# The Relationship Between Viral Load and Neutrophil Lymphocyte Ratio in HIV Patients Receiving Antiretroviral Therapy

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## ABSTRACT

Human Immunodeficiency Virus (HIV) is a virus that attacks the immune system and can progress to Acquired Immune Deficiency Syndrome (AIDS). Currently, HIV/AIDS remains incurable; however, viral replication can be controlled through Antiretroviral (ARV) therapy. The effectiveness of ARV is typically monitored through viral load testing. Several studies have also highlighted the Neutrophil Lymphocyte Ratio (NLR) as a biomarker that may reflect the severity of viral infection. This study aimed to examine the relationship between viral load and NLR in HIV patients undergoing ARV therapy, as well as to assess the influence of ARV therapy duration on these parameters. A quantitative approach with a cross-sectional design was employed, involving 50 HIV patients receiving ARV therapy at Bayu Asih Regional General Hospital, Purwakarta Regency. Viral load data were obtained from laboratory testing using the GeneXpert Rapid Molecular Test, while NLR was derived from complete blood count results measured with the Yumizen H500 Automatic Hematology Analyzer. Data analysis was conducted using the Chi-Square test. The results demonstrated a significant relationship between viral load and NLR ($p = 0.000$). In contrast, no significant relationship was found between viral load and the duration of ARV therapy ($p = 0.246$) or between NLR and the duration of ARV therapy ($p = 0.078$). Therefore, it can be concluded that an increase in viral load is associated with an increase in NLR, suggesting that NLR may serve as an inflammatory marker in HIV patients undergoing ARV therapy, whereas the duration of ARV therapy does not appear to affect these parameters.

**Keywords**: Viral load, Neutrophil Lymphocyte Ratio, HIV, Antiretroviral

## Introduction

Human Immunodeficiency Virus (HIV) is an RNA virus that specifically targets and weakens the human immune system. This condition may progress to Acquired Immune Deficiency Syndrome (AIDS), a collection of symptoms and diseases that arise due to impaired immune function caused by HIV infection (Alamsyah et al., 2020). HIV can be transmitted through several routes, including high-risk sexual intercourse, the use of contaminated needles, and mother-to-child transmission during pregnancy, childbirth, or breastfeeding (Roschmawati et al., 2021). To this day, To date, HIV/AIDS remains classified as an infectious disease with a continuously increasing number of affected individuals (Mutiara Hikmah et al., 2021).

According to data from the United Nations Programme on HIV and AIDS (UNAIDS), in 2023, approximately 39.9 million people were living with HIV worldwide. In the same year, there were 1.3 million new HIV infections and 630,000 AIDS-related deaths (UNAIDS, 2024). In Indonesia, the cumulative number of people living with HIV reached 598,271 as of June

2024, while the cumulative reported AIDS cases totaled 168,263. By June 2024, HIV/AIDS cases had been reported in 38 provinces across Indonesia. During the same period, cases were reported in 512 out of 514 regencies/cities nationwide (Kementerian Kesehatan RI, 2024). From 2016 to 2023, Purwakarta Regency recorded an annual increase in new HIV cases. During this period, the total number of individuals infected with HIV/AIDS reached 1,333 (RSBA, 2023). The Voluntary Counseling and Testing (VCT) clinic at Bayu Asih Regional General Hospital, Purwakarta Regency serves as the sole referral center for ARV services and functions as the designated facility for HIV/AIDS Care, Support, and Treatment (PDP) services in the regency (Kadar & Sartika, 2021).

To date, HIV/AIDS remains incurable; however, antiretroviral therapy (ART) can inhibit viral replication. Individuals living with HIV/AIDS must undergo lifelong ART to suppress viral progression within the body (Safitri et al., 2019). The effectiveness of antiretroviral therapy (ART) is monitored through viral load testing. An increase in viral load corresponds to accelerated HIV progression within the body (Arifa et al., 2022). Viral load testing is a laboratory examination that quantifies the number of viruses in the blood, allowing for the monitoring of viral replication and the assessment of antiretroviral therapy (ART) effectiveness (Thamrin et al., 2023). However, not all laboratories are equipped to perform viral load testing, and the procedure is further limited by its relatively high cost (Antoxida et al., 2021). Given the limitations of viral load testing, there is a need for alternative examinations that are widely accessible to patients and available at all healthcare facilities. In recent years, numerous studies have investigated the neutrophil-to-lymphocyte ratio (NLR), with recent findings indicating that NLR can serve as an indicator of inflammation in various diseases (Fauzi et al., 2021).

