



Monitoring Viral Load RNA And Cd4+ Count on HIV Patients Receiving ARV Therapy

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Human Immunodeficiency Virus (HIV) is a virus that threatens the quality of human life. HIV is a retrovirus that uses RNA as its genome so this virus can replicate very well. HIV will cause persistent disease so HIV-confirmed patients must be taking medication for life. HIV patients need to receive therapy and monitor Viral Load RNA and CD4+ count levels. Generally, routine checks are carried out every 3-6 months. Viral Load RNA levels show how much virus is in the blood while CD4+ count represents patient immunity. Normally Viral Load RNA and CD4+ count will show the same results inversely proportional. The higher the Viral Load RNA and the lower the CD4+ count,

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the more the patient's condition will get worse, and vice versa. Papua is one of the provinces in Indonesia with the highest HIV rate with faster spread compared to other provinces. To overcome this problem, the government has provided free therapy for the Indonesian people. This therapy called antiretroviral can be obtained free of charge and must be taken by people all patients are HIV positive

Aims: To determine Viral Load RNA levels and CD4+ count in HIV patients treated with ARV at Abepura District Hospital.

Place and Duration of Study: The research was carried out in the VCT medical records section of Abepura Regional Hospital from August 2023 to November 2023.

Methodology: This type of research is descriptive-analytical research with a design cross-sectional retrospective study using secondary data in the form of Abepura Regional Hospital medical records. The population in this study was treated HIV-positive patients ARVs at Abepura Regional Hospital from 2019 to 2022. This research uses a total sampling method. The research sample in this study were medical records of patients who were positive for HIV/AIDS and had been treated with ARVs at Abepura Regional Hospital from 2019 to 2022

Results: The results were obtained with more diverse patient characteristics female (52.9%), aged 25–49 years (68.6%), and heterosexual (81.4%). Overall the therapy showed success with an increase in undetected RNA patients were 24% and an increase in patients with normal CD4+ count of as much as 76% during three years of monitoring. The success of this therapy can occur if there is compliance in taking medication from the patient, there is good cooperation between staff health and patients, as well as support from the patient environment.

Conclusion: Data collection for this research will start from August 2023 until September 2023 and be obtained from hospital medical records Abepura Regional General. In this study, patients who were HIV positive and 85 people received ARV therapy at Abepura District Hospital There were 70 research samples that met the routine inclusion criteria control every 6 months.

Keywords: HIV; viral load; RNA; CD4+; ARV; ART.

1. INTRODUCTION

Human Immunodeficiency Virus (HIV) is a virus from the family Retroviridae genus Lentivirus. Retroviridae means these viruses use RNA as its genome and Lentivirus means non-oncogenic virus produces multi-organ disease and is characterized by a long incubation period and persistent infections. The Lentivirus genus is also dangerous because of its properties. The main thing is that it lasts a lifetime because of its ability to integrate with host chromosomes and can evade host immunity. This is due to the high mutation rate of the virus so that it can replicate, mutate, and undergo selection based on the host's immune response (Trickey et al., 2023). Human Immunodeficiency Virus attacks the immune system human body/immunity. When it enters the human body, the virus called gp120 will attach to the CD4 receptor and then enter into cells by endocytosis of coreceptors such as CXCR4 and CCR5. After entering the cell, the viral RNA will undergo reverse transcriptase and complement to DNA. Then the viral DNA will combine with cell DNA and mutate and replicate. High levels of virus in the body can cause Acquired Immunodeficiency Syndrome (AIDS) where the body's immunity is very low and

unable to fight disease. Human Immunodeficiency Virus positive is a person who has been infected with HIV. When a patient is HIV positive, they will be potential as a source of infection for others. (Trickey et al., 2023; Marta, 2019), HIV transmission is also known to be possible and occurs in various ways, generally, HIV is sexually transmitted however It can also be done through a syringe and from mother to child, such as from the placenta and breast milk (ASI). Until now, HIV is a big problem that threatens the world. The World Health Organization (WHO) in 2013 reported that around 78 million people have been infected with HIV with a death rate of 39 million per year. At that time, the data stated that the incidence rate was 1. The highest is in the ages 15-49 years and almost no country is free from it HIV. The large number of cases in the world means that this disease not only has an impact on health but also problems for social conditions and developing countries (Poltronieri et al., 2015).

