International Journal of Advances in Medicine
Pratikto BC et al. Int J Adv Med. 2023 Aug;10(8):596-600
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933
DOI: https://dx.doi.org/10.18203/2349-3933.ijam20232205

Original Research Article

Association between neutrophil-lymphocyte ratio and viral load with opportunistic pulmonary infections in human immunodeficiency virus/acquired immunodeficiency syndrome patients

Bella C. Pratikto, Ketut Suryana*

Wangaya Regional General Hospital, Bali, Indonesia

Received: 02 June 2023
Accepted: 03 July 2023

***Correspondence:**
Dr. Ketut Suryana,
E-mail: ketutsuryana@gmail.com

ABSTRACT

Background: Acquired immunodeficiency syndrome (AIDS) is a syndrome of an opportunistic infectious disease due to decreased immune system by human immunodeficiency virus (HIV) infection. Neutrophil-lymphocyte ratio (NLR) and viral load were used to assess inflammatory status and the amount of HIV virus in the blood. This study aims to determine the association between NLR and viral load in HIV/AIDS patients with the opportunistic pulmonary infections.
Methods: This study is an analytic observational study with a cross-sectional design. Data was collected through the medical records of HIV/AIDS patients at Wangaya General Hospital from January 2018 - April 2023. The data analysis method used was the Chi square test as bivariate tests.
Results: A total of 139 subjects, the majority of HIV/AIDS patients who had opportunistic pulmonary infections were Balinese ethnicity (45.3%), female (37.6%), age ≥36 years old (54.7%), used ART for ≥3 months (41.5%), viral load <40 copies/ml, NLR ≥2.81 (47.9%), had adherence (43.7%), types of ART were used combination of tenofovir lamivudine efavirenz (45.2%), and private employed (42.5%). A statistically significant association was found between age with opportunistic pulmonary infections (p=0.003; PR=3.082; 95% CI=1.516-6.266). NLR showed a significant association with the incidence of opportunistic pulmonary infections (p=0.003; PR=8.274; 95% CI=1.838-37.249). This study also showed pulmonary tuberculosis (42.37%) as the most common opportunistic pulmonary infections.
Conclusions: There is a significant association between NLR levels in HIV/AIDS patients with opportunistic pulmonary infections at Wangaya General Hospital, which the higher NLR levels correlates with higher opportunistic pulmonary infections.

Keywords: Human immunodeficiency virus, Acquired immunodeficiency virus, Neutrophil-lymphocyte ratio, Viral load, Opportunistic pulmonary infections

INTRODUCTION

Human immune-deficiency virus (HIV) is a ribonucleic acid (RNA) virus that belongs to the retroviridae family and the lentivirinae subfamily. Patients with confirmed HIV can develop acquired immunodeficiency syndrome (AIDS) if they are not given proper therapy. AIDS is some symptoms of opportunistic infections caused by this viral infection.[1] HIV can be transmitted via blood transfusions, sharing intravenous needles, sexually, and from the mother to child during the birth process and breastfeeding. Most patients diagnosed with HIV will develop AIDS within ten years if left untreated. Once a patient has been diagnosed with AIDS and they do not receive ART, they will probably die within two years.[2]

According to UNAIDS data in 2021, it was reported that globally 38.4 million people were living with HIV in 2021. 650.000 people died from AID-related illnesses in 2021.[3] The number of new HIV infections in Indonesia continues

to increase every year. Since it was first discovered in 1987 until March 2017, HIV-AIDS is spread in 390 (78%) of 498 regencies/cities in all provinces in Indonesia.[4] The prevalence of HIV/AIDS among people aged 15-49 years tends to be increased in the 2016-2020 period. Number of cases of HIV/AIDS in Bali province that were reported to the health service, continues to increase from year to year. Number of HIV/AIDS cases that were reported by voluntary testing and counseling (VCT) polyclinics and hospitals in Bali from 1987 to 2020, were 7.189 cases.[5]

The most important reason why pulmonary complications often occur in HIV infection is the anatomical consequences of the lungs so that they are chronically exposed to external (exogenous) infectious and non-infectious materials, on the other hand there is also hematogenous exposure to the HIV virus (endogenous) which weakens the immune system.[6] Pulmonological complications, especially due to opportunistic infections, are the main cause of morbidity and mortality and can occur at all stages with various manifestations.[7,8]

