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CD4 LYMPHOCYTE IN HIV / AIDS BEFORE AND AFTER ANTIRETROVIRAL THERAPY

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Abstract: Human Immunodefficiency Virus (HIV) is a virus that decreases the human immunity system, therefore the infected people become susceptible to any kind of infections. *Examination of CD4 lymphocyte count periodically is one of the antiretroviral therapy success indicators. The purpose of this research was to determine the difference of CD4 lymphocyte count before and after antiretroviral therapy at Ulin General Hospital Banjarmasin on 2013-2015. The method of this research was observational analytic with cross-sectional approach. The study population was 55 patients which were selected by inclusion and exclusion criteria. Results portrayed an increase of the CD4 lymphocyte count in 51 patients after being given four kinds of antiretroviral for 6 months with the mean increase in CD4 lymphocyte count was 92,72 cell/µL. Data analysis result with Wilcoxon test portrayed a difference of the CD4 lymphocyte count before and after antiretroviral therapy with p value=0,000. In conclusion, there was a significant difference of the CD4 lymphocyte count before and after antiretroviral therapy.*

Keywords*: Human Immunodeficiency Virus, CD4, lymphocyt, antiretroviral therapy*

INTRODUCTION

Human Immunodeficiency Virus (HIV) is a major problem that threatens Indonesia and many countries around the world.[1] HIV is a type of virus that lowers the immune system, therefore the people infected with this virus become susceptible to various infections.[2] *Acquired Immunodeficiency Syndrome* (AIDS) is a stage of infection that occurs when the immune system is damaged and a person becomes susceptible to infection. A person has been diagnosed with AIDS when CD4 lymphocytes count falls below 200 cells / µL. HIV is found primarily in blood, sperm fluid, vaginal fluid and breast milk.[2,3]

According to United Nations Programme on HIV/AIDS (UNAIDS) on 2012, there were 35.3 million people infected with HIV worldwide and 2.3 million more people each year.[4] The data of Indonesia Health Profile on 2012 showed that there were 21,511 new cases of HIV and increased by 35% to 29,037 new cases of HIV infection on 2013. On 2013, there were 174 new HIV cases in South Kalimantan.[5]

Drugs used for HIV currently are antiretroviral (ARV) with the aim of suppressing the development of virus to the maximum until undetected.[6] The standard guidelines for the management of HIV in Indonesia are the provision of 1 nucleoside reverse transcriptase inhibitors (NRTIs) and 2 non-nucleoside reverse transcriptase inhibitors (NNRTIs) known as combination therapy or ARV regimen as first line. It is expected that within six months of therapy there will be better clinical and immunological development.[6]

The success of ARV therapy programs can be achieved by following monitoring activities. A method of monitoring the success of therapy is by examining CD4 lymphocytes count every six months. Data of CD4 lymphocytes count when starting ARV therapy and the proliferation of CD4 lymphocyte counts evaluated every six months is necessary to determine immunological failure.[6]

It is essential to monitor ARV treatment responses through changes of CD4 lymphocyte count as a sign of an immunologic response. On the other hand, research on the evaluation of CD4 lymphocyte count responses in HIV patients who were given antiretroviral therapy requires more attention. In Indonesia, there are no a lot of researches reveal about the monitoring of antiretroviral therapy, especially at Ulin General Hospital Banjarmasin. Based on that reason, this research needs to be done.

RESEARCH METHODS

This research uses analytic observational method with retrospective cross-sectional approach. The populations of this research were patients diagnosed with HIV at Ulin General Hospital Banjarmasin on 2013-2015. The subjects of this research were taken from medical record data and laboratory results of HIV patients at Ulin General Hospital Banjarmasin using *purposive sampling* technique. The subjects were taken based on the inclusion criteria: the subjects should be 20-64 years old, have complete medical record data, has been receiving antiretroviral therapy for six months and has two data of CD4 lymphocytes count. The exclusion criteria for this research were patients who died before six months of antiretroviral therapy and pregnant HIV patients.

