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RESEARCH ARTICLE

Adherence of HIV/AIDS patients to clinical outcome in Semarang City

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Abstract

Background: The success of HIV therapy can be measured by clinical, immunological, and virological monitoring. Meanwhile, low adherence to antiretroviral therapy (ART) contributes significantly to the disease progression and emergence of drug-resistant HIV. **Objective:** This study aimed to determine the correlation between the adherence of HIV/AIDS patients to clinical outcomes in Semarang. **Method:** This was an observational and cross-sectional approach. The instrument used the Simple Medication Adherence Questionnaire (SMAQ), which was validated and distributed to 50 respondents. The data were analyzed using chi-square ($p < 0.05$), and the results showed a statistically significant relationship. **Result:** Respondents were male (96%), aged 26-45 years (76%), high school graduates (24%), working (88%), single (86%), without comorbidity (86%), length of treatment more than 12 months (80%), and general treatment (50%). A total of 31 respondents (62%) adhered to treatment with the combination regimen of Tenofovir/Lamivudine/Efavirenz (20%). There was a significant relationship ($p = 0.006$) between the length of treatment and patient adherence. The adherence results were not significantly related ($p > 0.05$) to virological outcomes. **Conclusion:** There is no significant relationship between the adherence of HIV/AIDS patients and clinical outcomes.

Introduction

Human Immunodeficiency Virus (HIV) is an infectious disease that attacks the cells of the immune system, thereby affecting health globally. HIV can cause the emergence of a disease commonly called acquired immunodeficiency syndrome (AIDS) because the virus has a mechanism of action by attacking and reducing the work of the human body system, characterized by severe immunosuppression, which can cause the emergence of various kinds of infections such as opportunistic, secondary neoplasms and neurological manifestations. The most advanced stage of this disease is AIDS, which can cause other infections with various symptoms and diseases. The number of HIV/AIDS sufferers in Indonesia increased from 30,935 in 2015 to 50,282 in 2019. Central Java was ranked as the fourth highest number of HIV sufferers, with 5,630 sufferers in 2019 (Kementrian Kesehatan RI, 2020); (WHO, 2021).

Management of HIV/AIDS involves rest, adequate macronutrient and micronutrient support, counselling, psychological and psychosocial approaches and the implementation of a healthy lifestyle. HIV sufferers need special drugs called Anti-Retroviral Therapy (ART) and use secondary infection therapy according to the infection and malignancy. The use of ART aims to reduce morbidity and mortality due to HIV/AIDS, optimally improve quality of life, restore immune function and effectively suppress viral replication (Nasronudin, 2014). Compliance with HIV/AIDS patients in taking antiretroviral drugs or ARVs is an important factor in the success of antiretroviral drug

therapy or ARVs if medication adherence reaches more than 95% (Kemenkes RI, 2017). Based on the research in one city in Indonesia, the majority of patients receiving ART reported good adherence to ART (Kusdiyah & Rahmadani, 2022). Patient adherence at Health Centre in Sorong City and West Java Province was reported to be high (76.5%) and (> 61.5%) respectively. Factors related to the adherence include employment status, ARV regimen (side effects), and family support. Feeling healthy, experiencing side effects, being busy, and being far from home often become reasons for not seeking treatment (Banna & Manoppo, 2019); (Ibrahim *et al*., 2020). The success of ART can be measured by clinical, immunological, and viral monitoring. ART monitoring is important to achieve treatment success, identify adherence issues, and decide on whether the ART regimen should be switched from first line to second line if treatment fails (WHO, 2021). Previous studies have agreed that adherence is associated with viral suppression (Wilson *et al*., 2020) and that adherence and CD4 increase have a significant relationship (Tchakoute *et al*., 2022). Nonadherence to ART may increase the risk of virologic failure (Pamplona *et al*., 2021). Viral load testing is highly recommended over clinical and immunological tests. It provides an earlier and more accurate indication of treatment failure and the need for a switch, reduces the accumulation of mutations of drug resistance, and improves clinical outcome. Assessing viral load helps differentiate between treatment failure, non-adherence, and increased adherence support (WHO, 2021). This study assesses the relationship between the adherence of HIV patients to virological outcomes in Semarang using a validated Simplified Medication Adherence Questionnaire (SMAQ). The aim of this study is to be able to formulate an effective strategy to increase medication adherence and optimize ART.

Methods

Design

This was observational research with a cross-sectional approach. Sampling used the probability sampling method in Semarang city. A sample of 50 HIV-positive patients met the inclusion criteria, namely having undergone treatment for at least 1 month, being ≥ 18 years, having positive viral load, having signed to an informed consent. This research was ethically approved by the ethical review committee of Universitas Islam Sultan Agung with reference number 32/I/2023/Bioethics Commission. Confirmation of permission was obtained from the Health Centre in Semarang City.