NLR assessment is a biomarker used to determine the prognosis of virus-induced infections and can serve as an indicator of potential disease severity. During inflammation, a physiological response characterized by a decrease in lymphocyte count and an increase in neutrophil count occurs due to an imbalance in the inflammatory response. Neutrophilia and lymphocytopenia form the basis for calculating the NLR (Vafadar Moradi et al., 2021). NLR is a simple, efficient, and reliable indicator of inflammation due to its high stability and sensitivity. An elevated neutrophil count indicates a non-specific destructive inflammatory process, whereas a reduced lymphocyte count reflects weakened immune system regulation (Nurdin et al., 2021).

A study by (Suhartini et al., 2024) found that increases in viral load in HIV patients are generally accompanied by rises in the neutrophil-to-lymphocyte ratio (NLR). This

phenomenon may occur because the body responds to elevated viral levels through specific immunological mechanisms, affecting the balance of white blood cells, particularly neutrophils and lymphocytes. However, the study had a limitation in that it did not account for the duration of antiretroviral therapy (ART) as a factor that might influence these changes. Therefore, the present study was conducted taking into consideration the length of ART received by HIV patients. Consequently, the researchers were interested in investigating the relationship between viral load and neutrophil-to-lymphocyte ratio in HIV patients undergoing antiretroviral therapy at Bayu Asih Regional General Hospital, Purwakarta.

## Materials and Methods

The research employed a quantitative descriptive design with a cross-sectional approach to investigate the relationship between viral load and NLR in HIV patients receiving antiretroviral therapy (ART). Additionally, the study aimed to examine whether the duration of ART influences viral load and NLR in these patients.

The study population comprised HIV patients undergoing ART at Bayu Asih Regional General Hospital, Purwakarta. The sample consisted of a subset of the population that represented it. A total sampling technique was used to determine the sample size, resulting in 50 participants. Inclusion criteria were HIV patients who had received ART for at least six months and had complete medical records at the Voluntary Counseling and Testing (VCT) clinic. Exclusion criteria included AIDS patients and HIV patients with co-infections.

Data collection involved both primary and secondary sources. Primary data were obtained directly from laboratory examinations: viral load was measured using the TCM GeneXpert system, and NLR was assessed using the Yumizen H-500 Hematology Analyzer at the Bayu Asih Regional General Hospital Laboratory. Secondary data, including the duration of ART for each patient, were obtained from medical records at the VCT clinic.

Data analysis included univariate analysis to identify the frequency distribution of respondent characteristics and all study variables. Bivariate analysis was conducted to evaluate the effect of each independent variable on the dependent variables. The Chi-square test was employed with the assistance of computer software. The relationship between two variables was examined by testing the research hypothesis, with a significance level (p-value) set at $<0.05$.

## Results and Discussion

Based on table 1, the majority of HIV patients were aged 33–43 years (46%) and were male (64%). Most respondents had a suppressed viral load (80%), had been on therapy for ≤2 years (72%), demonstrated adherence to therapy (58%), and belonged to the Men Sex with Men (MSM population group (34%). Based on Table 2, a p-value of 0.000 was obtained, indicating a significant association between viral load and NLR among HIV patients receiving ARV therapy. Based on Table 3, a p-value of 0.246 was obtained, indicating that there is no association between viral load and the duration of ARV therapy among HIV patients. Based on Table 4.4, a p-value of 0.078 was obtained, indicating that there is no association between NLR and the duration of ARV therapy among HIV patients.

