



## Relationship Between Multimorbidity, Nutritional Status and Duration of ARV Treatment to Major Signs of HIV at RSUD Dr. Soetomo Surabaya

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### Abstract

People living with HIV/AIDS (PLWHA) can have better health outcomes with early identification of the AIDS phase. In the first three years, PLWHA may progress to the AIDS stage. This cross-sectional study aimed to determine the relationship between multimorbidity, nutritional status and duration of Antiretroviral (ARV) treatment on major signs of PLWHA. This study was conducted in the Intermediate and Infectious Disease Treatment Unit (UPIPI) at regional public hospital (RSUD) Dr. Soetomo Surabaya from January to February 2023. As many as 52 PLWHA who started HIV treatment at RSUD Dr. Soetomo in 2020 to 2021 were sampled in this study, which was obtained from medical records. The dependent variable in this study was the major sign of HIV. Independent variables in this study were multimorbidity, nutritional status, and the duration of ARV treatment. This study found that 76.9% of PLWHA experienced major signs. Multimorbidity and duration of ARV treatment did not have an association with major signs of HIV ( $p$ -value  $> 0.05$ ). Nutritional status has a significant association with major clinical symptoms of HIV ( $p$ -value  $< 0.05$ ). PLWHA with underweight had higher odds of having a major sign ( $p$ -value = 0.017; PR = 1.507; 95% CI 1.131-2.008) than PLWHA with normal nutritional status. Thereby, it is hoped that the hospital will be assisted in determining health promotion needs such as screening and evaluation of nutritional status to monitor the nutritional status of patients, which will improve their health outcomes.

**Keywords:** ARV; major clinical signs for HIV/AIDS; multimorbidity; nutritional status; PLWHA

### INTRODUCTION

Since it was first discovered, HIV infection has been recognized as an epidemiological problem that is highly deadly and poses a danger to many countries around the world (Tesiman et al., 2017). Currently, no country is free from HIV/AIDS because this disease can cause multidimensional crises, including health, economic and humanitarian crises (Suharto et al., 2020). Older people living with HIV/AIDS (PLWHA) had a faster chance of progressing to the clinical stage of AIDS within 35 months (Munfaridah and Indriani, 2017). PLWHA will

enter the AIDS phase in the first three years, and the risk of getting AIDS is higher after ten years (Poorolajal et al., 2016). Early diagnosis of the AIDS phase is crucial. Most HIV-positive individuals will not develop to the AIDS stage and will live relatively everyday lives if they receive an early diagnosis and adequate therapies (Poorolajal et al., 2016).

Several factors affect HIV progressivity, including nutritional status, opportunistic infections, CD4 count, genetic factors and Antiretroviral (ARV) adherence (Rope, 2019;

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Candramawa, 2020; Supriono, 2020; Gayatri et al., 2021). The Indonesian AIDS Commission (KPA) describes the diagnosis of AIDS according to the World Health Organization (WHO) criteria established for epidemiological surveillance purposes. AIDS diagnosis is based on clinical symptoms, including major and minor signs. Individuals diagnosed with AIDS have a positive HIV test result and suffer from at least two major signs or one major sign and two minor signs (WHO, 2016). It can be concluded that the emergence of major signs is an early marker of HIV progressivity toward AIDS. The major signs include weight loss exceeding 10% in one month, chronic diarrhea for more than one month, prolonged fever for more than one month, loss of consciousness and HIV encephalopathy or dementia (Hidayati and Barakbah, 2018).

