

ASSOCIATION BETWEEN COMPLIANCE LEVEL ON FIXED-DOSE COMBINATION ANTIRETROVIRAL DRUG AND CD4 CONDITION AMONG HIV PATIENTS

Fadhil Ilham Mustafa, Nurfitri Bustamam, Andri Pramesyanti

Faculty of Medicine, Universitas Pembangunan Nasional Veteran, Jakarta

ABSTRACT

Background: People living with HIV / AIDS (PLWHA) have weak immune systems and are prone to infection. Therefore, PLWHA must take antiretroviral (ARV) to maintain their immunity. This study aimed to determine the relationship between the level of adherence to taking ARV fixed-dose combination (FDC) drugs and CD4 levels of HIV patients.

Subjects and Method: This was a cross-sectional study conducted at Pengayoman Cipinang Hospital, Indonesia, in 2018. Total of 91 HIV patient over 17 years of age, had or had received FDC ARV therapy for at least 1 year, and did not experience drug-induced hepatitis were enrolled in this study. The dependent variable was CD4 level. The independent variable was level of adherence to taking ARV fixed-dose combination (FDC). The data were taken from the Voluntary Counseling and Testing Poli Pengayoman Cipinang Hospital. This study used secondary data from the Overview of HIV Care and ARV Therapy. The data were analyzed using Chi-square.

Results: A total of 65.93% HIV patients had a good level of medication adherence and 79.12% had an increase of CD4 levels. There was a significant relationship between adherence to taking FDC ARV drugs and CD4 levels (OR = 6.50; 95% CI = 2.15 to 19.62; $p < 0.001$), and it was statistically significant.

Conclusion: There is a significant relationship between the level of adherence to taking FDC ARV drugs and CD4 levels. Therefore, patients must receive education and support to improve adherence to taking ARV drugs.

Keywords: antiretroviral, CD4, fixed-dose combination, adherence to taking medication, people with HIV / AIDS

Correspondence:

Fadhil Ilham Mustafa. Faculty of Medicine, Universitas Pembangunan Nasional Veteran, Jakarta. Jl. RS Fatmawati, Pondok Labu, South Jakarta. Email: fadhilimn@gmail.com. Mobile: 081283681755

BACKGROUND

Compliance is multidimensional phenomena that are determined by therapy, health system, environment, age, family support, patient motivation, and socioeconomic conditions. Strong commitment and close coordination from all parties are required in developing a multidisciplinary approach to solving patient non-compliance problems. Low adherence to drugs given by doctors can increase the risk of morbidity, mortality, and drug resistance both in patients and in the wider community (Purwanto, 2010).

Disease which is caused by by human immunodeficiency virus (HIV) to currently untreatable. The virus in the patient's body cannot be resisted by the immune system, so the patient must take antiretrovirals (ARV) for life and on time. The strict schedule of therapy with ARVs must not be missed in order to reduce the amount of virus in the body. If not disciplined, the virus will become resistant to drugs. HIV is a retrovirus that infects cells of the immune system, especially CD4 T cells and macrophages which are a vital component of the immune system. This is what makes people living with HIV/AIDS

(PLWHA) have a weak immune system and are prone to infection. Therefore, PLWHA must take ARVs to maintain their immunity.

In Indonesia, HIV/AIDS was first discovered in Bali Province in 1987. To date, HIV/AIDS has spread in 407 of 507 districts-/cities (80%) throughout the province of Indonesia. Various countermeasures have been made by the government in collaboration with various institutions at home and abroad (Ministry of Health, Republic of Indonesia, 2016).

The spread of HIV tends to increase in Indonesia. The cumulative number of HIV sufferers as of June 2016 was 208,920 people, while the cumulative total of AIDS cases was 82,556 people. HIV infection tends to increase and mostly occurs in the productive age group, namely the 25-49 age group and the 20-24-year age group (Ministry of Health, 2016).

The number of PLWHA who had received ARV in Indonesia until June 2016 was 164,155 people. A total of 69,954 people were still receiving ARV as of June 2016 with details of using the First Line Regimen of 53,433 people, one of the ARVs was replaced with another ARV which was still classified as the first line regimen as many as 14,427 people, and PLWHA who received 1 or 2 types of line ARV the second was 2,094 people. The rest who had received ARV, as many as 21,155 people died, 27,809 people lost follow-up, 12,622 moved to other service facilities, and 2,802 people stopped taking ARV (Ministry of Health, 2016).