The most commonly seen opportunistic pulmonary infections would be upper respiratory tract infections and acute bronchitis. HIV/AIDS patient for pulmonary disease, observation should be made of the patient's work of breathing, looking for signs of respiratory distress. Auscultation may reveal generalized or focal adventitious lung sounds, which may aid in the diagnosis of the pulmonary problem.[9]

Chronic proinflammatory states associates with HIV infection, even in patients receiving antiretroviral therapy (ART). There are 2 laboratory tests which are the focus of discussion in this study. There are viral load and neutrophil-lymphocyte ratio (NLR). When viral loads are low or undetectable, can be associated with worsened outcomes including mortality.[10] Viral load is an indicator to determine the response to therapy, the risk of transmission, and the risk of spreading infection.[11] NLR is a laboratory test that aims to determine the presence or absence of an inflammatory process. NLR is obtained from the absolute neutrophil count divided by the absolute lymphocyte count.[12] The higher the NLR value, the lower the CD4 value so that HIV/AIDS patients are susceptible to other infections. Therefore, NLR is used as a warning of the severity of infection.[1] One of the keys to success in reducing AIDS mortality and morbidity is increasing ART coverage. Related to this, another key to the success of ART for HIV is not late to give ART since the initial diagnosis of HIV.[13] The treatment of HIV requires the use of ART to suppress viral load and maintain CD4 counts. Various drug combinations are used to treat HIV, and the treatment is for life.[14]

The aim of this study is to be able to use laboratory tests such as NLR and viral load counts which are associated with the presence of opportunistic pulmonary infections in HIV/AIDS. The established marker of subclinical inflammation, NLR is easily determined from a complete blood count. Most inflammatory biomarkers are not measured in standard practice and may be expensive or impractical to monitor routinely. Viral load testing is the gold standard for HIV treatment monitoring. Periodic viral load tests are the most accurate way of determining whether antiretroviral therapy is working to suppress replication of the virus. Achieving viral suppression protects the body's immune system.

METHODS

This research is an analytic observational study with a cross-sectional approach. Researchers only make observations without giving treatment to the variables studied. This study is also retrospective because it uses data from patient medical records. This research was conducted at Wangaya General Hospital from January 2018 to April 2023. The sample for this study used the medical records of HIV/AIDS patients. The sampling technique used was consecutive sampling where samples were taken based on inclusion and exclusion criteria. The inclusion criteria included patients who had been diagnosed as positive for HIV/AIDS, complete medical record data of research subjects at the VCT polyclinic, patients who had regularly used ART for at least 1 month, and the age of the patients were 18-65 years. Exclusion criteria included patients with a history of chronic diseases, such as cancer, diabetes mellitus, hypertension, kidney failure, and cirrhosis of the liver. In this study, the sample size obtained was 139 subjects. The characteristics shown in the independent variables in this study were ethnicity, gender, age, ART duration, viral load, NLR, and control compliance. The dependent variable was opportunistic pulmonary infection. Data analysis was performed using the statistical product and service solutions (SPSS) program. The data analysis method in this study was the Chi square test as bivariate test. The presentation of the data is in the form of a frequency distribution table (one-way tabulation) and cross tabulation (two-way tabulation). The p value of <0.05 is considered significant.

RESULTS

The characteristics of the subjects, as shown in Table 1, the median age with opportunistic pulmonary infections was 43.00 (18.00-76.00). The median age without opportunistic pulmonary infections was 34.50 (22.00-64.00). The median NLR with opportunistic pulmonary infections was 3.22 (0.33-17.41). The median NLR without opportunistic pulmonary infections was 2.69 (0.04-18.86). Based on the median, the cut off points for age were divided into <36 and ≥ 36 years old. The cut off points were divided into <2.81 and ≥ 2.81.

Association of clinical profile with opportunistic pulmonary infections in HIV/AIDS are shown in Table 2. The majority of HIV/AIDS patients who had opportunistic pulmonary infections were Balinese ethnicity (45.3%), female (37.6%), age ≥ 36 years old (54.7%), used ART for

≥3 months (41.5%), viral load <40 copies/ml, NLR ≥2.81 (47.9%), had adherence (43.7%), types of ART were used combination of tenofovir + lamivudine + efavirenz (TLE) (45.2%), and private employed (42.5%). Based on the bivariate analysis results, a statistically significant association was found between age with opportunistic pulmonary infections in HIV/AIDS (p=0.003; PR=3.082; 95% CI=1.516-6.266). NLR showed a significant association with the incidence of opportunistic pulmonary infections in HIV/AIDS (p=0.003; PR=8.274; 95% CI=1.838-37.249). Meanwhile, the remaining factors, such as ethnicity, age, ART duration, viral load, and control compliance, were not statistically associated with the incidence of opportunistic pulmonary infections in HIV/AIDS (p>0.05). There are 59 HIV/AIDS patients who had opportunistic pulmonary infections. One patient can have more than one opportunistic pulmonary infections.

