels. One of the factors that influence the decrease in Hb levels was found to be the length of use of ARV therapy [4]. Recent research conducted at Adam Malik Hospital found 41.4% of PLWHA aged <16 years experienced anemia which was dominated by mild anemia. Anemia was common within 6 months of the use of ARV representing 51.4% of incidence. Also, this study found a relationship between duration of use AZT therapy for anemia [11].

Research in Eutopia related to risk factors for anemia in PLWHA users of AZT and TDF ARV therapy found the incidence of anemia; 20.3% in AZT users and 13.2% in TDF users after taking ARVs for more than 6 months (13). The case-control method research on PLWHA using TDF found Hb levels decreased by 4.2 g/dL after 11 months of ARV and at 5 months of ARVs, Hb levels decreased by 2.2 g/dL, while in PLWHA users on AZT decreased Hb levels by 3,8 g/dL occurs after 6 months of ARV use [12].

Previous research found that one of the factors causing the decrease in Hb levels was the use of ARV therapy which was reviewed based on the duration of therapy, therefore the formulation of the problem was found namely whether there was a correlation between the duration of the use ARV therapy with the incidence of anemia in PLWHA, while this study aimed to see the correlation between the duration of the use of ARV therapy based on the combination of AZT and TDF on the incidence of anemia in PLWHA at Balai Kesehatan Masyarakat Wilayah Semarang (Balkesmas). The findings in this study are helpful for government policyholders and health service providers for PLWHA to take steps to prevent the incidence of anemia in PLWHA and improve the quality of life of PLWHA.

2 Methods

This research is quantitative research with a retrospective correlation analysis method using secondary data. This research was conducted at the Semarang Public Health Center (Balai Kesehatan Masyarakat Semarang) during May-June 2022. This study used a total sampling technique based on inclusion and exclusion criteria. The sample in this study was 102 PLWHA on ARV users of a combination of AZT and TDF who had Hb levels examination results and did not experience anemia before ARV therapy. This study used data from the medical records of 102 PLWHA at Semarang Public Health Center (Balkesmas). Medical record data were collected and transferred into a computer application. The input data included name (initials), age, type of chlamydia, duration of use of ARV therapy, and Hb levels. The collected data were analyzed with statistical applications (SPSS 26 version) on the computer.

This research has received ethical approval from the Health Research Ethics Commission, Faculty of Nursing and Health Sciences, University of Muhammadiyah Semarang, with the number 0021/KEPK/VII/2022.

3 Results

3.1 Characteristics of PLWHA

This study found 102 PLWHA on ARV at Balkesmas Semarang until May 2022, of which 68 (66.7%) PLWHA were male and 24 (33.3%) PLWHA were female. The mean age of PLWHA in this study was 41.17 years with SD 11.28. The minimum and maximum age of PLWHA was 8 years and 79 years. Majority of PLWHA were from adult age group with 36.3% of late adults and 24.5% early adults. The type of combination ARV used by PLWHA included AZT combination ARV 64.7%, and TDF combination ARV 35.3%. Further, 33.3% PLWHA used anti-TB drugs along with their ARV combinations (Table 1).

3.2 Incidence of Anemia

This study found that, out of 102 PLWHA, 48% PLWHA had anemia with an average (\pm SD) Hb level of 12.92 ± 2.30 . Majority (31.4%) had mild anemia. Female represented 39.58% of anemia incidence with mean Hb level of 11.85 (SD = 1.67) while 61.22% of anemia incidence occurred among male with mean Hb level of 13.45 (SD = 2.40). Also, 55.9% of participating women and 44.1% of participating male had the incidence anemia.

The incidence of anemia in AZT-combined ARV users is 54.5%, which is greater than the incidence of anemia in TDF-combined ARV users, which is only 36.1%, while the incidence of anemia in ARV combined with anti-TB users is 50% (Fig. 1).

The duration of use of ARV therapy among PLWHA in May 2022 had an average value of 54.05 (SD = 37.54). The minimum and maximum duration of use of ARV therapy were one month and 154 months (12 years). Data suggests that all the PLWHA during the time of 6–12 months of ARV had anemia. Among them 57.1% had mild anemia, 28.6% had moderate anemia and 14.3% had severe anemia (Fig. 2).

