

Conference Paper

Functional Status and Incidence of Loss to Follow-up after Antiretroviral Therapy Initiation

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Abstract

Taking medication for lifetime puts Human Immunodeficiency Virus (HIV)-infected patients in challenging situations. The loss to follow-up (LTFU) is a major problem arising from their non-compliance. Information about functional status as a predictor of LTFU is limited. Therefore, this study was aimed to identify the association between the functional status and the incidence of LTFU among HIV patients at Saiful Anwar General Hospital, Indonesia. A retrospective cohort study was conducted in the tropical diseases and infections division of the Saiful Anwar General Hospital by observing 148 HIV patients who were diagnosed in 2015. Data were collected based on existing data in medical records. The log-rank test was used to compare the time of LTFU between groups. Cox proportional hazard was used to determine the effect of functional status after being controlled by other variables. This study found that 65.9% of HIV patients were able to retain on antiretroviral therapy for 39 months. Functional status had a significant association with the time LTFU occurred. Ambulatory patients had a higher risk of experiencing LTFU than working functional status (AHR = 2.289; 95% CI 1.106–4.738; p -value = 0.026). Identifying the patient's characteristic that has a higher risk of LTFU helps to determine the right strategy to ensure treatment adherence.

Keywords: antiretroviral therapy (ART), functional status, HIV, loss to follow-up (LTFU), Indonesia

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1. Introduction

The number of people infected with Human Immunodeficiency Virus (HIV) worldwide until 2019 has reached 75.7 million and 32.7 million of them died [1]. In 2019, it is estimated that around 1.2-2.2 million people are newly infected with HIV [1]. Asia and the Pacific region has a significant increase in HIV cases every year [1]. Nearly, 5.8 million people in that region are living with HIV in 2019, but only 60% of them accessed

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ARV treatment [1]. This is still very far from the WHO target, where 90% of people who know their HIV status should be able to access ARV treatment [2].

Nationally, the trend of newly HIV infected cases that are reported from year to year continues to decrease [3]. However, the number of HIV cases that die because of AIDS-related has increased by almost 60% in the last decade [3]. From 2005 – 2017, the cumulative number of HIV cases reached 280,623 people and 102,667 of them entered the AIDS phase [4]. The burden of this disease is getting heavier considering that only 17% of people who knew their HIV status had accessed the treatment [3]. It means that there are still 83% of people living with HIV (PLHIV) who have not received ARV treatment so the risk of HIV transmission in the community is very high.

To end HIV/AIDS epidemic, the strategies implemented are providing the widest possible access to PLHIV to find out their infection status, get ARV treatment, and successfully suppress the development of the virus after ARV initiation [2]. Indonesia's achievements in handling HIV/AIDS cases are still very far from the 90-90-90 target [3]. The Indonesian government continues to strive for achieving this target by optimizing the "test and treat" program. A loss to follow-up (LTFU) is a serious threat that can affect the success of HIV treatment programs. LTFU can lead to an increased risk of mortality, morbidity, drug resistance, and transmission of HIV/AIDS [5–8]. On average, LTFU occurs in 20% of PLHIV that initiate the ARV treatment [9]. Several previous studies also found that 4.3 - 56% of patients who were on ARV treatment were at risk for LTFU [10–14].

Functional status is known as a predictor of LTFU after ARV initiation [11–13,15–17]. However, most of the studies were conducted in the African region [11–13,15–17]. Studies that are conducted in countries with a high HIV burden in the Asian region are still limited. The findings of previous studies were also inconsistent. Some studies reported that ambulatory and bedridden had a higher risk of loss to follow-up from the treatment [11, 13, 15] whereas another study found the opposite result [12].

East Java is one of province in Indonesia that had the highest number of HIV cases [18]. The total HIV cases in that province are 43,399 people [18]. Saiful Anwar General Hospital is one of the HIV/AIDS referral hospitals in East Java Province. The association between functional status and LTFU after ARV initiation has not been identified. Hence, this study was carried out to assess the relationship between these two variables controlled by other covariate variables. Identifying the patient's characteristic that has a higher risk of LTFU helps to determine the right strategy to ensure treatment adherence.