The results of Ida Ayu and I Wayan's study in 2017 showed that there was a significant relationship with a strong correlation ($r= 0.601$) between the level of medication adherence and CD4 counts in HIV/AIDS patients at the clinic for the Voluntary Counseling and Testing Sanglah Hospital (VCT) period September-November, 2014. In that

study, the ARVs used were not a fixed-dose combination (FDC).

Based on this background, the study was conducted to determine whether there was a relationship between the level of adherence to taking FDC ARV drugs and CD4 levels of HIV patients at Pengayoman Cipinang Hospital. It is one of the referrals hospitals in East Jakarta, especially for people living with HIV who are under the auspices of the Ministry of Law and Human Rights of the Republic of Indonesia.

SUBJECTS AND METHOD

1. Study Design

This was a cross-sectional study conducted at Pengayoman Cipinang Hospital, East Jakarta, Indonesia.

2. Population and Sample

The population in this study was all data on the Care Summary of HIV/AIDS patients undergoing treatment at Pengayoman Cipinang Hospital during the 2014-2018 period. The subjects of this study were all HIV patients at Pengayoman Cipinang Hospital who met the criteria. The inclusion criteria were HIV patients over 17 years of age, had or had received FDC ARV therapy for at least 1 year, and did not experience drug induced hepatitis. This study used secondary data from the Overview of HIV Care and ARV Therapy.

The sample size was calculated using an unpaired categorical analytic formula with the total sample results were 82 people. This result was added by 10% in anticipation of a drop out, so that the sample size was 91 people.

3. Study Variables

The dependent variable was CD4 level. The independent variable was level of adherence to taking ARV fixed-dose combination (FDC).

4. Study Instruments

The secondary data were taken from the Voluntary Counseling and Testing of Pengayoman Cipinang Hospital.

5. Data Analysis

The data were analyzed using Chi-square.

6. Research Ethic

This study received Ethical Clearance from the Health Study Ethical Commission of the Veteran National Development University Jakarta (B/1317/IV/2018/KEPK) and a letter

permission from the Head of Cipinang Pengayoman Hospital.

RESULTS

1. Subject Characteristics

In Table 1, it can be seen that the majority of the subjects were male, belonging to the early adult age group, highly educated with high school education, not working, and not married.

Table 1. Subject Characteristics

| Characteristics | n | % |
|-----------------------------------|----|-------|
| Gender | | |
| Male | 79 | 86.81 |
| Female | 12 | 13.19 |
| Age | | |
| Late Adolescent (17-25 years) | 9 | 9.89 |
| Early Adult (26 - 35 years) | 40 | 43.96 |
| Late Adult (36 - 45 years) | 32 | 35.16 |
| elderly Early (46-55 years) | 8 | 8.79 |
| elderly Weekend (56-65 years old) | 1 | 1.09 |
| Seniors (65+) | 1 | 1.09 |
| Status of Education | | |
| Primary school | 12 | 13.19 |
| Junior high school | 28 | 30.77 |
| High school | 37 | 40.66 |
| College/University | 14 | 15.38 |
| Marital Status | | |
| Not Married | 47 | 51.65 |
| Married | 32 | 35.16 |
| Widow/widower | 12 | 13.19 |
| Job Status | | |
| Not Working | 53 | 58.24 |
| Working | 38 | 41.76 |

2. Overview Disease

Study subject can be seen in Table 2 that the biggest risk factors of HIV/AIDS in Cipinang Pengayoman hospital was drug with the

number of 57 subjects (62.63%). A total of 52 subjects were hospitalized and 54.9% were diagnosed as having stage III of HIV/AIDS.

