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Adherence to antiretroviral therapy, CD4 count, viral load and opportunistic infections in people with HIV/AIDS: a cross-sectional study

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ABSTRACT

Introduction: Globally, antiretroviral therapy (ART) has been successful in reducing the death rate due to human immunodeficiency virus (HIV). Different conditions in Indonesia mean the death rate due to HIV/AIDS is still high. The problem lies in the low compliance with ART. This study aimed to analyze the correlation between ART adherence with number of CD4, the opportunistic infection (OI) and viral load in PLHIV.

Methods: A quantitative survey with cross-sectional approach was conducted between August – September 2022. As many as 375 PLHIV were recruited and agreed to give consent as research respondents. All respondents completed a questionnaire about ART adherence, OI and had blood taken to check CD4 count and viral load. Analyses were performed using Chi-squared test SPSS version 21 with significance level p<0.05.

Results: A significant relationship was shown between ART adherence and OI (p value= 0.000 with <0.05). The respondents who reported adherence in ART also showed asymptomatic OI. The analysis also showed that ART adherence had significant relationship with CD4 count (p value= 0.000 with <0.05) and viral load (p value= 0.000 with <0.05), respectively. Respondents adherent to taking ART had better level of CD4 and suppressed viral load in the body.

Conclusions: Adherence of antiretroviral therapy is the important factor contributing to the immune status of PLHIV, which has an impact on reducing CD4 count and suppressing viral load, thereby preventing the emergence of OI.

Keywords: adherence, antiretroviral therapy, CD4, opportunistic infections, PLHIV, viral load

Introduction

Globally, antiretroviral therapy (ART) has been successful in reducing the death rate due to human immunodeficiency virus (HIV) by 48% (UNAIDS, 2017) and ART can effectively improve the immune status of people living with HIV/AIDS (PLHIV) with indicators of CD4 count, viral load and incidence of opportunistic infection (OI) (Wardhani and Yona, 2021). This condition is different from the situation in Indonesia, in contrast the death rate due to HIV/AIDS is still high. The problem lies in the low compliance with ART, which does not reach the national target from the Ministry of Health. Of the 96.69% of PLHIV who were recorded as receiving ART, unfortunately 22.89% experienced loss to follow-up on their therapy (Ministry of Health Republic of Indonesia, 2018). The low compliance of PLHIV is caused by low self-efficacy, hopelessness and perceived stigma (Andini, Yona and Waluyo, 2019; Nurfalah, Yona and Waluyo, 2019). The main impact that occurs in PLHIV leads to the increased number of CD4, preventing the

OI and suppressing the viral load (Wardhani and Yona, 2021). The current phenomenon is that many PLHIV are absent from ART, causing them to have low immunity due to a decrease in CD4 counts, an increase in viral load and making it easy for PLHIV to get OI.

In 2021, 38.4 million people in the world were living with HIV with new cases reaching 1.5 million and 650,000 will have died from HIV complications due to non-adherence to ART (World Health Organization, 2021). By the end of 2022, in Indonesia, positive HIV cases had reached 543,100 people, around 393,538 people with HIV were aware of their condition, 160,249 people received therapy and only 14% reported that ART had reduced the number of viruses over the last six months (Ministry of Health of Republic Indonesia, 2021). This condition shows that ART compliance in Indonesia is still lacking. The low level of ART in Indonesia means that many PLHIV show low CD4 counts (< 350) and viral loads increase to ≥ 40 copies/ml, the impact of which is an increase in the number of OI (Sutini et al., 2022). The most common OIs found in patients were oral candidiasis (58.6%), pulmonary tuberculosis (41.4%) and pneumonia (41.4%). Other infections found were hepatitis C, toxoplasmosis, cytomegalovirus, chronic diarrhea, tuberculous meningitis, and cerebritis. So far, government programs have been concerned with breaking the chain of transmission by increasing early detection of HIV cases in endemic areas, high risk groups and screening during pregnancy. The Indonesian government is also increasing the provision and retention of ART, as well as chronic care and expanding access to CD4 and VL testing including early infant diagnosis (EID) (Asmarawati et al., 2018).

Several factors influence non-adherence to ART in PLHIV, such as low level of knowledge (Martiana, Waluyo and Yona, 2019), not caring about their health status (Sefah et al., 2022), low motivation (Shrestha, Altice and Copenhaver, 2019), tired of taking medication (UNAIDS, 2017), hopelessness and trauma with side effects from treatment (Nursalam et al., 2021). Another study found that non-adherence of ART is also influenced by peer support, family caregivers, health service providers (Nursalam et al., 2020) and stigma or discrimination that comes from the public (Shrestha, Altice and Copenhaver, 2019; Agnes and Songwathana, 2021). If ART compliance is allowed to be low, more PLHIV will experience loss to follow-up and cause their immunity to decrease based on indicators of CD4 number, the OI and viral load. Therefore, this study aimed was to analyze the correlation between ART adherence with number of CD4, the OI and viral load in PLHIV.