2. Material and Method

The study design that was used in this study was a retrospective cohort study. This study was conducted at Saiful Anwar General Hospital, Malang. The population of this study was all of HIV/AIDS patients that were diagnosed in 2015 and registered at the medical record of Saiful Anwar General Hospital. The inclusion criteria used for selecting the exposed and unexposed groups were HIV patients that received first-line treatment. The exposure categories were classified based on the functional status of the patient at the start of ARV treatment. Patients with working status were categorized as the unexposed group while patients with ambulatory and bedridden status were classified as the exposed group. Patients who had incomplete data were excluded. Based on these inclusion and exclusion criteria, only 148 patients were enrolled in the study.

All the data were obtained from medical records. The outcome of this study was the time of LTFU. If the patients had not visited for three consecutive months after the last visit, they were categorized as LTFU [11, 12]. Functional status was a variable of interest in this study. Functional status was based on the baseline assessment of the patient when they started ARV treatment, namely working, ambulatory, and bedridden [11, 19]. Other covariates for which data were also collected in this study included sex, age, CD4 count, clinical stage, regimen, and opportunistic infection status.

The statistical analysis that was used to describe the cumulative probability of LTFU on HIV/AIDS patients and determine the relationship between the main independent variable and outcome variable was Kaplan Meier survival analysis and Cox Regression.

3. Results

Most of the HIV/AIDS patients in Saiful Anwar General Hospital were male (66.8%) and young. As many as 44.59% of them were under 30 years old, and 37.16% of patients were 31-44 years old. Based on their functional status, most of the patients had a working status (72.2%). This proportion was also almost the same as the number of patients who had CD4 levels < 200 cells/mm³ (72.97%). The assessment of the patient's clinical status at diagnosis showed that most of the patients were in stage III (35.8%) and IV (27.0%). As many as 29.7% of patients reported having opportunistic infections, such as candidiasis, diarrhoea, cryptococcal meningitis, pneumocystis pneumonia, cytomegalovirus, herpes zoster, herpes simplex, toxoplasmosis, or hepatitis. Based on the type of regimen consumed, 70.94% of patients were taking the TDF + 3TC + EFV regimen, and 18.91%

of them were taking the AZT + 3TC + NVP regimen. The characteristics of the study participants were shown in Table 1.

TABLE 1: The characteristics of HIV/AIDS patients in Saiful Anwar General Hospital.

No.	Variable	Frequency (n)	Percentage (%)
1	Sex		
	Male	99	66.8
	Female	49	33.1
2	Age (yr)		
	<30	66	44.5
	31–44	55	37.1
	>45	27	18.2
3	Functional status		
	Working	107	72.2
	Ambulatory	22	14.8
	Bedridden	19	12.8
4	CD4 count		
	<200 cell/mm ³	108	72.9
	>200 cell/mm ³	40	27
5	Clinical stage		
	I	34	22.9
	II	21	14.1
	III	53	35.8
	IV	40	27
6	Opportunistic infection status		
	Yes	44	29.7
	No	104	70.2
7	ART regimen		
	AZT+3TC+NVP	28	18.9
	AZT+3TC+EFV	12	8.1
	TDF+3TC+EFV	105	70.9
	Others	3	2.1

Source: Author's own work.

Based on the survival analysis with the Kaplan Meier method, the probability of the patient remaining on ARV treatment in the first ten months was 76.1%. In the next ten months, it decreased to 70.4%. The probability of HIV patients staying on ARV treatment continued to decline in the third ten months to 69.5%. At the end of the 39 months of observation, it was found that 65.9% of patients were still adhering to ARV treatment. The result of this survival analysis was shown in Figure 1.