The number of HIV cases in Indonesia continues to increase from year to year although it tends to fluctuate. Based on reports from the Ministry of Health of the Republic of Indonesia (KEMENKES RI), the highest HIV cases are in 10 provinces,

namely Papua, East Java, Special Capital Region (DKI) Jakarta, Bali, West Java, Central Java, West Papua, South Sulawesi, West Kalimantan and North Sumatra. The high number of HIV cases in Papua has now become a serious threat to the survival of all people in Papua. This is because the spread in Papua is faster than in other areas of Indonesia. Case HIV/AIDS in Papua It was first discovered in Merauke in 1992 where six HIV cases were recorded, consisting of 2 Indonesian citizens (WNI) who worked as commercial sex workers (PSK) and 4 foreign nationals (WNA), namely Thai fishermen. A year later there were 49 cases of HIV and 1 case of AIDS reported. 2 The high number of HIV/AIDS cases in Papua turns out to cause many problems, including the increasingly difficult performance of health workers accompanied by increased cost requirements, a decline in already poor health conditions, and an increasing number of people who will be at high risk of infection (Rabrageri et al., 2017). Based on national guidelines, the Indonesian Ministry of Health states that Antiretroviral therapy (ARV) is a treatment that patients must undergo HIV with Cluster Differentiation 4 (CD4) as a necessary parameter evaluated periodically. Cluster Differentiation 4 is a protein marker located on the surface of white blood cells, especially T lymphocytes has an important role in the human immune system. Clusters Differentiation 4 functions to stimulate the immune system to work well. Apart from CD4+, some parameters are no less important in therapy monitoring, namely the Viral load (VL) test. Viral load is the number of viruses HIV is in every milliliter of blood of people with HIV/AIDS (PLWHA) who are undergoing therapy. For PLWHA who comply with ARV therapy, CD4+ and Viral load levels should be inversely proportional to the positive response, namely CD4+ increases and Viral load L decreases (Poltronieri et al., 2015; Dewanti & Handayani, 2021).

There are also conditions for administering ARV therapy, namely that it has been confirmed positive for HIV/AIDS regardless of CD4+ count and Viral load. Apart from that, patients too must comply with taking ARV drugs every day and for life. An indicator of the success of ARV therapy is that the patient does not lose weight drastic increase or decrease, CD4+ increases, Viral Load decreases, and no opportunistic infections occur after first taking ARVs. Monitoring CD4+ counts and ARVs must be done regularly over some time The recommended time is 3-6 months (Dewanti & Handayani, 2021). Although this

therapy is not yet effective cures HIV completely and has the side effect of resistance to drugs, ARV therapy reduces mortality significantly. Personally, ARVs also improve the quality of life of PLWHA and raise the expectations of the wider community. Until now the majority of people have accepted HIV/AIDS as a disease that can be controlled although there are still some who still consider it taboo and scary (Gunawan et al., 2016). ARV therapy in Papua has also been implemented in the program HIV/AIDS management. Abepura Regional General Hospital (RSUD). became one of the hospitals that had an ARV therapy program and started routinely monitoring the VL and CD4+ of HIV patients every six months in 2019. This monitoring is not only to see the success of therapy but also to monitor the patient's quality of life and resistance to drugs. Most of the patients who were monitored had a positive response and were getting better, but A few also experienced lost follow-up, co-infection, or even death world. This negative response is due to non-compliance with taking medication, no regular evaluation, as well as co-infections obtained before or/after ARV therapy is given. Based on the ARV therapy process, the author is interested in researching VL RNA and CD4+ of HIV patients who were treated at Abepura District Hospital in 2018 2019-2022.

2. MATERIALS AND METHODS

2.1 Research Design

This type of research is analytical descriptive research with design cross sectional retrospective study using secondary data in the form of Abepura Regional Hospital medical records.