Table 1: Characteristics of sample.

Characteristics	Opportunistic pulmonary infections, median (min-max)	
	No	Yes
Age, years	34.50 (22.00-64.00)	43.00 (18.00-76.00)
NLR	2.69 (0.04-18.86)	3.22 (0.33-17.41)

Table 2: Association of clinical profile with opportunistic pulmonary infections.

Clinical profiles	Opportunistic pulmonary infections, n (%)		PR	95% CI	P
	No	Yes			
Ethnicity					
Balinese	52 (54.7)	43 (45.3)	0.691	0.331-1.441	0.422
Non-Balinese	28 (63.6)	16 (36.4)			
Gender					
Male	22 (47.8)	24 (52.2)	0.553	0.271-1.130	0.147
Female	58 (62.4)	35 (37.6)			
Age, years					
<36	46 (71.9)	18 (28.1)	3.082	1.516-6.266	0.003*
≥36	34 (45.3)	41 (54.7)			
ART duration (months)					
<3	4 (44.4)	5 (55.6)	0.568	0.146-2.215	0.635
≥3	76 (58.5)	54 (41.5)			
Viral load (copies/ml)					
<40	71 (56.3)	55 (43.7)	0.574	0.168-1.961	0.549
≥40	9 (69.2)	4 (30.8)			
NLR					
<2.81	18 (90)	2 (10)	8,274	1.838-37.249	0.003*
≥2.81	62 (52.1)	57 (47.9)			
Adherence					
Yes	76 (56.3)	59 (43.7)			0.219
No	4 (100)	0 (0.0)			
ART types					
Tenofovir + lamivudine + dolutegravir (TLD)	23 (67.6)	11 (32.4)			
Tenofovir + lamivudine + efavirenz (TLE)	57 (54.8)	47 (45.2)			
Lamivudine + zidovudine + nevirapine	0 (0.0)	1 (100)			
Occupation					
Not working	15 (60)	10 (40.0)			
Government employed	2 (33.3)	4 (66.7)			
Private employed	46 (57.5)	34 (42.5)			
Entrepreneur (self-employed)	8 (66.7)	4 (33.3)			
Farmer	5 (71.4)	2 (28.6)			
Others	4 (44.4)	5 (55.6)			

*Statistically significant (p<0.05)

The type of opportunistic pulmonary infections in HIV/AIDS patients can be seen in Table 3. The most common opportunistic pulmonary infections were pulmonary tuberculosis (TB) (42.37%). 9 patients (15.25%) had acute upper respiratory infection. 12 patients (20.34%) had pneumonia. 10 patients (16.95%) had bronchitis. 2 patients (3.39%) had coronavirus disease

(COVID-19). 9 patients (15.25%) had pneumocystis pneumonia (PCP).

Table 3: Types of opportunistic pulmonary infections.

Types of opportunistic pulmonary infections	n (%)
Acute upper respiratory infection	9 (15.25)
Pneumonia	12 (20.34)
Bronchitis	10 (16.95)
Pulmonary TB	25 (42.37)
COVID-19	2 (3.39)
PCP	9 (15.25)

*One patient can have more than one opportunistic pulmonary infections

DISCUSSION

This study showed 42.45% (n=59) of HIV/AIDS patients experienced opportunistic pulmonary infections, where opportunistic pulmonary infections were more common in HIV patients with risk group for Balinese ethnicity (45.3%), Female (37.6%), used ART duration ≥3 months, had adherence (43.7%), and private employed (42.5%). This study also showed 42.37% (n=25) of HIV/AIDS patients experienced pulmonary tuberculosis. Previous reports on the prevalence of opportunistic infections (OI) reported the prevalence of OI to be 12.3% (n=167) and the most common types of OI were tuberculosis infection (43%).[15] Study done by Inamdar et al in India found tuberculosis as the most common OI in HIV patients.[16]