The instruments of this research are medical record data and laboratory result of CD4 lymphocytes count of HIV patients at Ulin General Hospital Banjarmasin. The variables studied in this research were the CD4 lymphocytes count before and after ARV therapy expressed in units of cells / µL calculated by Alere Pima CD4 tool in Immunoserology Division of Clinical Pathology Laboratory of Ulin General Hospital Banjarmasin. The data is processed by using computerized system using SPSS programme for Windows.

Data analysis in this research begins with data of normality test using *Kolmogorov-Smirnov* test and continued with *Wilcoxon test*.

RESULTS AND DISCUSSION

From total of 55 patients, there was an increase of CD4 lymphocytes count in 51 HIV patients (92. 73%) who received ARV therapy at Ulin General Hospital Banjarmasin for at least six months. There was a decrease of CD4 lymphocytes count in 4 subjects (7.27%). These results are in accordance with Yasin et al's study that reported an increase of CD4 lymphocytes count after ARV therapy for six months is 92%.[7]

CD4 lymphocyte examination of HIV patients before and after ARV therapy at Ulin General Hospital on 2013-2015 can be seen in table 1. The result of the mean rate of lymphocyte count before antiretroviral therapy was 131.73 cells / µL with the highest number was 377 cells / µL and the lowest was 4 cells / µL. The results showed that the mean rate of lymphocytes count after ARV therapy was 224.45 cells /µL with the highest number was 666 cells /µL and the lowest was 16 cells / µL. The mean rate change of lymphocyte count after ARV therapy was 92.72 cells / µL. This is in accordance with Laboratory Guidelines for Enumerating CD4 from WHO on 2007 and Tsibris et al's study which expressed the expected increase of CD4 lymphocyte after therapy was 50-100 cells / µL in the first year of antiretroviral therapy.[8,9]

The normality test used in this research is the Kolmogorov-Smirnov normality test. Kolmogorov-Smirnov test results showed the distribution of CD4 lymphocyte count data before therapy was normally distributed with p = 0.010, whereas the distribution of CD4 lymphocyte count data after treatment was not normally distributed with p = 0.001.

Table 1. Changes of CD4 Lymphocyte count in HIV Patients Before and After ARV Therapy at Ulin General Hospital Banjarmasin on 2013-2015.

CD4 Lymphocytes Count Before Therapy (cell / µL)		CD4 Lymphocytes Count After Therapy (cell/µL)		The differences of CD4 Lymphocyte Count (cell / µL)
Highest-Lowest	Mean	Highest-Lowest	Mean	Mean
4-377	131,73	16-666	224,45	92,72

The data analysis test was continued with *Wilcoxon* test to know the difference between CD4 lymphocyte count group before and after ARV therapy because the data distribution of one group was not normal. *Wilcoxon* test results showed p = 0,000 (p <0.05) which showed significant difference between CD4 lymphocyte count before and after ARV therapy.

The results of this statistical test are consistent with the previous hypothesis that there is a significant difference between CD4 lymphocyte counts before and after ARV therapy. ARV therapy becomes an effective way to increase CD4 lymphocytes count in people with HIV.[3] CD4 lymphocytes are one component of lymphocytes that play a role in the immune system. HIV virus will enter, infect and replicate in CD4 lymphocytes.[3,10] This process of replication leads to progressive death and decreased CD4 lymphocyte count progressively.[10] ARV therapy is still the only effective way to increase CD4 lymphocytes count in people with HIV. The mechanism of action of ARV is to inhibit viral replication and CD4 lymphocyte death.[3] This result is in

accordance with research conducted by Siahaan (2010) with observational analytic method and *cross sectional* approach, it was found that there are 45 subjects have complete medical record data. Data analysis of CD4 lymphocyte count before and after ARV therapy conducted by Siahaan using T test showed significant difference of CD4 lymphocyte count before and after ARV therapy with p = 0.0001.[11]

The distribution of first-line ARV regimens administered to HIV/AIDS patients at Ulin General Hospital Banjarmasin on 2013-2015 can be seen in table 2. There are 34 subjects (61.82%) received a combination regimen of Zidovudine + Lamivudine + Nevirapine (AZT + 3TC + NVP) as the beginning of ARV therapy, followed by Zidovudine + Lamivudine + Epavirenz (AZT + 3TC + EFV) of 15 subjects (27.27%), Tenofovir + Lamivudine + Epavirenz (TDF + 3TC + EFV) of 4 subjects (7.27%), Zidovudine + Lamivudine + Nevirapin (TDF + 3TC + NVP) of 2 subjects (3.64%).