Materials and Methods

Study design and setting

A quantitative survey with cross-sectional approach was conducted in Dr. Soetomo General Hospital Surabaya, East Java, Indonesia. The study was conducted between August – September 2022 to evaluate ART adherence, CD4 count, viral load and the incidence of OI. This hospital was chosen as the research location because of its long experience in HIV/AIDS treatment, the large number of HIV experts conducting related research, and being one of the referral hospitals for ART therapy and HIV patients experiencing complications in Surabaya.

Participants

As many as 375 PLHIV were recruited and were willing to give consent as research respondents. Respondents were recruited directly by researchers with research assistants and assisted by doctors and nurses at the hospital to confirm data from PLHIV. Recruitment of respondents was carried out using a purposive sampling technique with criteria determined by the researcher as follows: 1) Having been diagnosed as HIV positive through three test methods (oncoprobe, intake and vikia) which were in accordance with the doctor's regulations; 2) Productive age, between 20 – 55 years; 3) Taking ART for at least six months; 4) Able to read and write well; 5) Able to communicate well with language; 6) Do not have mental illness; and 7) Do not have vision or hearing problems. Respondents who met the inclusion criteria were explained about the research procedures. After potential respondents agreed to participate in the research, they were asked to sign an informed consent form. All respondents agreed to sign the information form provided by the author and 100% of respondents filled out the questionnaire in accordance with the initial sample plan determined by the researcher. All respondents in this study were given souvenirs for their contribution.

Data Collection

Research data were collected based on the independent variable, namely adherence to antiretroviral therapy and the dependent variables were CD4 count, viral load and OI. All respondents who agreed to sign the informed consent to participate in this study were then asked to complete a questionnaire about ART adherence, OI and had blood taken to check CD4 count and viral load. They completed a questionnaire and had blood taken in a

special room provided to maintain the privacy of PLHIV from other respondents. The questionnaire in this study includes socio-demographic characteristics which collect age, gender, marital status, ethnicity, religion, educational history, employment, and income (Nursalam et al., 2021). ART adherence was identified based on two measures, in the last one week and last three months. If they self-reported taking ≥ 95% of ART medication in a 7-day period, they were determined as adherent category, then if they missed ≥ 1 dose of ART medication within this time period this was determined as non-adherent category. The second measurements described if PLHIV were following an ART medication routine ≥ 95% , if this was for a 3-month period, it was indicated as adherent and if they missed ≥ 3 doses of ART medication within this time period it was determined as non-adherent (Murphy et al., 2004; Wasti et al., 2012). Respondents were identified about OI using HIV/AIDS staging criteria with the criteria for stage 1 asymptomatic, stage 2 mild asymptomatic, stage 3 moderate asymptomatic and stage 4 AIDS (Bhatti, Usman and Kandi, 2016). CD4 count and viral load were checked by taking venous blood samples; 5 ml of blood was taken and divided into two test tubes. The examination results if the CD4 count < 350 were categorized as poor and ≥ 350 categorized as good, while if the viral load was ≥ 40 copies/ml in the blood sample then the viral load was detectable, otherwise a viral load < 40 copies/ml indicates it was not detectable (Cassenote et al., 2018).

Data Analysis

Descriptive analysis was performed to provide an overview of socio-demographic characteristic data and specific variables of percentage of ART adherence, OI, CD4 count, and viral load. Chi-squared test was used to detect the correlation between ART adherence with OI, CD4 count, and viral load. The independent variable was coded as binary (1=adherent and 2=non-adherent), dependent variable also was coded as binary (1= poor and 2 = good for CD4 count; 1 = detected and 2 = not detected for viral load, respectively), OI was coded as ordinally (1 = asymptomatic, 2 = mild asymptomatic, 3 = moderate asymptomatic and 4 = AIDS). All analyses were performed using SPSS version 21 with significance level $p<0.05$.

