

Highly active antiretroviral therapy adherence and its determinants in selected regions in Indonesia

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Abstrak

Latar belakang: Mengonsumsi obat antiretrovirus dapat mengurangi morbiditas dan mortalitas orang dengan HIV/AIDS (ODHA). Tetapi, hal tersebut bergantung pada adherens terhadap pengobatan. Penelitian ini bertujuan untuk menilai adherens obat antiretrovirus dan mengevaluasi karakteristik individu pasien (self-efficacy, tingkat depresi dan dukungan sosial) yang menentukan adherens terhadap obat antiretrovirus di beberapa daerah di Indonesia.

Metode: Studi potong lintang ini dilakukan di Jakarta, Malang, Bandung, Makasar, dan Banda Aceh. Subjek penelitian kami adalah ODHA yang berumur lebih dari 13 tahun dan telah mengonsumsi obat antiretroviral setidaknya satu bulan. Subjek diambil secara konsekutif kemudian ditanyakan jumlah pil yang mereka tidak minum sejak satu bulan yang lalu. Adherens dikatakan rendah apabila persentase rata-rata adherens di bawah 95%. Kami mengadaptasi HIV treatment adherence self-efficacy scale (HIV-ASES), Beck Depression Inventory (BDI-II) dan Interpersonal Support Evaluation List (ISEL) untuk menilai self-efficacy, tingkat depresi, dan dukungan sosial, secara berurutan.

Hasil: Pada penelitian ini didapatkan 96% subjek penelitian (n=53) memiliki adherens yang baik terhadap pengobatan antiretrovirus. Selain itu, tidak ditemukan adanya hubungan antara adherens dengan self-efficacy, tingkat depresi dan dukungan sosial. Penyebab utama rendahnya adherens pada penelitian ini karena faktor lupa tanpa adanya alasan yang spesifik.

Kesimpulan: ODHA di beberapa daerah di Indonesia memiliki adherens yang baik terhadap pengobatan antiretrovirus dan adherens tersebut tidak berhubungan dengan self-efficacy, tingkat depresi dan dukungan sosial. (*Med J Indones 2011; 20:50-5*)

Abstract

Background: Highly active antiretroviral therapy (HAART) can reduce morbidity and mortality of HIV-infected patients. However, it depends upon adherence to medication. The objective of this study was to examine the adherence to HAART and to evaluate individual patient characteristics i.e. self-efficacy, depression level, and social support and to finally determine HAART adherence in selected regions in Indonesia.

Methods: This cross-sectional study was conducted in Jakarta, Malang, Bandung, Makasar and Banda Aceh. The subject of the study was HIV-infected patients who were older than 13 years old and had taken HAART for at least a month. They were recruited consecutively then asked how many pills they had missed during the previous month. Poor adherence can be stated if the percentage of adherence rate is below 95%. HIV treatment adherence self-efficacy scale (HIV-ASES), Beck Depression Inventory (BDI-II) and Interpersonal Support Evaluation List (ISEL) was adapted to assess self-efficacy, depression level and social support, respectively.

Results: We found that 96 % (n=53) of the subjects adhered to HAART. There were no associations between adherence with self-efficacy, depression level, and social support. The main cause of non-adherence in this study was 'simply forget'.

Conclusion: Adherence to HAART was found to be high and not associated with self-efficacy, depression level and social support in some central regions in Indonesia. (*Med J Indones 2011; 20:50-5*)

Key words: adherence, depression, HAART, HIV, self-efficacy, social support

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV). The virus attacks human immunity response, hence HIV-infected patients would be easily infected by other pathogens. Since the discovery of HIV in 1983, it has become pandemic and a major cause of deaths by opportunistic infections.¹

According to Joined United Nations Programme for HIV/AIDS (UNSAID) data in 2007, there were 33.2 million HIV-infected patients in the world, 2.1 million of whom had died. The number of HIV-infected patients is increasing annually although less newly HIV-infected patients are recorded.² The HIV epidemic in Indonesia is among the fastest rising numbers in Asia.