2.2 Place and Time of Research

The research was carried out in the VCT medical records section of Abepura Regional Hospital in August 2023 to November 2023.

2.3 Population

The population in this study treated HIV-positive patients ARVs at Abepura Regional Hospital from 2019 to 2022.

2.4 Research Sample

This research uses a total sampling method. The research sample in this study was medical records of patients who were positive for HIV/AIDS.

2.5 Inclusion and Exclusion Criteria

2.5.1 Inclusion criteria

- HIV-positive patient at Abepura Regional Hospital.
- HIV patients receiving ARV therapy at Abepura District Hospital.
- Padien with complete personal data.
- Patients aged 18 to 65 years.
- Routine control every 6 months.

2.5.2 Exclusion criteria

- Patients with incomplete personal data.
- Patients who die in the middle of therapy.
- Patients lost follow-up.
- Patients under 18 years and over 65 years.

2.6 Research Instrument

This research uses research instruments in the form of medical records which was found in the VCT polyclinic of Abepura Regional Hospital in the 2019 period until 2022,

2.7 Data Analysis and Processing

The data that has been obtained during data collection will be tabulated and then processed using computer equipment. the data was

analyzed using the SPSS application. There are several steps to process data using a computer:

- Coding, to change data obtained during research be a suitable symbol for analytical purposes
- Data entry, entering data into computer software
- Validation, carrying out visual inspection of the data entered into the computer
- Computer output, prints the analysis results from several stages previously done by computers.

3. RESULTS AND DISCUSSION

3.1 Research Result

Data collection for this research will start from August 2023 until September 2023 and be obtained from hospital medical records Abepura Regional General. In this study, patients who were HIV positive and 85 people received ARV therapy at Abepura District Hospital and 70 research samples met the routine inclusion criteria control every 6 months. Data processing was carried out using the SPSS application version 27 and the data is presented in tables and graphs.

3.1.1 Sample characteristics based on gender

Table 1. Sample characteristics based on gender

Gender	Number (n)	Percentage (%)
Female	37	52.9
Male	33	47.1
Total	70	100.0

Based on the results of research on HIV-positive patients who received ARV therapy and had regular check-ups every six months as many as 37 people (52.9%) were women and 33 (47.1%) were men.

3.1.2 Sample characteristics based on age

Table 2. Sample characteristics based on age

Age (year)	Number (n)	Percentage (%)
18-24	9	12.9
25-49	48	68.5
≥ 50	13	18.6
Total	70	100.0

Based on age, there are three age groups. Group The majority of people aged 25-49 years were 48 people (68.6%), followed by 13 people aged ≥50 years (18.6%), and the fewest were 18-24 years old as many as 9 people (12.9%).

3.1.3 Sample characteristics based on sexual orientation

Table 3. Sample characteristics based on sexual orientation

Sexual Orientation	Number (n)	Percentage (%)
Heterosexual	57	81.4
bisexual	13	18.6
Total	70	100.0

The data showed that the majority of patients were heterosexual, 57 people (81.4%), while 13 other people were bisexual (18.6%).

3.1.4 Sample characteristics based on changes in viral load RNA levels

Table 4. Sample characteristics based on changes in viral load RNA levels FUM 1-12

Viral Load RNA Levels	FUM 01	Percentage (%)	FUM 06	Percentage (%)	FUM 12	Percentage (%)
< 200	50	71.4	58	82.9	62	88.6
≥ 200	20	28.6	12	17.1	8	11.4
Total	70	100.0	70	100.0	70	100.0

Table 5. Sample Characteristics Based on Changes in Viral Load RNA Levels FUM 18-30

Viral Load RNA Levels	FUM 18	Percentage (%)	FUM 24	Percentage (%)	FUM 30	Percentage (%)
< 200	62	88.6	65	92.9	62	88.6
≥ 200	8	11.4	5	7.1	8	11.4
Total	70	100.0	70	100.0	70	100.0

Based on the tables and graphs, it was found that the Viral Load RNA results amounting to ≥200 copies decreased every six months of monitoring except for the last examination. In the results, it can be seen that in the 24th and 30th months, the number of patients with Viral Load RNA levels ≥200 copies initially increased to eight. In contrast to the group of patients who had Viral Load RNA < 200 copies which experienced an increase every six months of examination and decreased at the 30th month. In the 30th month, the percentage (%) of the 24 groups of patients with Viral Load RNA levels <200 initially numbered sixty-five people, then decreased in the 30th month to sixty-two people.