Ethical Consideration

Ethics approval for this study was assessed and obtained from Dr. Soetomo General Hospital Surabaya with the approval number 070/0957/102.6.3.3/Litb/VII/2023. The researcher had first provided an explanation about research procedure to the research respondents and obtained informed consent by adhering to research ethical principles. Research data were processed by researchers and only data related to research were

Table 1. Demographic characteristics of the participants (N = 357)

Characteristics	Frequency	Percentage
Age		
20-25 years	28	7.5
26-35 years	140	37.5
36-45 years	134	35.7
46-55 years	73	19.5
Gender		
Male	196	52.3
Female	179	47.7
Education		
No school	7	1.9
Elementary School	43	11.5
Junior High School	78	20.8
Senior High School	209	55.7
University	38	10.1
Marital Status		
Single	116	30.9
Married	166	44.3
Divorced	79	21.1
Widowed	14	3.7
Tribes		
Java	332	88.5
Madurese	36	9.6
Dayak	2	0.5
Chinese	5	1.3
Religion		
Islam	349	93.1
Catholic	2	0.5
Christian	24	6.4
Work		
Self-employed	37	9.9
Private employees	150	40.0
Trader	27	7.2
Laborer	12	3.2
Housewife	123	32.8
Other	26	6.9
Income *		
≤ Minimum regional income	322	85.9
> Minimum regional income	53	14.1
Duration of ART		
1-5 years	358	95.5
6-10 years	6	1.6
>10 years	11	3.0
ART Adherence		
Adherent	248	66.1
Non-adherent	127	33.9
OI		
Stage 1 Asymptomatic	238	63.5
Stage 2 Mild asymptomatic	83	22.1
Stage 3 Moderately asymptomatic	52	13.9
Stage 4 AIDS	2	0.5
CD4 Count		
Less	185	49.3
Good	190	50.7
Viral Load		
Detected	101	26.9
Not detected	274	73.1

* Minimum Regional Income of Surabaya US$ 288 or IDR 4.375.479

Table 2. Correlation between ART adherence with OI, CD4, and viral load (n = 357)

Variable	Antiretroviral adherence				Total		OR	p
	Adherent		Non-adherent					
	n	%	n	%	n	%		
OI								
Stage 1 Asymptomatic	215	60.2	23	6.4	238	63.5	0.35	0.000*
Stage 2 Mild asymptomatic	23	6.4	60	16.8	83	22.1		
Stage 3 Moderately asymptomatic	10	2.8	42	11.8	52	13.9		
Stage 4 AIDS	0	0.0	2	0.6	2	0.5		
CD4 Count								
Less	61	17.1	124	34.7	185	49.3	0.29	0.000*
Good	187	52.4	3	0.8	190	50.7		
Viral Load								
Detected	0	0	101	28.3	101	26.9	0.44	0.000*
Not detected	248	69.5	26	7.3	274	73.1		

published. At the time of data collection, a respondent code was given to protect the confidentiality of the data and researchers did not force potential respondents, so that respondents participated in the research voluntarily.

Results

Table 1 shows the majority of respondents were aged between 26-35 years (37.5%), male (52.3%), senior high school degree (55.7%), married (44.3), Javanese by ethnicity (88.5%), Muslim (93.1%), private employee (40.0%), and income less than regional minimum (85.9%). Most of the respondents had been receiving ART for 1–5 years (95.5%) and the level of adherence just reached 66.1%. Of the 357 respondents, 238 (63.5%) reported being in stage 1 OI, namely asymptomatic, 190 (50.7%) had good category in CD4 count (>350) and 274 (73.1%) showed the viral load was not detected (< 40 copies/ml). Although the immunity level was good category, the level of less CD4 count was still high (49.3%) and viral load detected was 26.9%, it meant 22.1% of PLHIV had mild symptoms and 13.9% had moderate symptoms.

Table 2 shows the cross-tabulation and bivariate analysis between variables/ Based on cross-tabulation, PLHIV adherent category showed asymptomatic OI (60.2%), good CD4 count (52.4%) and not detected viral load (69.5%). A Chi-square test for the bivariate analysis demonstrated a significant relationship between ART adherence and OI (p value: 0.000, OR: 0.35). The respondents who reported adherent in ART also showed asymptomatic OI. The analysis also shows that ART adherence had a significant relationship with CD4 count (p value: 0.000, OR:2.9) and viral load (p value: 0.000, OR: 0.44), respectively. Respondents who were adherent to take ART had better level of CD4 and suppressed viral load in the body.