According to data from the United Nations Program on HIV/AIDS (UNAIDS) in 2021, the number of people with HIV/AIDS in the whole world amounted to 37.7 million. Global data shows that Southeast Asia is the second region with the highest HIV/AIDS-infected population, at 3.8 million people. A rapidly increasing HIV/AIDS epidemic is occurring among vulnerable populations in various countries, one of which is Indonesia, with a prevalence of 46.3% (UNAIDS, 2021). HIV/AIDS cases in Indonesia have tended to increase in the last 11 years. The number of PLWHA in Indonesia, classified by province in January to March 2021 was 7,650, with East Java Province as the province with the most cases (Directorate General of Diseases Prevention and Control, 2021). Data from the East Java Provincial Health Office stated that there was an increase in the number of new AIDS cases, from 470 in 2020 to 544 in 2021. In addition, there was also an increase in AIDS deaths; in 2020, there were 4,464 deaths, while 4,561 deaths in 2021. The rise in HIV/AIDS cases in East Java is dominated by several districts and cities, one of which is Surabaya City.

The higher incidence of HIV/AIDS also leads to a higher chance of multimorbidity among PLWHA, and the older the patient, the higher the prevalence of multimorbidity in PLWHA. Multimorbidity, or coexistence, is a condition where a person experiences two or more chronic conditions and has a special impact on safety issues (Sukumaran and Sabin, 2023). Multimorbidity has accounted for more than half of deaths in PLWHA (Pourcher et al., 2020).

Another factor that can affect the severity of clinical signs in HIV/AIDS patients is their nutritional status (Madhu et al., 2022). Nutritional status can be used to determine the progression of the disease, the functional status of all stages, and the quality of life of HIV/AIDS patients (Hanifa and Mahmuda, 2020). Adequate nutrition is a major factor in maintaining health and enhancing optimal immune function. This nutritional support can improve the clinical response of PLWHA and inhibit the progression of HIV/AIDS, which in turn can improve the quality of life and minimize deaths from HIV/AIDS (Amelia, 2021). The study of Diouf et al. (2016) proves that the energy intake of 100 g of ready-to-use peanut-based therapeutic food (RUTF), a type of agricultural food, is proven to be sufficient to optimize the use of other nutrients, which causes a significant increase in body mass, perhaps due to the amount of energy supplied by 100 g of RUTF (> 500 kcal). It is known that energy density is a determining factor in food consumption and can increase the chances of nutritional recovery in HIV-infected patients with severe malnutrition in Sub-Saharan Africa with a body mass index (BMI) of less than 17 kg m<sup>-2</sup> (Bolhuis and Forde, 2020).

Until now, there has been no known vaccine or drug to cure HIV/AIDS. However, to suppress the number of viruses, people with HIV/AIDS must take an ARV. ARV treatment is part of HIV/AIDS treatment to reduce the risk of HIV transmission, inhibit the worsening of opportunistic infections, improve the quality of life of HIV patients, and suppress the amount of virus (viral load) in the blood until it is undetectable (Ministry of Health, 2014). The CD4 count in PLWHA will increase during the first six months of taking ARVs. With reduced virus replication, T-CD4 lymphocytes will rise to protect the body's immune system from damage (Marta, 2019). ARV treatment can reduce viral load, prevent the worsening of HIV signs and symptoms, slow down disease progressivity, and improve the body's immune system. From year to year, there has been an increase in the use of ARVs in patients with HIV or AIDS. A total of 6,762 out of 7,650 people with HIV/AIDS received ARV treatment in 2021 (Directorate General of Diseases Prevention and Control, 2021).

The Ministry of Health of the Republic of Indonesia has established regional public hospital

(RSUD) Dr. Soetomo as a referral center for HIV/AIDS services and prevention since 2010. In 2018, the incidence of HIV was the third highest in the Outpatient Installation, with a total of 4,962 cases. In addition, there were 23,306 visits in 12 months. Based on the 2019 Internal Performance Report, it is known that there was an increase in HIV/AIDS case visits at the Intermediate and Infectious Disease Treatment Unit (UPIPI) of RSUD Dr. Soetomo Surabaya compared to 2018. Meanwhile, in 2020 to 2021, there were around 2,400 monthly visits for treatment and self-examination (RSUD Dr. Soetomo, 2019). So, it can be concluded that RSUD Dr. Soetomo Surabaya has handled many HIV/AIDS cases, and there is still limited research that discusses the determinants of the appearance of major clinical symptoms, which are one of the early markers of the AIDS phase. The majority of previous studies focused more on the determinants of HIV, AIDS and mortality, even though early detection of major clinical symptoms is important to anticipate mortality and death due to AIDS. Therefore, it is necessary to conduct a study to create a good health promotion strategy for HIV patients to prevent AIDS by knowing the relationship between the history of multimorbidity, nutritional status, and duration of ARV treatment and major signs in PLWHA at RSUD Dr. Soetomo Surabaya.