**Table 1**. Characteristics of HIV patients

| Characteristics | Total | |
|---|---|---|
| | Frequency (n) | Percentage (%) |
| Gender | | |
| Male | 32 | 64 |
| Female | 18 | 36 |
| Age (years) | | |
| 11-21 | 2 | 4 |
| 22-32 | 12 | 24 |
| 33-43 | 23 | 46 |
| 44-54 | 8 | 16 |
| 55-65 | 3 | 6 |
| ≥66 | 2 | 4 |
| Population Group | | |
| Men Sex with Men (MSM) | 19 | 34 |
| Married couple | 13 | 26 |
| Client of female sex worker | 11 | 22 |
| Female Sex Worker (FSW) | 4 | 8 |
| People who inject drugs | 3 | 6 |
| Viral Load | | |
| Suppressed | 40 | 80 |
| Not suppressed | 10 | 20 |
| NLR | | |
| Normal | 37 | 74 |
| High | 13 | 26 |
| Duration of ART (years) | | |
| ≤2 | 36 | 72 |
| >2 | 14 | 28 |
| Adherence | | |
| Adherent | 29 | 58 |
| Non-adherent | 21 | 42 |

Based on the findings of this study, the majority of respondents living with HIV were male (64%). This result is consistent with various previous studies reporting that HIV/AIDS cases are more prevalent among men than women. An analysis of 15 publications by (Sutrasno et al., 2022)(Sutrasno et al., 2022) also showed that most HIV/AIDS patients were male. This is further supported by the Ministry of Health, which recorded that based on sex distribution, 71% of cases were found in men and 29% in women, with a male-to-female ratio of 2:1 (Kementerian Kesehatan RI, 2024).

**Table 2**. The Relationship Between Viral Load and NLR

| Viral load | NLR | | | | Total | % | *p-value* |
|---|---|---|---|---|---|---|---|
| | Normal | | High | | | | |
| | n | % | n | % | | | |
| Suppressed | 37 | 74 | 3 | 6 | 40 | 100 | 0.000 |
| Not suppressed | 0 | 0 | 10 | 20 | 10 | 100 | |
| Total | 37 | 74 | 13 | 26 | 50 | 100 | 0.000 |

**Table 3**. The Relationship Between The Duration Of ART and Viral Load

| Duration of ART | *Viral load* | | | | Total | % | *p-value* |
|---|---|---|---|---|---|---|---|
| | Suppressed | | Not suppressed | | | | |
| | n | % | n | % | | | |
| ≤2 years | 27 | 54 | 9 | 18 | 36 | 100 | 0.246 |
| >2 years | 13 | 26 | 1 | 2 | 14 | 100 | |
| Total | 40 | 80 | 10 | 20 | 50 | 100 | |

**Table 4**. The Relationship Between The Duration of ART and NLR

| Duration of ART | NLR | | | | Total | % | *p-value* |
|---|---|---|---|---|---|---|---|
| | Normal | | High | | | | |
| | n | % | n | % | | | |
| ≤2 years | 24 | 48 | 12 | 24 | 36 | 100 | 0.078 |
| >2 years | 13 | 26 | 1 | 2 | 14 | 100 | |
| Total | 16 | 74 | 34 | 26 | 50 | 100 | |

In terms of age distribution, most respondents with HIV were within the productive age range of 33–43 years (46%), followed by the age groups 22–32 years (24%), 44–54 years (16%), 55–65 years (6%), and ≥66 years (4%). This aligns with the findings of (Hilmi Ramdan & Setiadi, 2023) who reported that individuals within the productive age group constituted the highest proportion of HIV/AIDS cases (46.9%). These results are consistent with data from the

Ministry of Health, which showed that most PLHIV were aged 25–49 years (63%), followed by those aged 20–24 years (19%) and ≥50 years (10%) (Kementerian Kesehatan RI, 2024).

This study also found that the majority of HIV patients belonged to the MSM population group (34%). This finding is consistent with the study by (Oktavia et al., 2024) and other previous research indicating that many HIV/AIDS cases among individuals aged 21–49 originate from the LSL population group, which is associated with active sexual behavior. In this age range, individuals typically experience increased sexual hormone activity, which elevates libido but is often not accompanied by adequate self-control or positive social influences, leading to curiosity and engagement in LSL-related activities. (Hardisman et al., 2018)reported that individuals identifying as MSM within this age group often cited increased sexual desire and fear of engaging in heterosexual intercourse as contributing factors. Many assume that same-sex intercourse avoids the risk of pregnancy, yet this behavior carries other consequences, particularly the transmission of infections such as HIV/AIDS.