Assessment

The research instrument used is the Simplified Medication Adherence Questionnaire (SMAQ), which was translated by a sworn translation agency. The questionnaire was also translated by a sworn translation agency. Among other things, the questionnaire consists of various sociodemographic categories including age, gender, education level, employment status, marital status, as well as distance between home and health centre. Clinical information collected included duration of treatment, co-morbidities, and current ARV drugs or therapy regimens. The SMAQ is a 6-item questionnaire that evaluates various aspects of patient adherence to medication including forgetfulness, routine, side effects, and quantification of omissions (Knobel *et al*., 2002). Patients classified as nonadherence if (1) they answered nonadherence question items, (2) if they either missed more than two doses in the last week or did not take medication at all for more than 2 days in the last 3 months. The data were analysed using SPSS. The relationship between the two variables was tested using the chi-square test with $p < 0.05$ as statistically significant.

Results

The sociodemographic data from 50 research respondents is presented in Table I. The responses were dominated by the following; male respondents (96%), those aged 26-45 years (76%), those who had a Bachelor's degree (44%), the employed (88%), the unmarried (86%), those who did not have any comorbidity (86%), although some respondents experienced complications from tuberculosis (2%), hypertension (6%) and other diseases (4%), those with a duration of treatment more than 12 months (80%), and respondents with general treatment in Semarang (50%).

Table I: Demographic profile of respondents

Profile	Respondents	Percentages (%)
Gender		
Male	48	96
Female	2	4
Age		
12-25 years	11	22
26-45 years	38	76
46-65 years	1	2
Education		
No school	0	0
Elementary school	0	0
Junior high school	3	6
Senior high school	16	32
College	9	18
Bachelor	22	44
Employment		
No	6	12
Yes	44	88
Marriage		
Not married	43	86
Married	6	12
Divorced	1	2
Comorbidities		
Tuberculosis	2	4
Hypertension	3	6
Diabetes mellitus	0	0
Kidney disorders	0	0
Cancer	0	0
No comorbidity	43	86
Other diseases	2	4
Duration of treatment		
6-12 months	10	20
> 12 months	40	80
Health insurance		
BPJS	24	48
General	26	52

The relationship between the sociodemographic relationship profile and adherence to ARV use is shown in Table II. Gender, age, education level, occupation, marital status, comorbidities and health insurance were not found to be significantly related to adherence (p > 0.05). Meanwhile, there was a significant relationship between adherence and the duration of therapy (0.006).

Table II: Correlation of sociodemographic profile with adherence to ARV use

Profile	Adherence level		*p*-value
	Adherence	Non-adherence	
Gender			
Male	29 (58%)	19 (38%)	0.258
Female	2 (4%)	0 (0%)	
Age			
12-25 years	6 (12%_	5 (10%)	0.346
26-45 years	25 (50%)	13 (26%)	
46-65 years	0 (0%)	0 (0%)	
Education			
No school	0 (0%)	0 (0%)	
Elementary school	0 (0%)	0 (0%)	
Junior high school	3 (6%)	0 (0%)	0.213
Senior high school	5 (10%)	4 (8%)	
College	11 (22%)	11 (22%)	
Bachelor	12 (24%)	4 (8%)	
Employment			
No	6 (12%)	0 (0%)	0.046
Yes	25 (50%)	19 (28%)	
Marriage			
Not married	24 (48%)	19 (38%)	
Married	6 (12%)	0 (0%)	0.083
Divorce	1 (2%)	0 (0%)	
Comorbidities			
Tuberculosis	2 (4%)	0 (0%)	
Hypertension	0 (0%)	3 (6%)	
Diabetes mellitus	0 (0%)	0 (0%)	
Kidney disorders	0 (0%)	0 (0%)	0.061
Cancer	0 (0%)	0 (0%)	
No comorbidity	27 (54%)	16 (32%)	
Other diseases	2 (4%)	0 (0%)	
Duration of treatment			
6-12 months	10 (20%)	8 (16%)	0.006
> 12 months	21 (42%)	19 (38%)	
Health insurance			
BPJS	16 (32%)	8 (16%)	0.544
General	15 (30%)	11 (22%)	
Total	31 (62%)	19 (38%)	

Table III shows the adherence of 50 patients who used ARV within which 62% of patients had adherence, while the remaining 38% did not have adherence to using drugs.

Table III: Level of adherence to ARV use

Adherence Level		Total
Adherence (%)	Non-Adherence (%)	
31 (62%)	19 (38%)	50 (100%)

Based on Table IV, most patients did not forget to take their medication (62%), were not careless (32%), did not stop (96%), always took medication (66%), with 94% taking it this weekend, and 60% always taking medication in the last three months.