3.1.5 Sample characteristics based on changes in CD4+ count

Table 6. Sample characteristics based on changes in CD4+ count M 1-12

CD4+ Count	FUM 01	Percentage (%)	FUM 06	Percentage (%)	FUM 12	Percentage (%)
< 200	12	17.1	13	18.6	8	11.4
200-499	41	59.6	37	52.9	43	61.4
≥ 500	17	24.3	20	28.6	19	27.1
Total	70	100.0	70	100.0	70	100.0

Table 7. Sample Characteristics Based on Changes in CD4+ count FUM 18-30

CD4+ count	FUM 18	Percentage (%)	FUM 24	Percentage (%)	FUM 30	Percentage (%)
< 200	9	12.9	5	7.1	3	4.3
200-499	42	60.0	38	54.3	37	52.9
≥ 500	19	27.1	27	38.0	30	42.9
Total	70	100.0	70	100.0	70	100.0

Based on the data, it was found that three groups of patients were in the results of monitoring CD4+ count, namely <200, 200-499, and ≥500. From the monitoring results, the group of patients with CD4+ count <200 decreased from the initial twelve people to three people. The group of patients with CD4+ count 200-499 also experienced a decrease from forty-one people to thirty-seven people. Meanwhile, the group of patients with CD4+ count ≥500 was the only group that experienced an increase, namely from seventeen people to thirty people.

3.2 Discussion

Human Immunodeficiency Virus (HIV) is a virus that causes a reduction in a person's ability to defend yourself. This is because HIV attacks cells in the human immune system, namely CD4 so that HIV positive patients will experience a decrease in CD4+ and an increase in the number of viruses. Number of viruses This is usually called the viral load. These two aspects should be checked regularly every three to six months for HIV sufferers who are running ARV therapy so that you can see the effect of treatment on recovery patients.

3.2.1 Gender

Based on research, it was found that HIV patients were women more than male HIV patients. From 70 samples research, there were 37 female patients (52.9%) and patients 33 men (47.1%). The results of this study are in line with research from Dewi et al., (2022). Who says that women are more vulnerable to HIV due to the excess mucosal surface of the genitals wider than men? Apart from that, there is also Awatiful's research Which states that women have a 2-4 times risk of being infected with HIV bigger than men. Not just because of the anatomical shape, this It can also occur through sperm during sexual intercourse. It said that the concentration of HIV in sperm is higher than in fluids other. Apart from that, there is also inadequate education, harassment, and exploitation of women, as well as sexual behavior unwanted or unsafe. (Aryani, et al, 2018; Azza, 2010).

However, some studies conflict with the results This research, for example, research from Lenci and Ratih stated that HIV patients were more likely to be men compared to women. According to Lenci and Ratih, this happened because men having more risky sexual relations and use injecting drugs (IDUs), while most patients.

Women are more frequently exposed to sexual contact. Apart from that, there is also research from Safitri et al., (2019) who also agree that the majority of patients HIV is male. According to the study, this can happen from sexual activity with commercial sex workers (PSK), IDUs, and there is also an increasing trend in the practice of men having sex with men (MSM).

3.2.2 Age

Based on the age factor, three groups of patients were obtained, The largest number was in the 25-49 year age group with 48 people (68.6%), then the age group ≥50 years, namely 13 people (18.6%), and the fewest is the 18-24 year age group, namely 9 people (12.9%). These results are in line with research conducted by Nadya who wrote that the largest age group of HIV patients is productive age from 25-49 years and Diah and Dina's research that HIV incidence and risk are highest in the 25-49 age group year. In Nadya's opinion, this result was caused by the possibility of unsafe sexual behavior is often carried out by a young age. Unsafe sexual behavior includes changing partners, not using condoms, and acts of trial and error, for example, injection drug use. Apart from unsafe sexual behavior, according to Herlina and Herri's research (Kusumah et al., 2016). It is stated that the age group 25-49 years old biologicals have a higher sexual drive in comparison with other age groups.

