**Original Research**

# VIRAL LOAD AND CD4+ AMONG HIV/AIDS PATIENTS RECEIVING ANTIRETROVIRAL THERAPY IN JAYAWIJAYA DISTRICT, PAPUA PROVINCE, INDONESIA

**Mirna Widiyanti[1], Moch. Irfan Hadi[2], Setyo Adiningsih[1], Evi Iriani Natalia[1], Dedi Ananta Purba[1]**
[1]Research and Development Center of Papua Health Office, Papua, Indonesia
[2]Department of Biology, Faculty of Science and Technology, UIN Sunan Ampel, Surabaya, Indonesia

## ABSTRACT

*Highly active antiretroviral therapy (HAART) is expected to reduce human immunodeficiency virus (HIV) morbidity and mortality. Antiretroviral therapy in HIV patients is given based on clinical conditions, CD4+ cell counts, and the number of viral copies in the blood. This study aimed to determine the profile of CD4+ levels and plasma viral load in HIV patients receiving antiretroviral therapy. This was a cross-sectional study conducted within six months at Voluntary Counseling and Testing (VCT) in Jayawijaya Hospital, Papua, Indonesia. The CD4+ levels were measured using CD4+ counter and viral plasma was checked using Polymerase Chain Reaction (PCR) for 90 patients. The results showed more female patients had a CD4+ level <200 cells/mm3, a higher number of copies of the virus in the blood plasma, and stages of disease 3 and 4. Statistically, there was a significant relationship between CD4+ levels and gender with a p-value = 0.00. HIV-infected males were more likely to have lower CD4+ cell counts and higher viral loads than females.*

***Keywords:*** *Viral load; CD4+; Jayawijaya; AIDS/HIV; human immunodeficiency*

**Correspondence:** Mirna Widiyanti, Research and Development Center of Papua Health Office, Jayawijaya, Papua, Indonesia. Email: ninawidhy@gmail.com

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**Highlights:**

1. Clinical conditions, CD4+ cell counts, and the viral copies number in the blood for AIDS/HIV were given antiretroviral therapy.
2. The profile of CD4+ levels and plasma viral load in HIV patients receiving antiretroviral therapy
3. The lower CD4+ cell counts and higher viral loads happen in HIV-infected's men.

## INTRODUCTION

According to the Indonesian Ministry of Health, the HIV/AIDS case in Indonesia is increasing at the end of October–December 2017 with 14,640 HIV cases and 4,725 AIDS cases spread throughout Indonesia. Antiretroviral therapy (ART) effectively suppresses the concentration of HIV-1 RNA in the blood and reduces HIV infectivity risk (Cohen et al. 2013). Early antiretroviral therapy has been recommended as a strategy to lower HIV incidence rate, clinical evidence, and mathematical models supporting the use of ART to control HIV transmission risk at the individual level and population (Cohen et al. 2016, Eaton et al. 2012, Sorensen et al. 2012).

Although antiretroviral therapy significantly reduces the incidence of pain and mortality associated with HIV-1 virus infections, a virology treatment failure often occurs. The plasma prognostic value of HIV-1 (viral load) and the number of Cluster Differentiation 4 ($CD4^+$) for clinical progression at baseline was measured in the patient population treated using antiretroviral (Farahani et al. 2016). Therapeutic failure can be seen from a variety of criteria, virological, immunological, and clinical. The best criteria are virological criteria. If there is no examination, it uses

immunological tests. The Indonesia Ministry of Health states that ODHA should use ARV for approximately six months before the stated failure of therapy in a state of good compliance.

$CD4^+$ is the best parameter to measure immune-deficiency. If used in conjunction with a clinical assessment, $CD4^+$ can be an early indication of progression disease, because $CD4^+$ counts decline earlier than the clinical condition. $CD4^+$ monitoring can be used to initiate ARV administration or drug replacement. $CD4^+$ counts may fluctuate according to the individual and the disease suffered.

$CD4^+$ speed reduction (both absolute and $CD4^+$ percentage) has been proven to be used as a guide for the development of AIDS disease. $CD4^+$ counts decline gradually during the disease. The speed of its decline over time averages 100 cells per year (Birhan et al. 2020). The increased rate of viral load (not an absolute number of viruses) can be used to estimate the development of HIV infection. Viral load increases gradually over time. In the first three years after the seroconversion occurred, viral load changed as if only in the patient with a tendency on AIDS at the time. After that time, the change in viral load can be detected, both in the accelerometer and absolute amount. However, only both can be used as a sign progression disease.