This is considered to result from the development of intravenous drug users (IVDUs) since 1999.^{2,3}

Although a cure for HIV infection is yet to be found, the infection can be controlled. By taking highly active antiretroviral therapy (HAART) regularly, viral replication in HIV-infected patients can be suppressed. In addition, drug resistance can be prevented in order to avoid morbidity and mortality of HIV-infected patients.⁴ However, these benefits depend upon adherence to medication due to the complexity of antiretroviral therapy by using triple regimens and due to the fact that this medication must be taken life-long. Some studies showed reduction of viral load and avoidance of chronic (opportunistic) diseases provided the adherence rate was above 95%.^{4,5}

There are many factors that may contribute to therapy adherence including self-efficacy, social support and depression level.⁶ Involvement of self-efficacy can be seen by their persistence i.e. high motivation, thoughts, cognition and affection to take the regimens to improve the quality of life of the recent condition.⁷ Depression level and social support affect adherence in psychological setting. Social stigma compels HIV-infected patients fall into depression. However, adequate social support may help them to overcome these psychological symptoms and to gain subsequently optimal medication adherence rate.⁶

The purpose of this study is to examine the proportion of adherence to HAART and to evaluate factors (self-efficacy, depression level, and social support) related to adherence in selected regions in Indonesia. We hypothesized that self-efficacy, depression level, and social support influence the adherence of taking medication in selected regions in Indonesia.

METHODS

Study Participants

This cross-sectional study was conducted in five regions by the Medical Faculties of five universities: Jakarta (Universitas Indonesia), Malang (Universitas Brawijaya), Bandung (Universitas Padjajaran), Makassar (Universitas Hasanuddin) and Banda Aceh (Universitas Syiah Kuala).

Between April 2009 and October 2009, in the five cities, participants were recruited consecutively from ambulatory care of each hospital or non-governmental organizations. The participants were older than 13 years and had been in treatment of HAART at least a month. HIV-

infected patients who were treated in the hospital and those who refused to participate in this study were excluded.

This study was approved by the Committee of Medical Research Ethics of the Faculty of Medicine Universitas Indonesia. Participants were given verbal and written information about the study. Written informed consent was obtained from all participants prior to inclusion into the study. No financial incentives were provided and all data were kept confidential.

In order to validate our questionnaires and to measure minimum sample size a preliminary study was conducted with fifteen subjects at ambulatory care of Dharmais and Cipto Mangunkusumo Hospitals, Jakarta. From this study, we obtained that 93% of the subjects (n=15) adhered to HAART therapy – the subsequent calculation of the minimum number for this study was 25 subjects.

Assessment Procedures

The data was collected by asking the participants to fill the questionnaires, which was accompanied by surveyors to avoid misunderstandings and unnecessary mistakes. Every participant took about 15 minutes to answer all the questions.

Measures

Demographics. Demographic data included participants' age, gender, marital status, education and employment.

Medication. We asked whether the participants had ever missed taking their antiretroviral medications. If they answered 'yes', there were 12 questions about the reasons with choices of "very rare", "rare", "often" or "very often". The frequency range described was scored from 0-3, respectively. Medication adherence was assessed with indirect methods by self-reporting, asking the participants how many pills they had missed to take during the previous month. Patients were classified as adherent when not more than three doses were missed and non-adherent if the patients admitted having missed at least four doses during the last month. We used one month recall period since we assessed self-efficacy, depression level and social support represented for the condition at that month.

Self-efficacy. HIV treatment adherence self-efficacy scale (HIV-ASES) developed by Johnson et al.⁸ was assessed with a 12-item scale of patient confidence to carry out important treatment-related behaviour plans for nutrition, exercise, etc. in front of barriers. Responses

range from 1 (cannot do it at all) to 10 (certainly can do it).⁸ Questions were translated to Indonesian language and a preliminary study was conducted to assess the validity and reliability of the questionnaire. Eight questions were valid with excellent internal consistency (Cronbach's $\alpha = 0.858$). In its adapted form, the scale consists of eight items with a score range of 0-80 with higher scores indicating higher confidence in ability to carry out treatment-related behaviours.

Depression Level. Beck Depression Inventory (BDI-II) which consists of 21-items self-report instrument was developed by Beck et al.⁹ to assess the existence and severity of symptoms of depression as listed in DSM IV. There is a four-point scale for each item ranging from 0 to 3. There are also cut score guidelines which can be adjusted according to the purpose of use.⁹ Questionnaires were also translated, then validity and reliability were tested in the same way as in the self-efficacy section. Fourteen items were valid and the questionnaire was shown to have excellent internal consistency (Cronbach's $\alpha = 0.88$). The cut score was also modified according to the number of items. In the total score, 0-8 is considered minimal range, 9-12 is mild, 13-18 moderate, and 19-42 is considered severe.

Social Support. Interpersonal Support Evaluation List (ISEL), which originally consists of 40 questions was developed by Cohen et al.¹⁰ to assess the perceived availability of the four separate functions of social support: appraisal items, tangible items, self-esteem items and belonging items as well as providing an overall functional support measure.¹⁰ In this study, we did not assess each function separately. The translated questionnaire was checked for validity: 12 items were valid and had reliable psychometric properties (Cronbach's $\alpha = 0.842$). Each question was scored ranging from 0 to 3. The modified ISEL consists of 12 items with a score range of 0-36 with higher scores indicating more social support.