Table IV: Characteristics of the drug adherence questionnaire

Questions	Response to adherence questions	Frequency
Do you ever forget to take your medicine?	Yes	19 (38%)
	No	31 (62%)
Are you careless at times about taking your medicine?	Yes	18 (36%)
	No	32 (64%)
Sometimes, if you feel worse, do you stop taking your medicine?	Yes	2 (4%)
	No	48 (96%)
Thinking about last week: How often have you not taken your medicine?	Never	33 (66%)
	1-2	13 (26%)
	3-5	1 (2%)
	6-10	3 (6%)
	>10	0 (0%)
Did you not take any of your medicine over the past weekend?	Yes	3 (6%)
	No	47 (94%)
Over the past three months, how many days have you not taken any medicine at all?	Never	30 (60%)
	1-2	17 (34%)
	>2	3 (6%)

Table V indicates that the respondents were more adherent to using the Tenofovir/Lamivudine/Efavirenz combination (20%). Meanwhile, more respondents did not adhere to using the Zidovudine/Lamivudine plus Nevirapine combination.

Table V: Correlation between ART regimen and patient adherence

Regimen	Adherence Level		Total
	Adherence (%)	Non-adherence (%)	
AZT/3TC + NVP	5 (10%)	7 (14%)	12
AZT/3TC + EFV	2 (4%)	1 (2%)	3
TDF/3TC/EFV	10 (20%)	6 (12%)	16
TDF/3TC/DTG	6 (12%)	2 (4%)	8
TDF + 3TC + EFV	6 (12%)	1 (2%)	7
AZT/3TC + LPR	1 (2%)	0	1
TDF/FTC + DTG	0	1 (2%)	1
TDF/FTC + LPR	1 (2%)	1 (2%)	2

AZT (Zidovudine), 3TC (Lamivudine), NVP (Nevirapine), EFV (Efavirenz), TDF (Tenofovir), DTG (Dolutegravir), LPR (Lopinavir/Ritonavir), FTC (Emtricitabine)

Table VI shows the results that adherence was not significantly related ($p > 0.05$) to virological outcome. A total of 49 respondents had undetectable viral load, and 30 of them were adherent respondents (60%), but one respondent had a viral load > 400 copies/ml.

Table VI: Correlation between medication adherence to virological outcomes

Adherence level	Virological outcome		*p*-value	OR
	Achieved	Non achieved		
	Frequency (%)			
Adherence	30 (60%)	1 (2%)	0.429	<0.001
Nonadherence	19 (38%)	0 (0%)		

Discussion

Employment showed a significant relationship to adherence ($p = 0.046$). This study is in line with research conducted by Haryadi et al. (2020) showing that work factors have a significant relationship to the compliance of patients with HIV in taking ARVs, the type of work affects respondents' compliance to take ARVs. Another study, Prabowo (2021), stated that respondents who had a good level of compliance occurred in those who worked by 80% but there was no relationship between employment status and compliance in taking ARV drugs. In research, Maulida et al. (2022) stated that high compliance was found in respondents who had jobs as private employees, civil servants, labourers and business owners, with an accumulation of 61%.

Duration of treatment showed a significant relationship with adherence ($p < 0.05$). This is in line with previous research that looked at the increase in adherence with a longer ARV use (Mbonye *et al*., 2013). HIV patients who had followed the ARV program for a long time had a high level of adherence and there was also a relationship between the length of therapy and adherence to ARV treatment (Sari *et al*., 2019). Patient adherence to the use of ARV drugs is very important for the success of therapy (Culig & Leppée, 2014). There are several factors that influence adherence such as adolescence, family, disease severity, treatment, and social regimen (Usitalo *et al*., 2014). Apart from that, self-awareness, support from family and health workers and side effects of ARV drugs are important factors that influence patient adherence (Arifa *et al*., 2022). Based on Oh & Han (2021) which included patients using single-tablet regimens (1 tablet/day), regimens containing (2-4 tablets/day), and regimens containing more than 5 tablets/day, the study showed that patients using single-tablet regimens (1 tablet/day) had a higher level of adherence and improved virological outcomes. Based on previous research (Adiningsih *et al*., 2023) the use of the Tenofovir/Lamivudine/Efavirenz combination as a single-tablet regimen is preferred for long-term combination therapy. In addition, the use of combination therapy with Tenofovir/Lamivudine/Efavirenz is safer than other ARVs as the preferred therapy for HIV patients. Tenofovir/Lamivudine/Efavirenz has fewer side effects than other combination regimens (Rukmangathen *et al*., 2020). Research in India showed the efficacy of using Tenofovir/Lamivudine/ Efavirenz as much as 98.7% and without high side effects (Sirohi *et al*., 2021). According to Nwaiwu et al. (2019) the use of antiretroviral drugs for 2 years was not significantly associated with virological outcomes (viral load) and immunological failure based on absolute CD4 counts.

Conclusion

There was no significant relationship between the adherence of HIV/AIDS patients to their respective clinical outcomes.

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