## MATERIALS AND METHOD

This cross-sectional study was conducted in the UPIPI RSUD Dr. Soetomo, Surabaya, from January to February 2023. All HIV/AIDS patients who enrolled in their first HIV treatment at RSUD Dr. Soetomo in 2020 to 2021 were the study population in this research. The inclusion criteria that were used to select the sample were at least 20 years old and had not been diagnosed with AIDS when they were registered as HIV/AIDS patients. Patients who had missing data and whose medical records were not found were excluded. As many as 52 patients who met the inclusion and exclusion criteria were enrolled purposively as a sample study.

A major sign of HIV was the dependent variable. Meanwhile, the independent variables in this study consisted of multimorbidity, nutritional status and duration of ARV treatment. All data from each variable were collected from medical records. Patients were considered to

have major signs of HIV if they experienced any of the following signs: i.e., weight loss of more than 10% in one month, chronic diarrhea for more than one month, prolonged fever for more than one month, consciousness loss, dementia or HIV encephalitis (Ngoma, 2010; Hadiatma and Triyono, 2023). Multimorbidity was classified into two categories: patients with two types and patients with more than two health problems (Sukumaran and Sabin, 2023). Nutritional status was calculated based on the BMI. Patients were categorized as underweight if their BMI was less than  $18.5 \text{ kg m}^{-2}$  and standard if the BMI was around  $18.5$  to  $25 \text{ kg m}^{-2}$  (Minister of Health, 2014). Meanwhile, the duration of ARV treatment was categorized into 13 to 24 months and 25 to 36 months (Nurmawati et al., 2019). Univariate analysis was conducted to present the distribution of respondents' characteristics in the frequencies and percentages. The association between independent and dependent variables was assessed using Chi-Square with a 5% alpha and 95% confidence interval. This research had fulfilled the Ethical Clearance by the Ethics Committee of RSUD Dr. Soetomo with certificate number 0590/KEPK/II/2023.

## RESULTS AND DISCUSSION

This study enrolled 52 patients as a sample. Most patients were male (76.9%) and aged between 20 and 40 (61.5%). This study also found that all the respondents had multimorbidity, and more than half had more than two health problems or chronic conditions (63.5%). Based on nutritional status, respondents had a normal nutritional status of 57.7%. However, respondents who were underweight reached 42.3%. All the respondents had received ARV treatment. The majority of them had accessed ARV treatment around 25 to 36 months (76.9%). The result of major sign identification among the respondents showed that more than three-quarters of respondents experienced major signs (76.9%). The distribution characteristics of respondents are presented in Table 1.

As previously mentioned, all respondents had co-morbidities other than HIV/AIDS. The co-morbidity that most respondents suffered from was tuberculosis (65%), anemia (32.7%) and visual impairment (25%). Other comorbidities suffered by respondents can be seen in Table 2.