Participants were informed that their answers in self-efficacy, depression level and social support sections should represent their condition in the past month.

Statistical Analysis

Bivariate associations of numerical variables (social support score and self-efficacy scale) with medication adherence were analyzed using unpaired t-test or Mann-Whitney test as an alternative. Kolmogorov-Smirnov test was used to examine normality of data. For analyzing depression level with medication adherence, Mann-Whitney test was used. Probability

value of ≤ 0.05 was considered significant. All analyses were performed with SPSS® Statistic 17.0.

RESULTS

Description of the participants

Demographic characteristics are shown by adherence status in Table 1. The average age of patients (n=53) was 32 years, 77.4% were male, 83% of our participants had a senior high school degree or more, and approximately half of them were married. There were 6 unemployed participants (11.3%) in this study.

Most patients (n = 28 or 52.8%) had ever missed taking their medications. Among them, 64.29% forgot to take their medication in the night, followed by 28.57% who forgot it in the morning and the rest in the afternoon. The major reasons affecting their adherence were simply "forget" without any specific reasons (score = 34), followed by "busy with other things" (score = 25), "run out of medications" (score = 19) and "ashamed if seen by others" (score = 18). There were 2 participants (3.8%) who were classified as non-adherent indicating that they missed at least four doses of their antiretroviral medications over the previous month.

The mean of self-efficacy was 70.11 (SD = 13.4) with the highest score of 80. The distribution of these data was not normal ($p < 0.001$). The depression level was 47.2% scored minimal, 17% mild, 17% moderate, and 18.9% scored severe. The mean of social support score was 25.49 (SD = 5.95) with the highest score of 36. The data distribution was normal ($p = 0.200$).

Bivariate Analysis of associations between self-efficacy, depression level and social support with antiretroviral adherence

In this study, we found that adherence was neither associated with self-efficacy ($p = 0.962$), social support ($p = 0.474$) nor depression level ($p = 0.709$).

Although we did not hypothesize any relationship between self-efficacy, social support and depression level, we found that they were significantly related to each other. The depression level was not categorized and distribution of the data was not normal ($p = 0.007$), hence Spearman test was used. The correlation between self-efficacy and depression level was weak ($r = -0.304$, $p = 0.027$); as was the correlation between self-efficacy and social support ($r = 0.286$, $p = 0.038$); while correlation between depression level and social support was moderate ($r = -0.461$, $p = 0.001$).

Table 1. Sociodemographic characteristics of participants by adherence status

Characteristics	Total Participants (n=53)	Adherent (n=51)	Non-adherent (n=2)
City			
Jakarta	45.3% (n= 24)	45.1% (n=23)	1
Malang	26.4% (n=14)	27.5% (n=14)	-
Bandung	17% (n=9)	15.7% (n=8)	1
Makassar	7.5% (n=4)	7.8% (n=4)	-
Banda Aceh	3.8% (n=2)	3.9% (n=2)	-
Age in years, mean±SD	31.55±7.92	31.94±7.79	21.5±4.95
Gender			
Male	77.4% (n=41)	78.4% (n=40)	1
Female	22.6% (n=12)	21.6% (n=11)	1
Education level			
Junior high school	17% (n=9)	17.6% (n=9)	-
Senior high school	45.3% (n=24)	43.1% (n=22)	2
Academic/university	37.7% (n=20)	39.2% (n=20)	-
Marital status			
Unmarried	43.4% (n=23)	43.1% (n=22)	1
Married	49.1% (n=25)	49% (n=25)	1
Widow/-er	7.5% (n=4)	7.8% (n=4)	-
Unemployment	11.3% (n=6)	11.8% (n=6)	-
Employment			
Employer	37.7% (n=20)	39.2% (n=20)	-
Private sector	28.3% (n= 15)	29.4% (n=15)	-
Public sector	3.8% (n=2)	3.9% (n=2)	-
Student	3.8% (n=2)	2% (n=1)	1
Housewife	15.1% (n=8)	13.7% (n=7)	1

DISCUSSION

In this study, 96 % HIV-infected patients adhered to HAART therapy. This result suggests that Indonesia has higher adherence to the treatment compared to other countries, such as India (60%),¹¹ Brazil (74.27%)¹², Nigeria (62.9%)¹³ and United States (66%).¹⁴ This excellent result might be supported by the implementation of 3 of 5 WHO programs for HAART in Indonesia since 1999¹⁵ and may be influenced by the location where the survey took place. In HIV centres and clinics, the majority of attending HIV-infected patients have already understood the concept of HAART therapy and accepted their HIV status. In addition, they may do HAART therapy as one of their regular activities. Furthermore, the self-reporting method might affect the way the questions were asked: to prevent prejudicial judgement, patients should be notified that they were not being judged and surveyors sought a true answer.¹⁶

We found that there was no association between medication adherence of HIV patients and self-efficacy. However, many studies had shown correlation between them. Berg, et al.¹⁷ found that adherence of HIV patient is partially correlated with self-efficacy. Another study by Johnson, et al.⁸ demonstrated that self-efficacy

mediated the relationship between positive provider interactions and medication adherence. Pinheiro et al.¹⁸ conducted a study with 195 HIV-infected patients in Brazil also showing that self-efficacy was the most important predictor of adherence.