Table 2. Disease Description of Study Subjects

| Disease Description | n | % |
|---------------------|----|-------|
| Risk Factors | | |
| Drugs | 57 | 62.63 |
| Heterosexual | 26 | 28.57 |
| Homosexual | 6 | 6.59 |
| Bisexual | 2 | 2.20 |

| | | |
|-----------------------|----|-------|
| Care Status | | |
| Outpatient | 39 | 42.86 |
| Inpatient | 52 | 57.14 |
| Clinical Stage | | |
| Stage I | 10 | 10.99 |
| Stage II | 12 | 13.19 |
| Stage III | 50 | 54.95 |
| Stage IV | 19 | 20.88 |

3. Compliance Level of Subjects in Taking FDC ARV Medication

The majority (65.93%) of study subjects had a good level of adherence to taking medication (Table 3).

4. An overview of CD4 levels

Overview of CD4 levels can be seen in Table 4 shows that after being treated with ARV,

most of the subjects (79.1%) experienced an increase in CD4.

5. Compliance Levels of FDC ARV drugs and CD4 levels

The results of the Chi-square test showed that there was a relationship between the level of adherence to taking FDC ARV drugs and CD4 levels (OR= 6.50; 95% CI= 2.15 to 19.62; p< 0.001) (Table 5).

Table 3. Compliance Level of Subjects Taking FDC ARV Medication

| Compliance Level | N | % |
|---------------------|-----------|-------------|
| Good (≥ 95%) | 60 | 65.93 |
| Sufficient (80-95%) | 26 | 28.57 |
| Less (<80%) | 5 | 5.59 |
| Total | 91 | 100% |

Table 4. Overview of CD4 Levels

| Levels CD4 | N | % |
|-----------------|-----------|------------|
| Raised | 72 | 79.12 |
| Fixed/Decreased | 19 | 20.88 |
| Total | 91 | 100 |

Table 5 Compliance Levels of FDC ARV Medication and CD4

| Compliance | CD4 Levels | | | | TOTAL | OR | 95% CI | P | |
|----------------------|------------|------|---------------------|------|-------|-----|--------|---------------|--------|
| | Increase | | Constantly/Decrease | | | | | | |
| | N | % | N | % | | | | | |
| Good | 54 | 90 | 6 | 10 | 60 | 100 | 6.50 | 2.15 to 19.62 | <0.001 |
| Enough + Less | 18 | 58.1 | 13 | 41.9 | 31 | 100 | | | |

DISCUSSION

A total of 79 out of 91 subjects (86.81%) were male. A similar result was obtained by the Ministry of Health (2012) which

states that more men have HIV/AIDS than women with a ratio of 2: 1.

The high proportion of men who suffer from HIV/AIDS is assumed to be due to the large number of men who have

risky sexual intercourse and injecting drug users (IDUs) than women who get it more often from their sexual partners. This is supported by Yusri et al. (2012) in his study at RSUP H. Adam Malik Medan which stated that of the 163 study subjects with sexual transmission, the highest proportion was male, 119 people (73.0%). Likewise, of the 58 subjects with blood transmission and blood products, the highest proportion (77.6%) were male.

In this study, the highest prevalence of HIV/AIDS cases at Pengayoman Cipinang Hospital was in the category of early adulthood - late adulthood or aged 26-45 years which was included in the category of productive age. The results of this study are in accordance with data from the Ministry of Health (2013) that the highest cumulative percentage of AIDS (1987-June 2013) is in the 20-29 years age group (35%), 30-39 years age group (28.2%), and the 40-49-year age group (10%). The results of this study indicate that most AIDS sufferers are in the productive age group (20-49 years).

The majority (40.7 %) of the study subjects had high school education. This is in accordance with the results of Husnul's study in 2015 in the working area of the Simpang Tiga Community Health Center, Marpoyan Damai sub-district, with the result that 67.9% of HIV/AIDS sufferers have the latest high school education/equivalent. Other studies have shown sexually transmitted infections, including HIV infection, to be more prevalent in the group with high school education status and above. This is thought to be related to the level of economic stability which is getting better, so that it has an impact on the development of prostitution service providers for adult

male groups with a good economic level (Karim, 2012).

In this study, 53 out of 91 subjects did not work. In contrast, the results of Yowel's (2016) study in West Papua showed that 61.3% of working subjects and married subjects were 61.3%. This difference is due to the fact that most of the study subjects at Pengayoman Cipinang Hospital are inmates so that the subject does not work.