Table 1. Characteristics of respondents

Variable	Category	Frequency	Percentage (%)
Gender	Male	40	76.9
	Female	12	23.1
Age	20 – 40 years	32	61.5
	> 40 years	20	38.5
Multimorbidity	2 health problems	19	36.5
	> 2 health problems	33	63.5
Nutritional status	Underweight	22	42.3
	Normal	30	57.7
Duration of ARV treatment	13 – 24 months	12	23.1
	25 – 36 months	40	76.9
Major sign	Yes	40	76.9
	No	12	23.1
Total		52	100.0

Table 3 presents the association between independent variables and the outcome. It was known that as many as 84.8% of HIV/AIDS patients who had more than two health problems experienced major signs among patients who only experienced two types of comorbidities—as many as 63.2% experienced major signs. However, the difference was not statistically significant ( $p$ -value = 0.095). Multimorbidity had no significant association with the occurrence of major signs among HIV/AIDS patients. The duration of ARV treatment was also found not to be statistically associated with the occurrence of major signs ( $p$ -value = 0.253). The proportion of major sign occurrences in the group who had only been taking ARV for two years and the group who had been taking it for more than two years did not differ significantly. Of the three independent variables, only nutritional status had an association with the occurrence of major signs. Underweight respondents had 1.5 times higher odds of experiencing major signs than respondents with normal nutritional status ( $p$ -value = 0.017; PR 1.507; 95% CI 1.131–2.008).

#### Association between multimorbidity and major signs

The results of this study explained that there was no relationship between a history of multimorbidity and major clinical signs in PLWHA. Multimorbidity is often described as two or more chronic disease conditions diagnosed in an individual (Brown and Guaraldi, 2016). The findings of this study are in line with the research of Wong et al. (2017) that there is no relationship between a history of multimorbidity and the

severity of HIV, including the clinical manifestations suffered by sufferers which are caused by the early initiation of ARV therapy, which then results in an improved quality of life for PLWHA (Wong et al., 2017). With the improvement in HIV-infected individuals' survival, the probability of other diseases is increasing, like in the general population (Lerner et al., 2020). According to reports from the WHO, ARV may affect and progress non-communicable diseases that can cause a multimorbidity (Hadavandsiri et al., 2023). ARV consumption is proven to be able to increase the appetite of every HIV/AIDS patient, which will improve the patient's nutritional status (Iheme, 2023).

Concerning the results of this study, most patients had normal nutritional status. The survey by Iheme (2023) also states that HIV/AIDS patients with normal nutritional status who experience multimorbidity have a low risk of experiencing HIV/AIDS severity. Meanwhile,

Table 2. Co-morbidities suffered by respondents

Co-morbidities	Frequency	Percentage (%)
Tuberculosis	32	65.0
Anemia	17	32.7
Visual impairment	13	25.0
Myalgia	7	13.5
Joint pain	6	11.5
Respiratory disorders	6	11.5
Metabolic syndrome	5	9.6
Mental health disorders	4	7.7

based on the results of this study, it was also found that as many as 65% of HIV patients also had tuberculosis, which means that these patients were also undergoing TB-HIV treatment. In 2015, the success of TB-HIV treatment reached 88.5% (Ambadekar et al., 2015; Ali et al., 2016). In addition to reducing the severity of HIV, early initiation of ARV therapy has also been shown to improve the quality of life of TB-HIV patients. It is supported by the consumption of anti-tuberculosis drugs (OAT) with good medication adherence (Aung et al., 2019). The study from Kamkuemah et al. (2022) shows that beyond healthcare, the findings of high levels of food insecurity and multidimensional poverty reinforce the need to address the social, economic, and environmental exposures that coexist with and perpetuate non-communicable disease risk that can cause a multimorbidity.

**Association between nutritional status to major signs**

The results of this study explained that there is a relationship between nutritional status and major clinical signs. The study by Gebremichael et al. (2018) also demonstrated that malnutrition and food insecurity are associated with increased mortality and poor clinical outcomes among individuals with HIV/AIDS. Nutritional problems have been proven to be significant and contribute to morbidity and mortality in people with HIV/AIDS. The study by Gizaw et al. (2018) stated that people who are well-nourished are less likely to develop AIDS more quickly, but the opposite is true for people who are malnourished because their bodies are too weak to fight infections. So, it proves that nutritional status is associated with the occurrence of major

clinical signs. Nutritional status modulates the immunological response to HIV infection, influencing symptoms as well as overall manifestations (Jesson and Leroy, 2015; Muenchhoff et al., 2018). Undernutrition is the major factor in ensuring treatment effectiveness and thus, nutritional assessments, care and support for HIV/AIDS patients should be strengthened (Daka and Ergiba, 2020).