There are also studies with contradictory results, one of which is research from Lenci and Ratih 10 which was carried out in Semarang (Aryani et al, 2018). This research states that the age group of HIV patients is 18-24 years old. This is because it is in the city of Semarang Respondents had their first sexual activity before the age of 13 years and the majority have sexual relations with risk groups. Meanwhile, in research conducted at the Abepura Regional Hospital group 18-24-year-olds are the age group least exposed to HIV. So differences in data results in Semarang and Abepura are possible due to different lifestyles (Marshalita et al., 2020; Rohmatullailah et al., 2021).

3.2.3 Sexual orientation

Based on sexual orientation, patients at Abepura Regional Hospital with homosexual sexual orientation do not complete ARV treatment with two possibilities: lost follow-up or death. The data shows that the majority of HIV patients are people with Heterosexual sexual orientation 57

people (81.4%) and the fewest were bisexual, namely 13 people (18.6%). These results are consistent with Erli and Arulita's research Widiastuti & Fibriana, (2022) which says that most HIV patients are heterosexual. This happened because according to Widia and Fitriani Astuti & Rayasari, (2017) the behavior of heterosexual patients tends to be more aware of the disease and its recovery so consciously go to the hospital, have an examination, and be obedient with treatment. Meanwhile, homosexual patients will be more closed from examination and treatment. Different results were also obtained in research by Herlina and Herry (Kusumah et al., 2016) which shows that as many as 82.2% of HIV patients in Garut are homosexual. This is because in theory, Homosexuals are 1.97 times more at risk of contracting HIV due to relationships. Sexual intercourse is carried out through oral and anal means, the majority of which does not use a condom. This sexual behavior will cause injury to The oral and anal mucosa are thin and facilitate the entry of fluids to the HIV-infected partner.

3.2.4 Viral load RNA

During ARV therapy, monitoring changes in Viral Load RNA and CD4+ count is a necessity to see the patient's progress and ensure whether therapy is going well or not. Ascension Viral Load levels correlate with increasingly specific viruses that attack the immune response. Generally, the more specifically toxic the virus will be on T lymphocytes. ARV therapy will be said to be good if Viral Load RNA decreases and CD4+ count increases. Research Currently, Viral Load RNA is divided into two categories, namely Viral Load RNA levels <200 coffee/ml and ≥200 coffee/ml. This group division is due to the sensitivity of the examination tool for which the Viral Load calculation limit is calculated at 200, so if the Viral Load is less than 200 copies, a mark will be written undetected. Meanwhile, if Viral Load RNA is still ≥200 copies then the patient is still counted as an HIV-positive patient (Stanford, 2023). From the data, it was found that Overall Viral Load RNA decreased from the first month of control until the thirtieth month. In the 1st to 12th month There was a decrease in Viral Load RNA in patients with Viral Load RNA ≥200 coffee/ml which was originally 28 people (28.6%) became 8 people (11.4%), then from the 12th month to the 18th month the same results were obtained still 8 people (11.4%). After that, there was a decline from the 18th month to the 24th month, which was initially 8 people (11.4%) and

became 5 people (7.1%). However, there was an increase again in the 30th month to 8 people (11.4%) (Harrison et al, 2019). This is due to the way ARVs work in two phases namely cell fusion and reverse transcription. In cell fusion, ARV will block the part of the cell where the HIV attaches. In this phase, there are three inhibitors, namely CCR5 blockers, GP120 inhibitors, and gp41 inhibitors with different functions. CCR5 blockers will prevent the attachment of the virus and interrupt the HIV cycle at the stage beginning. Then gp120 inhibitors and gp41 inhibitors will both block the gp120 and gp41 parts which are the closest parts to the CD4+ receptor, this means the virus cannot enter attack CD4+ and replicates.