Table 1. Characteristic of PLWHA

Category	n	%
Gender		
Male	68	66,7
Female	34	33,3
ARVs Combination		
AZT combination	66	64,7
TDF combination	36	35,3
AZT and TDF + Anti TB	34	33,3
Age Category ^a		
Child (5–11 years old)	2	2,0
Late teens (17–25 years old)	3	2,9
Early adulthood (26–35 years old)	25	24,5
Late adulthood (36–45 years old)	37	36,3
Early elderly (46–55 years old)	24	23,5
Late elderly (56–65 years old)	10	9,8
Seniors (>65 years old)	1	1,0

a: Depkes RI, 2009

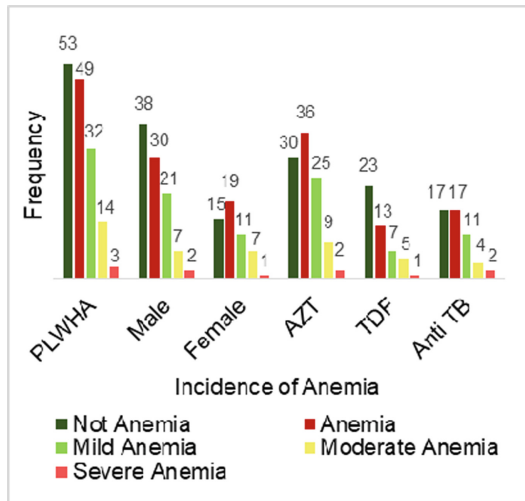


Fig. 1. Incidence of Anemia

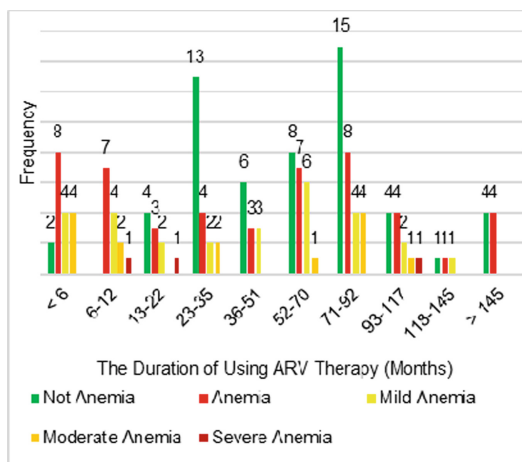


Fig. 2. Anemia Incidence Based on Long Use of ARV Therapy (Months)

Table 2: Correlation Analysis

Indicator	Regression Coefficient	P
Duration of Use of ARV Therapy Based on Combination of AZT and TDF	0,110	0,272 ^a
Duration of Use of AZT Combination ARV Therapy	0,034	0,789 ^b
Duration of TDF Combination ARV Therapy	0,196	0,253 ^b

a: Sperman’s Rho, b: Pearson Correlation

3.3 Correlation Analysis

The results of the correlation analysis between the duration of use of ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA in this study found that there was no significant correlation between the length of use of ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA with p -value = 0.272 (Table 2).

4 Discussion

4.1 Characteristics of PLWHA

This study found that HIV/AIDS sufferers were dominated by male sex representing 66.7% of total sample. This is in accordance with reports related to the incidence of HIV/AIDS in Indonesia for the period January to March 2021 which reported that PLWHA was dominated by men because they had the behavior of risky sexual [13]. The results of this study are similar to previous studies conducted in Nepal confirming

that the majority of PLWHA are male [14]. While another study in Ethiopia found that majority of PLWHA were female [15].

In this study majority (64.7%) of ARV included combination with AZT which is in line with previous research findings suggesting that the combination of AZT was more widely used [16]. The results of this study are different from other studies which state that the combination of AZT is rarely used because it can trigger anemia [17]. The combination of AZT is the main combination that is often recommended by the government for people living with HIV without blood and liver problems, although in some conditions AZT can trigger side effects such as anemia [18, 19]. This study found that as many as 33.3% of PLWHA used anti-TB drugs, previous studies found that 40% of PLWHA were positive for TB and used anti-TB drugs [11].

In this study majority of PLWHA were from adult age group with 24.5% from early adulthood and 36.2% from late adulthood. This study is similar to previous research which found that most of PLWHA were adults because adulthood is a sexually active period which is a risk factor for HIV/AIDS [19–21].

4.2 Incidence of Anemia

The results of this study found that as many as 48% of PLWHA on ARV experienced anemia, this study was supported by findings in previous studies that the incidence of anemia in PLWHA on ARV was still relatively high [22]. The high incidence of anemia in PLWHA is influenced by several factors such as the high clinical stage that can cause anemia because HIV can increase the production of pro-inflammatory cytokines which indirectly suppress the process of hematopoiesis [23]. The high clinical stage can reduce the CD4 count so that opportunistic infections appear which indirectly trigger anemia [24, 25]. Opportunistic infections such as TB and the use of anti-TB drugs can cause anemia due to malabsorption of nutrients [26].

