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Factors Affecting Adherence to Antiretroviral Therapy

Nanda Safira[1], Rahayu Lubis[2], and Mohammad Fahdhy[3]

[1,2]Department of Public Health, University of Sumatera Utara, Medan City, Indonesia
[3]Obstetric and Gynecology Department, General Hospital Haji Adam Malik, Medan City, Indonesia

Corresponding Author:
Nanda Safira
safiraa25@gmail.com

Abstract

The success of highly active antiretroviral therapy (HAART) for treating human immunodeficiency virus (HIV) disease depends on maintaining a high level of adherence. Non-adherence is associated with a poor short-term virological response and accelerates the development of drug-resistant HIV. The shift to combination therapies for treating HIV-infected individuals has increased the challenges of adherence for both patients and health-care providers. The cumulative number of people in April 2015 who were eligible for HAART but had not yet started the therapy at the Adam Malik Hospital in Medan City Indonesia was 1,669 out of 6,033 people (27.66%). The cumulative number of absentees and loss to follow-up at >3 months was 1,273 out of 4,364 people (29.17%) up to April 2015.This study was a cross-sectional investigation of the factors associated with adherence to antiretroviral consumption for HIV-infected individuals at the Adam Malik Hospital in 2015. The sample size was 65 people, using consecutive sampling. The data were collected from medical records, observations, and an interview with a questionnaire. The data analysis included descriptive study, the chi-square test, Fisher's exact test, and logistic regression, using STATA software. The results showed pill adherence in 28 patients (43.08%) and non-adherence in 37 patients (56.92%). The principal factors associated with non-adherence in the logistic regression were patient-related, including occupation (p = 0.062; OR = 0.22) and pill burden (p = 0.080; OR = 6.20). However, another factor that may have contributed was the system of health insurance (p = 0.015; OR = 5.00). The probability of the meaningful factors, based on the results of a multivariate analysis using the logistic function formula, is 0.7365 or 73.65%. The major reasons of HIV-infected individuals for not taking their medications were being employed, pill burden consideration, and without health insurance. Improving adherence probably requires the provision of the easy health insurance system with adequate patient preparation, innovative interventions and must fit into the socio cultural context of each setting.

Keywords: adherence, antiretroviral, health insurance, occupation, pill burden

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1. INTRODUCTION

Human immunodeficiency virus (HIV) infected individuals have experienced progressive reductions in HIV-associated morbidity and mortality over the years. Recent studies have shown marked improvements in life expectancy for patients with HIV [13]. Over the last 5 years, there has been a rapid change in the treatment strategies for HIV infection. With the advent of newer antiretroviral (ARV) drugs, the treatment has shifted from monotherapy and bi-therapy to triple-drug therapy, or highly active antiretroviral therapy (HAART), which consists of three or more ARV medicines to be taken in combination. In order to achieve the ARV therapy goal of undetectable levels of the HIV virus in the blood, patients are required to maintain more than 90–95% adherence [11].

The national ARV therapy guidelines by the Ministry of Health, the Republic of Indonesia (MoH R.I.), state that the expected ARV adherence is 100% for HAART, which means that all the combinations of drugs should be taken in the right way at the corresponding correct time without exceeding the proper dosage. There are three levels of adherence to ARV treatment: an adherence rate of ≥95% (good adherence), if fewer than 3 doses of ARVs are missed within a 30-day period; an adherence rate of 80–95% (moderate adherence), if 3–12 doses of ARVs are missed within a 30-day period; and a level of adherence of <80% (poor adherence or non-adherent), if more than 12 doses of ARVs are missed within a 30-day period (Directorate of Environmental Health and Disease Control MoH 2006).

There are 4 main barriers to good adherence around the world: (1) patient factors (e.g., age, education, medical knowledge, literacy); (2) community empowerment and community barriers, such as stigma, family support, and community involvement or existence of a community; (3) structural barriers such as the cost of treatment, the ease of access to services, nutritional support, and the availability of drugs; (4) loss to follow-up—namely, the difficulties faced by health workers in tracing the HIV patients who are undergoing treatment, due to the lack of involvement of the community or society as a treatment support [3].