This study found that age was associated with opportunistic pulmonary infections. The age group ≥36 years had a significant relationship to the incidence of opportunistic pulmonary infections. This was following research reports in the United States that aged 13-24 years, 35-44 years, and 45-54 years had risky behavior.[17] Another following research reported the majority of diagnosed HIV patient were 46-65 years (70.69%) and male (68.97%). The report also showed 13.79% (n=8) were HIV with TB.[18] A study from Congo showed the most represented group with OI in HIV patients were 36-45 years (31.8%).[19]

NLR has been used as an inflammatory marker to predict the severity of various diseases that can be easily obtained at low cost. Inflammation plays a significant role in the pathogenesis of opportunistic pulmonary infections. The inflammatory process causes neutrophil apoptosis, which disrupts the function and number of neutrophils and makes HIV patients susceptible to bacterial infection.[20] The other finding in this study showed that NLR had a significant relationship with opportunistic pulmonary infections in HIV/AIDS patients. This was following the previous study that HIV patient with TB had statistically significant relationship with NLR ($p<0.05$) with the mean NLR of 6.05±2.67.[21] Another following study by Kusnadi et al found NLR was significantly higher in subjects with bacterial infections in HIV patient ($p<0.05$) and the mean NLR was 12.80±9.19. The study concluded that NLR can become a marker of bacterial infection in HIV-infected patients.[22]

In this study, it was found that viral load was not associated with the incidence of opportunistic pulmonary infections in HIV/AIDS patients (p=0.549). These results were in line with studies conducted by Kurniawati et al and Ogbenna et al.[23,24]

While research conducted by Ekwaru et al obtained different results, it found an association between having had an opportunistic illness and short-and long-term effects on HIV RNA viral load among people taking ART. Participants who had an OI following an assessment in which their HIV RNA viral load was undetectable had four times the odds of having a detectable HIV RNA viral load in the following three-month assessment compared to when there was no episode of an OI (OR=3.8; 95% CI=1.7–8.4; p=0.001).[25]

Limitations

The limitations of our study were due to the limited scope of this study as it was only conducted by consecutive sampling and samples were taken without further follow up. Author also realized that the results of this study still had several weaknesses where the risk factors affecting NLR and viral load were not studied further, thus affecting the validity value obtained in this study. These risk factors included regular NLR and viral load tests in the short and long term.

CONCLUSION

This study identified the association NLR and viral load with opportunistic pulmonary infections in HIV/AIDS patients. This study found that age and NLR were statistically associated with the incidence of opportunistic pulmonary infections in HIV/AIDS patients. NLR is a cheap and easy-to-obtain biomarker that is associated with opportunistic pulmonary infections in HIV/AIDS. Viral load was not associated with the incidence of opportunistic pulmonary infections in HIV/AIDS patients. Samples were taken without further follow up might be the cause of it. However, ethnicity, age, ART duration, and control compliance were not associated with the incidence of opportunistic pulmonary infections in HIV/AIDS patients. Further studies can conduct research using another sampling method and other independent variables.