In this study, 57 people (62.6%) had the risk factors for drugs. The increase in HIV infection is increasingly evident in drug users. Injecting drug users have a high risk of contracting HIV. The cause is the use of shared and repeated needles that are commonly used by narcotics users. One syringe is shared between 2 to more than 15 people who use narcotics. A survey conducted at the Drug Addiction Hospital in Jakarta showed an increase in the prevalence of drug users who were undergoing rehabilitation and suffering from HIV from 15% in 1999 to 40.8% in 2000 and 47.9% in 2001 (Zubairi, 2014).

The results showed that the majority of the subjects at Pengayoman Cipinang Hospital were diagnosed with stage III (54.9%). Different results were obtained in Estie's study in 2011-2013 in Jakarta. As many as 59.1% of subjects with HIV/AIDS were diagnosed as stage IV. This difference was due to Estie taking the study subject only to the Inpatient section. According to the Ministry of Health in 2011 when PLWHA was at stage I, PLWHA did not experience any significant symptoms. Symptoms of unexplained weight loss and new infection are felt by PLWHA when they are at stage II or III. When PLWHA already feels these symptoms, then the patient goes to a doctor. This is what causes the majority of PLW-

HA in Cipinang Pengayoman Hospital to be diagnosed at stage III HIV/AIDS.

The results showed that 60 (65.93%) subjects had good adherence to taking medication. This data is in accordance with the results of Ida Ayu's study in 2014 at Sanglah Hospital Bali, with the results that 77.8% of study subjects had a good level of adherence in taking ARVs. A good level of adherence means that the subject takes > 95% of the drug in a month. This 95% adherence rate can be analogous to if a person with HIV/AIDS is required to take medication twice a day, then the total drug consumption in a month must be 60 pills (100% compliance rate). If the study subjects took only 57 pills out of a total of 60 pills, the adherence rate of the study subjects was classified as 95%. If interpreted into the results of the Morisky Medication Adherence Scale (MMAS), 95% will be classified as subjects with moderate adherence (a maximum of forgetting 2 tablets of medicine a month). Adherence really determines how successful ARV treatment is in increasing CD4 cells, because if a person forgets to take a dose, HIV can multiply. Therefore, high adherence is needed considering that HIV is a mutating virus. If you do not comply with the rules for using ARV drugs, the drugs you are taking can no longer slow down the virus, so they need to be replaced with a higher dose.

Study by Adriani et al. (2014) for PLHIV in Lancang Kuning Support Group Pekanbaru who were treated with ARVs instead of FDCs, it showed that only 22 people with HIV/AIDS had good medication adherence (26.7%). This shows that the use of ARV FDC is expected to increase the subject's medication adherence. Study subjects with FDC ARVs only needed to take one tablet compared to

PLWHA who had not yet consumed FDC ARVs who would take several tablets as a combination of ARV drugs.

As many as 72 out of 91 subjects (79.12%) had increased CD4 levels after being treated with ARV and 19 subjects (20.88%) had fixed/decreased CD4 levels. In the study, it was found that the majority of HIV/AIDS study subjects at Pengayoman Cipinang Hospital had increased CD4 levels. This is in line with Andriani's study in 2014 at Lancang Kuning Support Group Pekanbaru, with the result that 90% of subjects experienced an increase in CD4 levels. This is due to the good level of compliance with taking ARV drugs at Pengayoman Cipinang Hospital. Monitoring the number of CD4 cells in the blood is a reliable indicator to monitor the severity of the immune damage caused by HIV. A high CD4 level indicates a recovered body immunity for PLWHA (Zubairi, 2014).

The test results Chi-square level for taking ARV FDC drugs and CD4 levels showed that there was a relationship between the level of adherence to taking ARV FDC drugs and CD4 levels (OR= 6.50; 95% CI= 2.15 to 19.62; $p < 0.001$). According to Bachmann (2006), ARV therapy requires a high level of adherence. It is hoped that high levels of adherence to ARV therapy can achieve treatment success and prevent resistance. This study is in line with Ida Ayu's study (2014) with the results of the Pearson correlation test which showed a statistically significant relationship with a strong correlation strength ($r = 0.601$) between the level of medication adherence and CD4 counts in subjects with HIV/AIDS. at the VCT Polyclinic of Sanglah Hospital for the period September - November 2014 ($p < 0.05$).