2. MATERIALS AND METHODS

2.1. Study Setting

This was an analytical observational study with a cross-sectional design. It was conducted at the Voluntary Counseling and Testing (VCT) clinic, the special service center called Pusyansus in the Out-Patient Department (OPD) at Adam Malik Hospital, Medan City, Indonesia, between January and July 2015. This center was established in 2005 as a counselling center for HIV/AIDS in North Sumatra. Every patient, before starting ARV therapy, undergoes three sessions of adherence in the form of pre-test counseling, post-test counselling, and pre-ARV drug adherence counselling within the first three months [14].

2.2. Sample

A list of patients fulfilling the inclusion criteria was updated from the Pusyansus register, and the patients to be included in the study were selected by the consecutive sampling method.

TABLE 1: Individual questions on the adherence questionnaire scale.

Adherence Questionnaire Items	Frequency	
	n = 65	%
Have a reminder system for medications	50	76.92
Have sometimes forgotten medications	59	90.77
Have considered the long-term of ARV therapy	65	100.00
Have forgotten medications during the last week	52	80.00
Have had treatment interruptions because the pills are considered to be a burden	9	13.85
Have had known side-effects of ARV therapy		
Have had an opportunistic infection	41	68.33
Have consumed ARV while having a stigma from health care	61	93.85
Have rarely been to counseling for ARV therapy	53	81.54
Have easy access to the Pusyansus	49	75.38
	39	60.00

2.3. Sample Size

The sample size of 65 was calculated with a hypothesis test for a population proportion (two-sided test) by using the sample size determination in a health studies software program version 2.0.21 of the W.H.O. Collaborating Centre for Health Informatics and the Medical Informatics Programme of the National University of Singapore. The confidence level was 95%, the power of the test was 80%, the test value of the population proportion was 0.62, and the anticipated value of the population proportion was 0.45, in order to have sufficient variation in the population characteristics (e.g., sex, education, economic status) that may influence adherence. All the patients who were aged 18 years or above and had taken ART for a duration of at least 6 months were included in the study. Informed consent was taken from all the patients. An institutional ethical committee approval to conduct the study was obtained on 2 April 2015.

2.4. Tools of Data Collection

In this study, adherence was measured using the recommendations of the international Network for the Rational Use of Drugs-Initiative on Adherence to Antiretroviral therapy (INRUD-IAA) methods, i.e., adherence monitoring of patients with HIV/AIDS through (1) patient reports (self-reported in exit interviews), and if the patient is unable to speak, the report is obtained from a family member or companion patient currently taking the medicine; (2) the number of days that patients received the drug; (3) patient visits; and (4) the calculation of the amount of the drug along with reports of the patients in clinical records [4]. In addition, a closed-ended, self-reported questionnaire was used to collect data regarding the number of medications taken, the number of doses missed, sociodemographic information, family and peer-group support information, and the reasons for not taking the medications as prescribed. Patients who attended the Pusyansus during the study period, satisfied the inclusion criteria, and who were willing to participate in the study were given the adherence assessment questionnaire.

2.5. Data Analysis

The adherence rate was calculated by looking at whether only one dosage was missed in the last week for one month after the prescription started (counted from the last

visitation), the number of pills expected to be taken divided by the number of pills reported missed multiplied by 100, and the last-ARV-taken report from the Pusyansus pharmacy. Adherence was defined as a resulting value ≥95%. A logistic regression analysis was undertaken to explore the factors associated with lower adherence to provide odds ratios (ORs) and 95% confidence intervals (CIs). The variables found to be associated with lower adherence in the bivariate analyses were included in the multivariate analysis. A p value of <0.05 was considered significant. Based on the results of a multivariate analysis using the logistic function formula was undertaken to know the probability of the meaningful factors. Analysis was done using STATA 11.2 (STATACorp, LP, college Station, Texas, USA).

3. RESULTS

A total of 65 patients were included in the study. An adherence rate of more than 95% was reported by 28 patients (43.08%) and non-adherence by 37 patients (56.92%). A total of 24 patients (36.92%) had 100% adherence to their medication over the last 1 month, 4 patients (6.15%) had missed 1 dose over the last week for a month, 10 patients (15.38%) had missed 2–3 doses, and 27 patients (41.54%) had missed more than 3 doses.