Among enrolled women 55.9% had anemia while among enrolled male 44.1% had anemia. Previous studies also found that women were susceptible for anemia because women had risk factors for anemia such as menstruation and pregnancy [14].

This study found that the incidence of anemia was more common (54.5%) in PLWHA using AZT combination ARV, this was supported by previous studies which found that anemia was more common in AZT users than TDF because the AZT combination has the potential to inhibit the proliferation of red blood cells [25, 27]. The incidence of anemia in anti-TB users in this study was 50%, this is in line with previous studies which found that anemia in anti-TB users was 42.9% [11]. HIV infection and TB infection have a close relationship because HIV infection can cause TB infection while TB infection is an early manifestation of the AIDS stage [28].

Among anemic PLWHA, majority (31.4%) had mild anemia. Also, among PLWHA with ARV combination with AZT, 37.9% had mild anemia while 19.4% of PLWHA receiving ARV combination TDF had mild anemia. This study is in line with previous studies which found that the incidence of mild anemia dominated in PLWHA using AZT and TDF [25].

The Incidence of Anemia based on The Duration of ARV Therapy Use are all the PLWHA receiving ARV therapy for 6–12 months had anemia. Among them 57.1% had mild anemia, 28.6% had moderate anemia, and 14.3% had severe anemia. Among PLWHA receiving ARV therapy for less than 6 months, 80% had anemia; 40% had mild anemia and another 40% had moderate anemia. While the incidence of mild anemia occurred in 100% of PLWHA with ARV therapy duration >145 months. Previous studies have found that AZT can cause anemia at 3 months after taking ARV therapy [19]. Another study found that 75% of PLWHA using ARVs experienced anemia after >6 months of taking ARVs, while chronic anemia was found in 2.2% of PLWHA who did not experience anemia at the beginning of taking ARV [9]. Another study also found the highest incidence of anemia occurred in ARV use >6 months, the incidence of anemia that occurred >12 months on ARVs was associated with anemia during 6 months of ARV therapy [15]. 3–6 months of ARV use is expected to create clinical improvement, but 3–6 months of ARV use is also a time where therapy failure or drug toxicity can occur, causing clinical worsening such as anemia, if clinical deterioration is detected, changes are recommended ARV therapy line [18].

4.3 Correlation Analysis

This study did not find a significant correlation between the duration of use of ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA. This study excluded PLWHA who experienced anemia before ARV therapy. This study is in line with previous studies, which also did not find a correlation between the duration of therapy and the incidence of anemia, but this study did not exclude the incidence of anemia before ARV therapy [23]. Different studies have found that prolonged use of ARV therapy can cause a decrease in Hb levels [4]. Another study found that one of the factors associated with anemia in children less than 16 years old with HIV/AIDS was the duration of therapy more than six months [11].

This insignificant correlation can be caused by the occurrence of anemia which is more common in the duration of short-term ARV use, which is <52 months (4 years) compared to long-term ARV use >52 months (4 years). The high incidence of anemia during short-term use of ARVs can be influenced by the unfavorable clinical condition of people living with HIV, characterized by low CD4 cell counts, high viral loads, opportunistic infections, and poor nutritional status. Previous studies have found that a decrease in CD4 cell count is in line with a decrease in Hb levels exacerbated by malnutrition in people living with HIV [29]. Another study found that an increase in CD4 cell count began to be seen in ARV use >18 months [30]. This study found that the incidence of anemia in long-term use of ARVs was lower, perhaps because people living with HIV had experienced many clinical improvements.

5 Conclusions

The results of this study found that 66.7% of PLWHA were male and the combination of AZT was more widely used by PLWHA as much as 64.7%. The incidence of anemia in this study was found to be 48% and was dominated by mild anemia. The incidence

of anemia was more common in PLWHA using AZT 54.5% compared to TDF users, while the incidence of anemia in anti-TB users along with ARV therapy was 50%. This study found that there was no significant relationship between the duration of use of ARV therapy based on a combination of AZT and TDF on the incidence of anemia in PLWHA. For health service providers, related parties need to educate about the side effects of using ARV therapy that triggers anemia and conducts regular reviews or screening within 3–6 months to anticipate the occurrence of worse anemia. Furthermore, the researcher advises PLWHA to control the side effects of ARVs and prevent anemia by consuming nutritious foods that are also high in iron.

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