Data from some cohort studies showed that $CD4^+$ cell counts remained steady or continued to increase in patients using ART, although there was an increase in the plasma viral load of HIV-1 in the blood. The level of immunosuppression or immunocomics determines the progression of the disease, and the $CD4^+$ count becomes a better predictor than the viral load for patients who receive ART event though predictive value of viral load that will increase with the length of infection (Shoko & Chikobvu 2019). Moreover, viral load states the measure of inhibition, while individuals with the low viral load will press the transmission rate to below (Hughes et al. 2012).

This study aimed to identify immunological clinical progression profile of $CD4^+$ levels, virology with viral load, and clinical value using clinical stage in HIV patients who have received therapy over six months in Jayawijaya Regency, Papua, Indonesia.

## MATERIALS AND METHODS

This study was a descriptive-analytical study with cross-sectional design of the latitude in HIV/AIDS patients who underwent routine treatment at VCT Wamena Hospital. The research was conducted for six months from April-October 2017. $CD4^+$ and viral load were examined in 90 HIV/AIDS patients. $CD4^+$ test was conducted using a $CD4^+$-FacsPresto (BD, Bioscience, USA), while viral load was measured using the qPCR (Bioneer, Korea) technique. Sampling and recording of medical records conducted in VCT RSUD Jayawijaya, $CD4^+$, and viral-load analysis were conducted in the Laboratory of Immunology, Research and Development Center of Papua Health Office.

PCR viral load and $CD4^+$ examination, 400 ul HIV plasma extracted with viral test kit load Exiprep DX Viral RNA Extraction Kit (Cat: K-4773), and the Accupower Kit quantitative HIV PCR Kit 96 using the Machine Exiprep TM 16 (Bioneer, Korea). The results of the extraction in the elution tubes were inserted in the Vortex-spin tool (EXI-spin), and Exi-Cycler 96. Quantitative PCR results were then analyzed using Exi-CYCLER3 software. The results of the analysis were in the form of data which reflected the quantity (ml) of the virus blood samples of HIV patients.

A total of 100 ul whole blood was conducted $CD4^+$ examination using BD FacsPresto (Paint: 651000) and BD Facspresto Cartridge Kit (Cat: 655495). The $CD4^+$ test results showed an absolute value and presentation. The test result was inserted in the Excel chart for further analysis. Demographic and clinical characteristics data were obtained from patient medical records and interviews.

Quantitative PCR using Exi-Cycler could read the viral load up to >50 copies/ml of the viral RNA. The result of the <50 copies/ml entered in the category was not detected, while >50 copies/ml were detected. Data were analyzed using SPSS for $CD4^+$ frequency distribution, viral load, and clinical stage. To know the relationship of clinical progression profile and gender of patients using Chi-Square test with confidence level 0.05.

This study had been approved by the Health Research Ethics Committee, Board of Health Research and Development, Health Ministry of the Republic of Indonesia, under a decree No. LB.02.01/5.2/KE.064/ 2017.

## RESULTS

Results of laboratory examination and medical record data obtained results in the form of clinical profiles of patients that include immunological, virological, and clinical parameters.

Table 1. Clinical profile of HIV/AIDS patients in RSUD Jayawijaya

| Variable | Frequency | Percentage |
|---|---|---|
| Gender | | |
| Male | 45 | 50 |
| Female | 45 | 50 |
| Age | | |
| 17-35years old | 62 | 68.9 |
| >35 years old | 28 | 31.1 |
| CD4+ levels | | |
| <200 cell/mm$^3$ | 13 | 14.4 |
| >200 cell/mm$^3$ | 77 | 85.6 |
| Viral Load | | |
| Detected | 52 | 57.8 |
| Not detected | 38 | 42.2 |
| Opportunistic infections | | |
| TB | 5 | 5.6 |
| Non-TB | 85 | 94.4 |
| Type of Therapy | | |
| EFV Based | 78 | 86.7 |
| NVP Based | 12 | 13.3 |
| Clinical Stadium | | |
| Stage 1&2 | 14 | 15.6 |
| Stage 3&4 | 76 | 84.4 |
| Duration of therapy | | |
| 6-24 months | 15 | 16.7 |
| >24 months | 75 | 83.3 |

Table 2. Relationship between progression profile and gender

| Characteristics | Gender | | p-value | Odds ratio | 95% CI interval | |
|---|---|---|---|---|---|---|
| | Female | Male | | | Lower | Upper |
| CD4+ levels | | | | | | |
| <200 cell/mm$^3$ | 12 | 1 | 0.00* | 16.00 | 1.98 | 129.27 |
| >200 cell/mm$^3$ | 33 | 44 | | | | |
| Viral Load | | | | | | |
| Detected | 27 | 25 | 0.83 | 1.20 | 0.51 | 2.77 |
| Not detected | 18 | 20 | | | | |
| Opportunistic infections | | | | | | |
| TB | 1 | 4 | 0.36 | 0.23 | 0.02 | 2.17 |
| Non-TB | 44 | 41 | | | | |
| Clinical stadium | | | | | | |
| Stadium 1&2 | 5 | 9 | 0.38 | 0.50 | 0.15 | 1.63 |
| Stadium 3&4 | 40 | 36 | | | | |