Table 1 describes the patients' responses on individual questions in the adherence questionnaire scale. It was observed that 76.92% of the patients had some reminder system for medicines, while 90.77% of the respondents confessed to sometimes forgetting medications, and 80.00% had forgotten pills in the last week before the interview. Most of these patients were reminded to take their pills by family members. A few used alarm watches or alarms on their mobile phones to remind themselves. In addition, 13.85% patients had not taken their medications on time due to the pill burden, −68.33% patients had experienced side effects during therapy, 93.85% patients had had an opportunistic infection, 81.54% patients had been stigmatized while consuming the ARV, 75.38% had rarely gone to ARV therapy counseling, 60.00% had easy access to the Pusyansus, and 53.85% patients had national health insurance coverage for taking the ARV.

TABLE 2: Univariate and multivariate analysis of factors related to adherence.

Independent Variables		Adherence				p	Odds Ratio (OR) (95% CI)
		Non adherence		Adherence			
		n = 37	%	n = 28	%		
Patient Individual Factors							
Age (years)	<34 years	15	57.69	11	42.31	0.919	1.030 (0.581–1.828)
	≥34 years	22	56.41	17	43.59		
Sex	Male	26	63.41	15	36.59	0.167	1.480 (0.858–2.555)
	Female	11	45.83	13	54.17		
Education	Primary School & Above	9	50.00	9	50.00	0.344	0.816 (0.527–1.265)
	Up to Secondary School	21	63.64	12	36.36		1.000 (0.456–2.194)
	Bachelor's and Above	7	50.00	7	50.00	1	
Marital status	Single	15	71.43	6	28.57	0.103	1.750 (0.837–3.660)
	Married	22	50.00	22	50.00		
Occupation	Unemployed	7	31.82	15	68.18	0.003	0.443 (0.259–0.758)
	Employed	30	69.77	13	30.23		
Income (annual family income)	≤Rp 900,000	25	51.02	24	48.98	0.146	0.510 (0.208–1.249)
	>Rp 900,000	12	75.00	4	25.00		
Opportunistic infection history	Yes	35	58.33	25	41.77	0.644	1.440 (0.663–3.128)
	No	2	40.00	3	60.00		
Pill burden	Yes	28	68.29	13	31.71	0.016	1.971 (1.142–3.402)
	No	9	37.5	15	62.5		
Health Care-Related Factors							
ARV availability	Always Available	34	58.62	24	41.38	0.453	0.724 (0.356–1.474)
	Not Available	3	42.86	4	57.14		
Have experienced stigma in health care	Yes	5	33.33	10	66.67	0.043	0.540 (0.323–0.903)
	No	32	64.00	18	36.00		
Have national health insurance	Yes	15	42.86	20	57.14	0.013	2.143 (1.108–4.142)
	No	22	73.33	8	26.67		
Have adherence counseling	Rarely	26	53.06	23	46.94	0.385	0.666 (0.303–1.460)
	Always	11	68.75	5	31.25		
Social Community Factors							

Independent Variables		Adherence				p	Odds Ratio (OR) (95% CI)
		Non adherence		Adherence			
		n = 37	%	n = 28	%		
Have family support	Yes	26	52.00	24	48.00	0.234	1.800 (0.741–4.372)
	No	11	73.33	4	26.67		
Have peer group support	Yes	4	40.00	6	60.00	0.306	1.500 (0.823–2.735)
	No	33	60.00	22	40.00		

Table 2 describes the univariate and multivariate logistic regression analysis of the factors related to adherence among the individual patient factors, health care-related factors, and social community factors. In the bivariate analysis, occupation, pill burden, stigma experience in health care, and having national health insurance were significantly associated with adherence. Male patients, those who were employed, those who had a good income (>Rp 900,000), those who had a pill burden, those who had no stigma experience in health care, those who has no national health insurance, and those without family support were more likely to have poor adherence.

In the multivariate analysis, pill burden was significantly associated with adherence. Patients who had pill burdens were less adherent than patients who had no pill burden. Patients who had no national health insurance were less adherent than patients who had national health insurance. Patients who were employed were less adherent than patients who were unemployed. Patients who felt a pill burden were 6.2 times more likely to be non-adherent than patients who did not feel a pill burden. Patients who did not have national health insurance had 5 times more risk of non-adherence. Patients who were employed were 0.216 times more likely to be more adherent, which means that the occupation variable was a protective factor, as those who were unemployed were more adherent than patients who were employed.