MSM individuals are considered a high-risk population for HIV infection. This is influenced by frequent engagement in anal intercourse, compounded by other high-risk sexual behaviors such as inconsistent condom use (Hasby & Sudaryo, 2021). During anal intercourse, the likelihood of mucosal injury is high because the anus is not anatomically designed for sexual activity. Such injuries facilitate viral entry into the body (Oktavia et al., 2024). The Ministry of Health also reported that 30.5% of HIV cases originated from the MSM population (Kementerian Kesehatan RI, 2024). These characteristics highlight the need for targeted promotive and preventive interventions focusing on MSM individuals as a high-risk population for HIV transmission.

Furthermore, this study examined other factors, including biological indicators that may influence HIV infection progression. Statistically, a significant association was found between viral load and NLR in HIV patients undergoing ART (p-value = 0.000). This finding indicates a strong relationship between the level of HIV replication in the body and systemic inflammatory response measured through NLR. As viral load increases, the body tends to exhibit a heightened inflammatory response reflected by elevated NLR. This result aligns with the study by (Suhartini et al., 2024), which showed that an increase in viral load is often followed by an increase in NLR.

Chronic inflammation associated with HIV infection can trigger neutrophil activation and lymphocyte suppression, ultimately increasing NLR. According to (Luthfiyah et al., 2024) a low white blood cell count (leukopenia) or a low neutrophil count (neutropenia) may indicate a high risk of infection. In HIV/AIDS or immunosuppressive therapy, hematological

examinations commonly show a reduction in lymphocyte count (lymphopenia). NLR has been identified as an inflammatory biomarker capable of reflecting disease severity and the effectiveness of immune response. Consistent with the findings of (Vafadar Moradi et al., 2021), NLR can serve as a prognostic biomarker for viral infections and may indicate the potential severity of disease. During inflammation, physiological responses include lymphocyte reduction and neutrophil elevation due to an imbalance in inflammatory regulation. These findings suggest that NLR may serve as an additional indicator for monitoring HIV progression and treatment response. While viral load remains the gold standard for HIV monitoring, NLR provides supplementary information regarding the patient's inflammatory status, which may help inform clinical decision-making. As noted by (Luthfiyah et al., 2024), integrating immunological and non-immunological examinations can offer a comprehensive overview of a patient's immunological status, aid diagnosis, evaluate complications, and guide appropriate clinical management. Early detection and effective management play an essential role in preventing complications caused by immunodeficiency, including the importance of ART in HIV/AIDS patients.

Contrary to the initial hypothesis, no significant association was found between viral load and duration of ART among HIV patients (p-value = 0.246). This finding indicates that within this study population, the duration of ART did not statistically influence viral load levels. This may be attributable to variations in patient adherence to ART. As widely known, ART effectiveness is highly dependent on consistent adherence. Patients who fail to take their medication as prescribed may experience increases in viral load regardless of the duration of therapy. This result aligns with the study by (Hayatiningsih et al., 2017), which reported no association between duration of ART and adherence among HIV patients. Factors such as treatment fatigue after six months of ART, routine medication schedules, feelings of improved health, drug side effects, financial burden, and social stigma may all contribute to reduced adherence. These findings emphasize the importance of assessing and supporting ART adherence through interventions such as counseling, medication reminders, and family or peer support to optimize treatment outcomes.

Similarly, this study found no significant association between NLR and duration of ART (p-value = 0.078). This suggests that the duration of ART in this population did not statistically influence systemic inflammatory levels as measured by NLR. Other factors, such as opportunistic infections, comorbidities, or lifestyle-related variables, may have a greater impact on NLR. Individual variations in inflammatory response to HIV and ART may also contribute to the absence of a significant association.

Despite these findings, this study has several limitations. Future research is encouraged to use larger sample sizes to obtain more comprehensive results. Additionally, patient adherence to ART should be assessed more thoroughly as a potential confounding factor that may influence its relationship with viral load and NLR. Such measurements should not solely rely on observations at the time of ART retrieval. Further studies may also expand the scope of analysis by evaluating additional inflammatory biomarkers or assessing the influence of comorbidities on NLR changes in HIV patients, including CD4 count dynamics.

## Conclusion

Based on the findings of this study, it can be concluded that there is a significant association between viral load and NLR in HIV patients receiving antiretroviral therapy (ART). However, no significant association was found between viral load and the duration of ART, nor between NLR and the duration of ART among HIV patients.

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