Based on the functional status of HIV patients, Kaplan Meier graph showed that the probability of patients with working status staying on ARV treatment for 39 months was

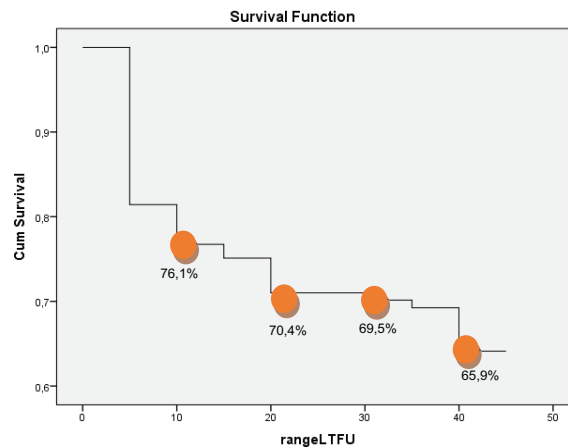


Figure 1: Survival estimate for LTFU. (Source: Author’s own work.)

71.5%, in patients with ambulatory status was 40%, and in patients with bedridden status was 60%. In all groups, the majority of LTFU events occurred in the first ten months of ARV treatment (Figure 2).

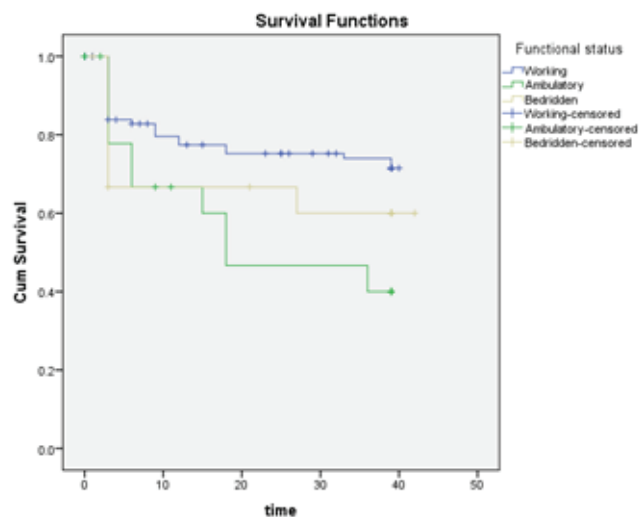


Figure 2: Survival estimate for LTFU by functional status. (Source: Author’s own work.)

In univariable analysis (Table 2), ambulatory status was associated with LTFU (p-value = 0.026), but all covariates (sex, age, CD4 count, clinical stage, opportunistic infection status, and ART regimen) were not found to be associated with LTFU. In multivariable Cox Regression (Table 2), only functional status remained in the final model. Patients with ambulatory status had higher risk of experienced LTFU than patients with working status. The risk for experiencing LTFU among ambulatory patients was two times higher (HR 2.29; 95% CI 1.11 – 4.74; p-value = 0.026). Bedridden status did not have significant association with LTFU (p-value = 0.303).

TABLE 2: Association between functional status and LTFU.

No.	Variable	Univariable		Multivariable	
		HR (95% CI)	Sig.	AHR (95% CI)	Sig.
1.	Functional status				
	Working	Ref.	0.073	Ref.	0.073
	Ambulatory	2.29 (1.11–4.74)	0.026*	2.29 (1.11–4.74)	0.026*
	Bedridden	1.55 (0.67–3.56)	0.303	1.55 (0.67–3.56)	0.303
2.	Sex				
	Female	Ref.		–	–
	Male	1.56 (0.80–3.14)	0.186		
3.	Age (yr)				
	<30	Ref.	0.246	–	–
	31–44	0.81 (0.40–1.63)	0.56		
	>45	1.56 (0.75–3.23)	0.236		
4.	CD4 count				
	> 200 cell/mm ³	Ref.			
	<200 cell/mm ³	1.32 (0.63 - 2.74)	0.459	–	–
5.	Clinical stage				
	I	Ref.	0.423	–	–
	II	1.17 (0.36–3.83)	0.796		
	III	1.97 (0.79–4.90)	0.146		
	IV	1.79 (0.68–4.73)	0.237		
6.	Opportunistic infection status				
	No	Ref.		–	–
	Yes	1.06 (0.56 - 2.00)	0.857		
7.	ART regimen				
	AZT+3TC+NVP	Ref.	0.671	–	–
	AZT+3TC+EFV	0.41 (0.09–1.85)	0.247		
	TDF+3TC+EFV	0.75 (0.38–1.49)	0.412		
	Others	0.79 (0.10–6.09)	0.818		