No association between depression level and adherence was found in this study, while HIV-infected patients who were in severe depression still had good adherence. Leserman et al.¹⁴ showed correlation between depressive symptoms and adherence; however, the odd ratio was only 1.05 and clinically not significant. Johnson et al.⁸ performed behavioural interventions teaching how to overcome stress on HAART adherence among HIV-infected patients. The result left uncertainty on the relative increase in the intervention group as compared to controls. The authors kept doubts about the clinical significance of this difference and presumed that it was only because of increased attention by the trial staff.⁸ According to Kalichman et al.¹⁹ depression was not also significant predictors of medication self-efficacy and/or medication adherence in HIV-infected patients. On the other hand, Fulk et al.²⁰ and Safren et al.²¹ found that relief from depression could potentially increase medication adherence which would in turn affect the illness severity and progression.

There was no association between social support and adherence in this study. Paasche-Orlow et al.²² stated the same result like we do. Their study showed that low social support was not associated with lower adherence. Indeed, trends in their data suggest the possibility that low social support may be associated with a higher odd of adherence and virologic suppression.²² The previous study by Johnson et al.⁸ found an indirect influence of social support on antiretroviral adherence by improving patient's self-efficacy.

The causes of non-adherence in this study were more affected by simply forgetting, being busy with other things, running out of medication or being ashamed if seen by others than feeling depressed or by low self-efficacy and low social support. The result is similar with other studies that also showed that most reasons were 'simply forget'.^{13,23-25}

Simply forget could happen because there was no self-reminder to take the regiments. Furthermore, using direct observation of medication ingestion may help to deal with this problem. Tyndall, et al.²⁶ demonstrated the positive impact that a comprehensive directly observed therapy (DOT) programme could have on increasing HAART adherence and outcomes. However, Santos, et al.²⁷ found that only 17% of their study participants would voluntarily participate in DOT program. Commonly mentioned concerns regarding DOT were loss of privacy, interference with family, work or home life and coercion.²⁷ However, it needs courage of the patients to accept their condition and keep their confidence.

Being "busy with other things" may probably be due to jobs that cannot be set aside; therefore patients forget and miss the schedule to take their medication. Moreover, to schedule an appointment with a doctor is difficult due to the permission by the employer and the fear to be known as an HIV-infected person. Poorly distributed medication to rural areas and socio-economic factors also affect non-adherence, especially when patients run out of their medicine.

To control the prevalence of HIV-infected patients, the Indonesian Government initiated a program in 2004 to subsidize the cost of ART. By 2005, the program provided low-cost HAART at 50 hospitals. Yet, only 20 percent of HIV-infected patients received HAART in 2006 according to UNDAID. This is well below the country's target.³

Antiretroviral drugs can only be provided at hospitals in urban areas whereas some HIV-infected patients live

in rural areas. Consequently, when the drugs have run out, these patients have difficulties in acquiring medication, which forces them to miss taking HAART for days, months or even years. In addition, unemployed patients and low paid workers are unable to get their medicine despite of low prices. Stigma to HIV-infected patients also affects them to hide their condition and results in fear to take HAART in front of others. They are deliberate to pass their medication because of feeling ashamed.⁶

In this study, we found that self-efficacy, depression level and social support were correlated to each other. Depressive symptoms could be reduced when there was social support to HIV-infected patients. However, the social support may also be influenced by depression, which causes loss of interest to join the society. Because of the social stigma, people with HIV tend to become depressed, worried and stressed. Adequate social support may help them to overcome these psychological symptoms. Consistent with the previous study by Reynolds et al.²⁵ with over 900 individuals naive to HIV medication treatments, we found that lower self-efficacy about adherence was associated with increased stress, depression, and symptoms of distress. On the other hand, higher self-efficacy was associated with higher functional health, social support, and higher education ($p < .001$).²⁵

In conclusion 96% of our subjects were found to be adherent to HAART, although there were no associations between medication adherence and self-efficacy, depression level and social support in this study. The reasons of non-adherence were mostly "simply forget", followed by "busy with other things", "run out of medication" and "ashamed if seen by others".

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