Discussions

The proportion age was slightly greater in 26-35 years, which is similar to a study from Bandung, Indonesia that reported the average age of PLHIV was in productive age (between 20-40 years) (Wardhani and Yona, 2021). Male patients were dominant in this study; this contrasts with study conducted in Lampung where HIV positive cases occurred in women (Irmayati, Yona and Waluyo, 2019). HIV is more dominant in males because of the potential for a high risk of HIV transmission, because males like heterogeneous sex, male with male relations, as well as job factors, injecting drugs and tattoos (Katz et al., 2018). Mostly, respondents had jobs as private employees and the salary was less than the minimum regional income, which is one of the factors that make patient compliance low. The cost of treatment for PLHIV is quite high, and even though ART in Indonesia receives a free program from the government, the need for medication and other immune-boosting supplements is also very large Which impacts on PLHIV compliance, because they need supplements and vitamins to increase their immune status so they don't easily fall into worse conditions (Sukartini, Nursalam and Arifin, 2021). Senior high school as moderate education level influences ART adherence because higher education determines the quality of respondents' knowledge, thereby increasing respondents' awareness. Adequate adherence contributes to the success of ART treatment and minimizes the prevalence of antiviral resistance during treatment. However, lack of knowledge makes respondents and caregivers not aware of this fact (Van Nguyen et al., 2021). The majority of respondents were Javanese and Muslims, both of which were related to the culture and religion adhered to by Indonesian society as a country with diversity; moreover, the cultural and religious values of Indonesian society encourage each partner to always be loyal to each other even in sick conditions (Gamarel and Golub, 2015; Eidhamar, 2018). Most of the respondents were married which makes a big contribution to the support system between partners

of PLHIV; even though the partner has HIV in their body, the marital relationship makes them more accepting of each other (Wardhani and Yona, 2021).

This study revealed the level of adherence only reached 66.1%, although they had been receiving ART on average for 1–5 years. Many factors are related to the low adherence to ART among respondents, especially beginners and those who have been around for a long time, because ART will cause side effects that are considered by PLHIV to be excruciating when taken (Martiana, Waluyo and Yona, 2019) and when not taken it also causes more serious problems (Shi et al., 2022). PLHIV feel uncomfortable and reduce their coping, coupled with low support, stigma and discrimination from society. The level of lower CD4 count was still high and viral load was still detected according to the research results, affecting to low immunity status. ART as a means of suppressing the number of viruses means that PLHIV must consume every day; the existence of the treatment makes them have better health and live longer (Van Nguyen et al., 2021). Suppressing the number of viruses contributes to reducing the amount of the body's immunity that has to fight the virus, so that more of the body's immunity survives. The body's immunity that maintains this condition in PLHIV is CD4 (Shukla, Ramirez and D'Orso, 2020). ART compliance for PLHIV is key if you want to stay healthy and live longer, because one copy of the virus can produce tens of millions of new active viruses (Fauk et al., 2021).

The analysis showed that adherence to ART had a significant relationship with OI; the more PLHIV adhere to ART, the more minimal the incidence of OI will be, because their immune system is better. ART as a treatment for PLHIV does not function as a curative or curing disease, but rather the persistence of both residual viremia and long-lived cells carrying latent, intact proviruses (Hong and Mellors, 2015). Early taking on of ART makes PLHIV get life expectancy and quality of life close to normal persons (Walker and Hirsch, 2013). Non-adherent ART for a long time results in the patient's immunosuppressed condition which results in more frequent or more severe OI, and can be the cause of serious morbidity and even mortality (Duff, 2019). Preventing OI can be initiated by vaccination, such as meningococcal infection, pneumococcal infection, hepatitis A and B, influenza and varicella, but it is not the most effective solution (Cao et al., 2022). Other major OI requires prophylactic antibiotics or antiviral medications (Sangeda et al., 2018), so it is very important for them to increase ART. The adherence to taking ART had a significant correlation with CD4 count and viral load among PLHIV; the more they adhere to treatment, the more CD4 counts increase and viral load can be suppressed. Proper adherence to ART is sufficient to suppress viral load in plasma and it makes viral load not achieved ongoing viral replication and prevents progressive depletion of CD4 through direct and indirect roles (Sempa et al., 2020).

Our study has some limitations that need to be addressed. Our results were focused to patients from one hospital in Surabaya. Furthermore, due to the methodology design, it may not be generalized to all PLHIV in Indonesia. Future research needs to add sample size or conduct research nationally so it can find some heterogeneous characteristics of respondents and type of ART adherence.

Conclusion

Adherence of antiretroviral therapy is the important factor contributing to the immune status of PLHIV, which has an impact on reducing CD4 count and suppressing viral load, thereby preventing the emergence of OI. The correlation between ART adherence has statistical significance to CD4 count, viral load and OI. Furthermore, it can be implied in the hospital that improving the immunity level of the PLHIV should focus on improving the quality of ART adherence in PLHIV. Future research that focuses on HIV/AIDS ART adherence research is expected to examine the impact of ART adherence on other PLHIV outcomes. Research can also be carried out that focuses on therapy to increase ART adherence for PLHIV, because ART for PLHIV is very important and should not be missed altogether.

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Conflict of interest

The researcher declares that in preparing and carrying out the research there was no conflict of interest with any party.

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