*P-value < 0.05

HR: Hazard ratio; AHR: Adjusted hazard ratio

Source: Author's own work.

4. Discussion

In this study, it was found that the survival estimate for LTFU ART was 65.9%. It was lower than the finding of the Ethiopia study that reported 75% of HIV/AIDS patients remained in the ARV treatment [12]. This different finding might be caused by the difference in the time observed. A study in Ethiopia only followed up the outcome status for 24 months, while the outcome of this study was observed for 39 months [12]. Besides, differences in

the management of HIV/AIDS patients might also have contributed to these differences in findings. In Ethiopia, there was a good engagement between HIV/AIDS patients and medical personnel. The health facilities often monitored the patients via cellular phones to early identify the problems-related to ARV treatment that occurred [12].

The main finding of this study showed that functional status had a significant association with the incidence of LTFU, but it was only found in ambulatory status. A similar finding was also found in studies that were conducted in Ethiopia [11, 13, 15, 16]. Ambulatory patients had a higher risk to end up in LTFU compared to patients with working status. This association might be attributed to socioeconomic status. Patients in this status generally had financial limitations due to their inability to work [11, 13, 15]. Because they had to visit health facilities regularly, the costs that were spent, both direct and indirect costs, might be quite large. This financial limitation led them to not adhere to ARV treatment [11, 13, 15, 16]. Patients with ambulatory status might also experience social disadvantageous. They were more likely to have a lower motivation and felt hopeless with their condition [11, 13, 15]. They also reported experiencing more side effects in the initial stage of the treatment compared to patients with working status [11]. So, intensive monitoring in these patients needs to be optimized to prevent loss to follow-up. Bedridden patients were not a predictor of LTFU. Compared to patients with working status, the incidence of LTFU among those categories was not significantly different. Patients who had bedridden functional status usually under close supervision by the health providers [12]. The physical weakness of the patient could be a barrier to adherence to ARV treatment. They could not do a routine follow-up every month to the VCT clinic. Patients who were in bedridden status also had a higher risk of death [12, 20].

Limitations in the data completeness and access to medical were the causes that could affect the validity of the results. However, this study could explain the causal relationship between functional status and the incidence of LTFU because this study was conducted using a retrospective cohort design.

This study showed that functional status can cause loss to follow-up in HIV patients. This study was conducted in one of the countries in the Southeast Asia region that had the highest HIV burden, considering that previous studies were only conducted in African countries, especially Ethiopia. The findings indicated that monitoring of treatment of HIV patients needs to be done strictly, especially at the start of ARV treatment. If it can be identified early, then the incidence of loss to follow-up can be prevented. Building a good relationship between the patient, the patient's family, and health workers can facilitate a better monitoring process. Providing counselling to patients and their

families is also aimed to increase patient's motivation and family support to ensure the adherence to the ARV treatment. Thus, patients can get favourable health outcomes.

5. Conclusion

Functional status had a significant association with LTFU. Patients with ambulatory status had a doubled risk of experiencing LTFU than the working category, whereas bedridden status did not have a significant association with LTFU. In all categories of functional status (working, ambulatory, and bedridden), most of LTFU occurred in the first ten months after starting the ARV treatment. Increasing patient's knowledge and understanding about the importance of undergoing treatment regularly might be able to reduce the incidence of loss to follow-up. Health workers need to more pay attention and monitor the patient's treatment process.

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Conflict of Interest

The authors state that there is no conflict of interest.

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