Treatment with ARVs is expected to reduce the viral load or the amount of HIV in the body. HIV attacks the immune system. The success of therapy can be seen from the clinical symptoms of the subjects who improve after therapy, one of which is the absence of opportunistic infections. CD4 count was the strongest predictor of HIV complications.

Based on this study, it can be concluded that there is a significant relationship between the level of adherence to taking FDC ARV drugs and CD4 levels. Therefore, patients should receive education and support to increase their level of adherence to ARV therapy.

REFERENCE

- Andriani R, Sandhita (2014). Hubungan kepatuhan mengkonsumsi anti-retroviral virus (ARV) dengan kenaikan jumlah CD4 ODHA di lancang kuning support group Pekanbaru. *Scientia Journal* 2(3)
- Bachmann MO (2006). Effectiveness and cost-effectiveness of early and late prevention of HIV/AIDS progression with antiretrovirals or antibiotics in Southern African adults. Oxfordshire: Taylor & Francis.
- Djoerban Z, Djauzi S (2014). Buku ajar ilmu penyakit dalam jilid i edisi vi: hiv/aids di Indonesia. Jakarta: Interna Publishing.
- Kambu Y, Waluyo A Kuntarti (2016). Umur orang dengan hiv aids (odha) berhubungan dengan tindakan pencegahan penularan hiv. *Jurnal Keperawatan Indonesia*; 19:3.
- Karim QA, Humphries H (2008). Reducing HIV infection in young women in Southern Africa: the key to altering epidemic trajectories in a generalized, hyperendemic setting. Washington: USAID.
- Kementerian Kesehatan Republik Indonesia (2011). Pedoman nasional tata-laksana klinis infeksi hiv dan terapi antiretroviral pada orang dewasa. Jakarta: Direktorat Jenderal Pengendalian Penyakit dan Penyehatan Lingkungan Kemenkes RI.
- Kementerian Kesehatan Republik Indonesia (2012). Perkembangan HIV-AIDS di Indonesia triwulan III Tahun 2012. <http://www.depkes.go.id/article/print/2186/perkembangan-hiv-aids-di-indonesia-triwulan-iii-tahun-2012.html>.
- Manuaba, Wasita IAK, Yasa, IWPS (2017). Tingkat Kepatuhan Mengkonsumsi Obat Antiretroviral dengan Jumlah CD4 Pada Pasien HIV AIDS di Klinik VCT RSUP Sanglah dalam Periode September-November 2014. *E-Jurnal Medika Udayana*, 6(1): 2303-1395. <https://ojs.unud.ac.id/index.php/eum/article/view/28437>
- Ministry of Health (2016). Situasi Penyakit HIV AIDS di Indonesia. <http://www.depkes.go.id/resources/download/pusdatin/infodatin/Infodatin%20AIDS.pdf>.
- Notoatmodjo S (2012). Metodologi Penelitian Kesehatan. Jakarta: Rineka Cipta
- Puspitasari E, Yunihastuti E, Rengganis I Rumende CM (2016). Prediktor mortalitas pasien HIV/AIDS rawat inap. *Jurnal Penyakit Dalam Indonesia*, 3(1). doi: <http://dx.doi.org/10.74-54/jpdi.v3i1.29>
- Saktina PU, Satriyasa BK (2017). Karakteristik penderita aids dan infeksi oportunistik di Rumah Sakit Umum Pusat Sanglah Denpasar periode Juli 2013 sampai Juni 2014. *E-Jurnal Medika Udayana*, 6(3). 2303-1395. <https://ojs.unud.ac.id/index.php/eum/article/view/29100>

Umam H, Dewi YI Elita V (2015). Identifikasi karakteristik orang risiko tinggi HIV dan AIDS tentang program pelayanan voluntary counseling and testing (VCT). *Jurnal Mahasiswa UNRI*, 2(1).

Widiyant M, Hutapea H (2015). Hubungan jumlah cluster of differentiation 4

(CD4) dengan infeksi oportunistik pada pasien HIV/AIDS di Rumah Sakit Umum Daerah (RSUD) DOK II Jayapura. *Jurnal Biologi Papua*, 7(1). doi: <https://doi.org/10.31957/jbp.42>