Table 2. Distribution of First-line ARV regimen in HIV/AIDS Patients at Ulin General Hospital Banjarmasin

First line ARV regimen	Total (%)
AZT+3TC+NVP	34 (61,82%)
AZT+3TC+EFV	15 (27,27%)
TDF+\3TC+EFV)	4 (7,27%)
TDF+3TC+NVP)	2 (3,64%)

This result is in accordance with research conducted by Yasin et al at a Jogjakarta Education Hospital, it was showed that the Zidovudine + Lamivudine + Nevirapin (AZT + 3TC + NVP) regimen was the most widely used of 61.97%, followed by AZT+3TC+EFV, TDF+3TC+EFV and TDF+3TC+NVP. The use of all four types of regimens at Ulin General Hospital Banjarmasin is in accordance with national guidelines for the management of HIV/AIDS infection and antiretroviral therapy in adults with the most widely used AZT + 3TC + NVP and AZT + 3TC + EFV regimens.[6,7]

The mean rate of CD4 lymphocyte counts of HIV/AIDS patients based on the type of ARV regimen showed a varied increase in the four types of ARV regimens. The AZT + 3TC_NVP regimen showed a mean rate change of 101.94 cells /µL, the AZT + 3TC + EFV regimen showed a mean rate change of 93.53 cells /µL. The TDF + 3TC + EFV regimen showed a mean rate change of 73.5 cells / µL. The TDF + 3TC + NVP regimen showed a change of -31.5 cells / µL. The mean of this change can be seen in table 3.

Table 3. Mean Rate Changes of CD4 Lymphocyte counts in HIV / AIDS Patients by Regimen Type

First line ARV regimen	Mean Rate Changes (sel/μL)
AZT+3TC+NVP	101,94
AZT+3TC+EFV	93,53
TDF+\3TC+EFV)	73,5
TDF+3TC+NVP)	-31,5

The distribution of types of opportunistic infections in people with HIV/AIDS at Ulin General Hospital Banjarmasin on 2013-2015 can be seen in table 4. HIV/AIDS patients at Ulin General Hospitals on 2013-2015 mostly suffer from oral candidiasis. There are 33 (60%) subjects suffering from oral candidiasis, 19 (34.54%) subjects suffering from pulmonary tuberculosis, 5 (9.09%) subjects suffering from chronic diarrhea and 1 (1.81%) subject suffering from herpes zoster. This can be seen in table 3. This result is in accordance with Hutapea research at VCT clinic HKBP Balige Hospital which reported that most opportunistic infections suffered by HIV patients at HKBP Balige Hospital are oral candidiasis of 97 (89,8%) subjects and the least case is 1 (0.9%) subject suffering from herpes zoner.

Table 4. Distribution of Types of Opportunistic Infections in HIV/AIDS Patients at Ulin General Hospital Banjarmasin

Types of Opportunistic Infections	Total (%)
Oral Candidiasis	33 (60%)
Pulmonary Tuberculosis	19 (34,54%)
Chronic Diarrhea	5 (9,09%)
Herpes Zooster	1 (1,81%)

CONCLUSIONS

Based on the research results, the mean rate of CD4 lymphocytes count in HIV patients before antretroviral therapy at Ulin General Hospital Banjarmasin was 131.73 cells / Ml; whereas, the mean rate of CD4 lymphocytes count in HIV patients following antiretroviral therapy at Ulin General Hospital Banjarmasin was 224.45 cells/µL. From these two results, it can be concluded that there is a significant difference of CD4 lymphocytes count in HIV patients before and after antiretroviral therapy at Ulin General Hospital Banjarmasin.

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