Referring to Table 3, it is known that 95.5% of patients with a low nutritional status experience major clinical sign. The nutritional status of HIV patients is a matter that must be reviewed in more detail in their treatment because it is related to the patient’s functional status, disease progression, survival and quality of life (Rezazadeh et al., 2023). Poor nutritional status in HIV patients is caused by inadequate nutritional intake, especially energy and protein, changes in the body’s metabolic rate, changes in the performance of the digestive system, and the effects of drugs with nutrients, which then cause malnutrition, which worsens immunity, increases the risk of opportunistic infections, and reduces the ability to absorb ARVs. Therefore, poor nutritional status in HIV patients can accelerate the progression of the disease to AIDS, increase mortality and lower life expectancy (Dewi, 2017; Tesiman et al., 2017).

**Association between duration of ARV treatment to major signs**

The results of this study explained that there was no relationship between the duration of ARV treatment and major clinical signs. The results of this study are in line with research conducted in Vietnam, which found that in the first year of ARV treatment, there was a decrease in quality of

Table 3. Association between multimorbidity, nutritional status and duration of ARV treatment with major sign

Variable	Major sign				p-value	PR	95% CI
	Yes		No				
	n	%	n	%			
Multimorbidity							
> 2 health disorders	28	84.8	5	15.2	0.095	0.744	0.513 – 1.080
2 health problems	12	63.2	7	36.8			
Nutritional status							
Underweight	21	95.5	1	4.5	0.017	1.507	1.131 – 2.008
Normal	19	63.3	11	36.7			
Duration of ARV treatment							
13 – 24 months	11	91.7	1	8.3	0.253	1.264	0.979 – 1.633
25 – 36 months	29	72.5	11	27.5			

life. This condition was also due to the side effects experienced by patients observed in Vietnam and several other regions. So, it proves that the longer duration of giving ARVs can also worsen the quality of life of HIV patients and make them vulnerable to a more severe condition (Tran, 2012). It can be said that treatment with a long duration cannot always have a good impact on the patient. A study by Liping et al. (2015) stated that the duration of ARV treatment did not describe a significant relationship with the increased quality of life of PLWHA, including the clinical manifestations they suffered, which are caused by individual immunity, poor medication adherence, drug side effects and the patient's nutritional status (Karyadi, 2017; Nugroho and Wardan, 2021; Novita, 2022).

The level of CD4 cell count is an important immunological parameter to assess the effect of ARV therapy (Iheme, 2023). The CD4 growth rate was high during the first year of ARV consumption (Liping et al., 2015). Still, it would fluctuate due to changes in immune function, medication non-adherence, drug side effects, and other factors. It will, of course have an impact on the quality of life of every patient, including clinical manifestations and disease progression towards the AIDS phase. Therefore, the effect of the duration of giving ARVs to each individual will be different (Liping et al., 2015). It can be concluded that the duration of ARV treatment does not affect the emergence of major clinical signs suffered by HIV patients.

### Limitation and implications

This study only used two years, so the sample size was relatively small. It cannot represent the population. However, the association between nutritional status and a major sign found in this study had a statistical power of 82%. The results of this study can be used to help determine the health promotion needs of HIV patients to prevent AIDS. Patients with poor nutritional status can be given special nutrition screenings routinely and continuously. It can inhibit the progression of the disease towards AIDS.

### CONCLUSIONS

This study found that multimorbidity and nutritional status did not have an association with the occurrence of major signs among PLWHA. Only nutritional status had an association with it. Being underweight made them more likely to

experience major signs. Monitoring the nutritional status of PLWHA should be carried out optimally to help reduce the risk of major sign occurrences and improve their quality of life. Further studies are needed to consider other factors, such as each patient's diet and medication adherence.

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