Table 1 showed that patients with a range of 17-35 age-years who were getting antiretroviral therapy >24 months were more dominated by CD4+ levels >200 cells/mm$^3$, and more viral loads were still detected in the range of Stage 3 and stage 4. The viral load number was highly detected in 2 patients, i.e., 2.07 x 106 and 2.38 x 106 copies/ml, and the lowest viral load ranged from 11 copies/ml and 15 copies/ml of blood. CD4+ levels <200 cells/mm$^3$ the lowest was 15 cells/mm$^3$.

From the Table, the composition of male and female patients was balanced, so that the analysis of the relationship to identify the relationship between the gender and characteristics progressivity of the patient's disease could be obtained (Table 2).

Table 2 illustrated a meaningful relationship between gender and profile progression, and the patient was a CD4+ level with p: 0.00 (<0.05). This suggested that female patients were more at risk of having lower CD4+ values (<200 cells/mm$^3$) than male patients.

## DISCUSSION

Gender contributes to the pathogenesis of diseases of various infectious diseases, including HIV (vom Steeg & Klein 2016). Most studies suggested that females had a lower viral load of HIV at infection onset, but despite these differences, progression diseases were comparable between genders (İnkaya et al. 2019). Females had a higher CD8 T cell activation at certain HIV viremia levels (Kovacs et al. 2010), whereas males had one log10 higher viral load activation (Meier et al. 2009). Similarly, the gene expression was stimulated to higher interference in females when controlling the viral load of HIV (Chang et al. 2013). Given immune activation's role in encouraging the progression of HIV disease and in the comorbidity that arose during the effective use of ART, the gender differences in immune set points had clinical consequences (Schwartzman-Morris & Putterman 2012).

This study showed that female HIV patients were more likely to have lower CD4+ levels than male patients. It was proven that progression disease was faster in females. Previous studies showed that disease progression in females was faster than in men. It was attributed to females who were less likely to start an ART or receive treatment for opportunistic infections and were more susceptible to suffering from anemia at the period of initiation of ART (Maskew et al. 2013).

Some contributing factors to gender differences and manifestations of the disease were the risk factors of behavior and epidemiological, socio-economic, differential expression of genes, and levels of sex steroid hormones (Ruel et al. 2011). The mechanisms underlying gender differences and manifestations of the disease HIV-1 had been investigated in In vitro. The results showed that plasmacytoid dendritic cells (pDCs) of females were more significant producing interferon-alpha (IFN-α) in response to HIV-1 derived from Logan Toll-Like Receptor (TLR) compared to plasmacytoid dendritic cells from males (Meier et al. 2009, Wang et al. 2012). Nevertheless, molecular mechanisms underlying sexual dimorphism in immune function were still researched.

Previous attempts to explain sex differences and HIV infections were focused on the various effects of the primary female sex steroid immunomodulation (Ruel et

al. 2011, Ziegler & Altfeld 2016), particularly on hormone estrogen and progesterone. Receptors for estrogen and progesterone were expressed by most types of immune cells, and these hormone levels affected the expression of CCR5, $CD4^+$ T cells, and the production of several cytokines (Mo et al. 2005, Biswas et al. 2022). This exogenous hormone was natural and fluctuated during the ovulation cycle and modulated the innate and adaptive immune response, so that it could affect the HIV replication rate (Hel et al. 2010). The viral load value illustrated the disease progression and risk of death. Periodical checking concerning the number of CD4+ and viral loads could determine the progress of the disease and identified the exact requirements to start or change the antiretroviral regimen.

**Strength and limitation**

The strength of this study is that it provides important information on the profile of CD4+ levels and plasma viral load in HIV patients receiving antiretroviral therapy in a specific setting in Indonesia. The study findings may be useful for healthcare providers in improving HIV treatment and management in the study population. Limitations of this study include its cross-sectional design, which only provides a snapshot of the CD4+ levels and plasma viral load in HIV patients at a specific time point.

## CONCLUSION

The clinical progression of HIV-1 patients in the Jayawijaya Regency, Papua, Indonesia, showed that there were more females with HIV who had a $CD4^+$ level of <200 cells/$mm^3$, higher or still detectable number of copies of the virus content per ml, and with the stage of the disease of stage 3 or 4.

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**Conflict of interest**

None.

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None.

**Author contribution**

DAP,MW,MIF,SA and EIN were conseptual design and collected and analysis data. MW write the manuscript.

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