According to Teguh's research, there have been Karyadi, (2017) increases in VL RNA decreasing in the middle of the therapy period;, one of the reasons is resistance virus against the ARV used. Apart from virus resistance, there is also Another cause of the increase in VL RNA, namely, adherence is a major factor in the success of therapy. In ARV treatment Patients are required to take medication according to the dosage, on time, no can forget, and can not break. Compliance with taking medication is influenced by several factors including gender, social economics, education, stigma, drug side effects, and patient lifestyle. It was explained that the patient's lifestyle had quite an influence on compliance, feeling that there would be no recovery, alcohol consumption, drug abuse, and anxiety or depression. Apart from internal factors from patients, patients can also be negligent in taking medication if the communication between health workers and patients does not go well. Results This research is different from the results obtained by Nunu et al where obstacles in adherence to ARV therapy are due to service poor health. The respondents complained that it was difficult to consult a doctor and distance to health facilities was difficult. Apart from that, some admitted to having internal difficulties regarding hospital registration fees, transportation, and no support from family.

The theory also explains that the viral load experiences changes from time to time. In the first few weeks after HIV-positive patients, the viral load will usually be very high, reaching hundreds of thousands or even millions of copies/ml. In this phase, patients are very at risk transmit the virus. Next, the viral load will begin to decrease and stabilize around 50,000 copies/ml with a fairly high risk of infection.

However, if the patient starts ARV therapy and adheres to taking the medication, within the term Within three to six months the majority of patients experience a positive response and the viral load will decrease steadily. Many patients will achieve an undetectable viral load.

3.2.5 CD4+

CD4+ is a marker cell on the surface of leukocytes, so if the CD4+ count decreases then the immune system's ability to fight infection will also decrease. In HIV patients CD4+ is very high. It is important to monitor to see whether immunity is high or not patient. When undergoing ARV therapy, HIV patients are expected to experience an increase in CD4 levels. In the research, the data obtained shows good and significant results. In the initial patient, 12 people had CD4 levels <200 cells/ml in the 1st month (17.1%) increased to 13 people (18.6%) in the 6th month. Then in the 12th month, it decreased to 8 people (11.4%) and rose again to 9 people (12.9%) in the 18th month. After that, the number of patients whose CD4+ levels were <200 cells/ml decreased to 5 people (7.1%) in the 24th month and then to 3 people (4.3%) in the 30th month. The same was true for patient groups previously, patients with CD4 levels of 200-499 also experienced a positive decline. In the 1st month, there were 41 people (58.6%) then decreased to 37 people (52.9) in the 6th month. On the moon 12th increased again to 43 people (61.4%) and decreased to 42 people (60%) in the 18th month. Then in the 24th month, it dropped to 38 people (54.3%), and finally 37 people (52.9) in the 30th month. Then the last was the group of patients who experienced the most positive increase, namely those who had CD4+ \geq 500. On data obtained that in the 1st month, there were 17 people (24.3%) then increased to 20 people (28.6%) in the 6th month. On the moon in the 12th month, it fell to 19 people (27.1%) and was stable until the 18th month. In the 24th month, this group of patients became 27 people (38.6%) and again increased to 30 people (42.9%).

Overall, the data shows that the majority of patients have CD4+ count >200 cells/ml which means the level of drinking compliance The patient's medication is quite good. This is in line with research from Rihaliza et al., (2019) most of the respondents also experienced the same thing. According to him, this occurs when the patient's level of compliance with taking medication reached 72%.

4. CONCLUSION

Overall Viral Load RNA levels decreased. Patients whose Viral Load RNA was undetected experienced an increase of 24% during three years of monitoring. Overall, the CD4+ count of HIV patients treated with ARVs also increased has improved. Patients who have normal CD4+ count experience an increase of 76% after three years of monitoring.

CONSENT

It is not applicable.

ETHICAL APPROVAL

As per international standards or university standards written ethical approval has been collected and preserved by the author(s).

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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