One function of the logistic regression test was to determine the predictive models in order to determine the probability of the risk factors [5]. The probability of the meaningful factors, based on the results of a multivariate analysis using the logistic function formula, is 0.7365 or 73.65%. It showed that if the respondents had no pill burden, were unemployed, and had national health insurance, the adherence probability will be 73.65% to improve the consumption of HAART.

4. DISCUSSION

This study focused on adherence to ART that was provided free of cost to the patients. This definition is based on how patients theoretically would have completed the exit interview if they had taken at least 95% of the prescribed doses. The adherence formula calculates adherence over the last one month before the interview. In the present study, the adherence rate, as calculated by the adherence questionnaire scale, was lower than the adherence data from the hospital. This could be because the adherence questionnaire scale and the hospital adherence measurement method were different. Moreover, adherence is lower over longer periods of recall. In this study, the level generalization of research only at second external validation was an affordable population who were representing the target population. This means that all the patients with HIV/AIDS who made repeat visits and had been taking ARV drugs for at least 6 months in the VCT clinic at Pusyansus did not necessarily represent adherent patients with HIV/AIDS in the province of North Sumatra. This is because the study was conducted in only one VCT hospital clinic.

The most common reasons for pill burden were the length of consumption (which should be the whole lifetime), the number of pills, and being afraid that the HIV status would become known to others [8, 18]. One study found that the number of doses to be taken every day and being tired of consuming ARVs were the most common causes of pill burden, while another study showed that adherence has declined, even in people who are very obedient. This phenomenon is called "pill saturation" or "therapy saturation" [19].

The results showed that patients who had health insurance did not have to spend as much money to buy drugs, although the cost of transportation and the cost of CD4 testing is still a problem because there is no government policy to eliminate the fee. Some patients have health insurance but do not use it because the health insurance system is very complicated today and requires the patient to pay a premium fee every month for the health insurance card to remain active, and a delay in the payment of the dues will be fined. While the results of one previous study in Bandung City and Cimahi were in line with the results of the analysis in this study, the important structural obstacles to adherence were the burdens of the cost of treatments or medications (Yuniar et.al 2012). Overall qualitative research on adherence constraints in Botswana, Uganda, and Tanzania showed that transport costs, registration and health service fees, and the loss of income are the most important financial barriers to good adherence [3].

Some research in dr. Kariadi Hospital in Semarang is consistent with the indication that the resistance to ARV treatment is partly because respondents had difficulty in leaving a job if they had to take ARV drugs. Another obstacle is the fear of being cut out of jobs when frequent permission is required to leave work to take the medicine [2]. Fishermen who usually go to sea for 3–4 months also experience difficulties if they should take the drug every month (Yuniar et.al 2012). This study showed that unemployed people had time to visit the Pusyansus clinic any time they wanted. This is related to the lifestyle and daily activities such as being too busy or forgetting. People living with HIV should have the ability to adjust their schedules to take the medication.

Women were less adherent than men in some studies [15], but we did not find any statistically significant relationship between gender and adherence. In the present study, age was found to be significantly associated with adherence. Age has been found to be significantly associated with adherence in other studies, too [1, 12].

In the present study, the level of education and income were not found to have statistically significant associations with adherence. This may be because the treatment was provided free of cost. Income and education have been shown to have an impact on adherence in other studies [10, 16].

Living alone and lacking support have been associated with non-adherence to ART [17]. Social isolation is predictor of non-adherence [9]. According to Eraker et al. (1984), not living alone and having a partner, social or family support, peer interactions, and better relationships are characteristics of adherent patients [7]. In our study, merely being married or having support from friends or family was not significantly associated with adherence.

To conclude, more attention should be paid to patients feeling pill burden during counseling sessions. For employed patients who have trouble remembering medications, someone should be identified who can remind the patient. When possible, patients should be referred to case management and wraparound services for help with issues such as a lack of transportation, housing, child care, or access to insurance.

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