ACKNOWLEDGEMENTS

Authors would like to thank Internal Medicine Department, Wangaya General Hospital, Denpasar, Bali, Indonesia for reviewing the work and general support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Handayani K, Katu S, Bakri S, Halim R, Aman AM, Rasyid H, et al. Correlation of CD4 Count And Neutrophil- Lymphocyte Ratio in Human Immunodeficiency Virus-Acquired Immuno-deficiency Syndrome (HIV- AIDS) Patients. Eur J Mol Clin Med. 2020;7(8):985-93.
2. Poorolajal J, Hooshmand E, Mahjub H, Esmailnasab N, Jenabi E. Survival rate of AIDS disease and mortality in HIV-infected patients: a meta-analysis. Public Health. 2016;139:3-12.
3. UNAIDS. Global HIV & AIDS Statistics – Fact sheet. 2022. Available at: https://www.unaids.org/en/resources/fact-sheet. Accessed on 27 May 2023.
4. Kementerian Kesehatan Republik Indonesia, Direktorat Jenderal Pencegahan dan Pengendalian Penyakit. Laporan Perkembangan HIV-AIDS & Penyakit Infeksi Menular Seksual (PIMS) Triwulan I Tahun 2017. 2017.
5. Dinas Kesehatan Provinsi Bali. Rencana Strategis (RENSTRA) Dinas Kesehatan Provinsi Bali Tahun 2018-2023. 2021.
6. Rich EA. Activation-inactivation of HIV-1 in the lung. J Biomed Sci. 1998;5:1-10.
7. Segreti J. Pulmonary complications of HIV disease. Current medical diagnosis & treatment. 2006;39:414-23.
8. O'neil KM. The changing landscape of HIV-related lung disease in the era of highly active antiretroviral therapy. Chest. 2002;122:768-71.
9. Chu C, Pollock LC, Selwyn PA. HIV-Associated Complications: A Systems-Based Approach. Am Fam Physician. 2017;96(3):161-9.
10. Hanberg JS, Freiberg MS, Goetz MB, Rodriguez-Barradas MC, Gibert C, Oursler KA, et al. Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios as Prognostic Inflammatory Biomarkers in Human Immunodeficiency Virus (HIV), Hepatitis C Virus (HCV), and HIV/HCV Coinfection. Open Forum Infect Dis. 2019;6(10):ofz347.
11. Lundgren JD, Babiker AG, Gordin F, Emery S, Grund B, Sharma S, et al. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. N Engl J Med. 2015;373(9):800-3.
12. Wahyuni RD, Sallatu NAPRS, Harun H, Rasjid M. Perbandingan Rasio Neutrofil Limfosit (RNL) pada Pasien TB Paru BTA Positif dan BTA Negatif di RSU Anutapura Palu Tahun 2017. Continuing Medical Education. 2019;1(1):1-9.
13. Nachega JB, Uthman OA, Del Rio C, Mugavero MJ, Rees H, Mills EJ. Addressing the Achilles' Heel in the HIV Care Continuum for the Success of A Test and Treat Strategy to Achieve an AIDS-free Generation. Clin Infect Dis. 2014;59(1):21-7.
14. Cihlar T, Fordyce M. Current status and prospects of HIV treatment. Curr Opin Virol. 2016;18:50-6.
15. Sutini, Rahayu SR, Saefurrohim MZ, Al Ayubi MTA, Wijayanti H, Wandastuti AD, et al. Prevalence and Determinants of Opportunistic Infections in HIV Patients: A Cross-Sectional Study in the City of Semarang. Ethiop J Health Sci. 2022;32(4):809-16.
16. Inamdar SA, Kosambiya JK, Modi A, Gohil A, Mehta A, Patel T. Age and Opportunistic Infections: Prevalence and Predictors among Older People Living With HIV. Natl J Community Med. 2018;9(8):610-3.
17. Brooks JT, Buchacz K, Gebo KA, Mermin J. HIV infection and older Americans: the public health perspective. Am J Public Health. 2012;102(8):1516-26.
18. Fatimatuzzuhro, Sundari SA, Indriati DW. The Prevalence of Pulmonary Tuberculosis Among Newly Diagnosed HIV/AIDS Individuals Admitted in Gresik, Indonesia. Malaysian J Med Health Sci. 2020;16(16):4-8.
19. Bongenya BI, Bulanda BI, Bukongo RN, Chuga D, Botomuito HT, Kabasele JYD. Prevalence of Opportunist Infections among the Professionals Sex Workers and Their Customers Living with the VIH under ARV in Kinshasa. Open Access Library J. 2022;9(5):1-7.
20. Emokpae MA, Aruomaren AI, Mrakpor BA. Association of Neutrophil-tolymphocyte ratio with Respiratory burst enzymes in Human Immunodeficiency virus type 1 infected Africans. J Med Discov. 2017;2(2).
21. Sulastri N, Alisjahbana B, Livia R, Sahiratmadja. Higher Neutrophil-lymphocyte Ratio in TB/HIV Co-infection Compared to Pulmonary Tuberculosis. Indones Biomed J. 2021;13(4):375-82.
22. Kusnadi D, Liwang MNI, Katu S, Mubin AH, Halim R. Correlation between the neutrophil-lymphocyte count ratio and bacterial infection in patient with human immunodeficiency virus. IOP Conference Series: Earth and Environmental Science. 2018;125(1):012-29.
23. Kurniawati V, Harioputro D, Susanto A. Evaluasi Kadar Sel CD4, Viral Load, Dan Neutrophil Lymphocyte Ratio (NLR) Terhadap Infeksi Oportunistik Pada Pasien HIV/Aids. Biomedika. 2022;14(2):99-107.
24. Ogbenna AA, Meloni S, Inzaule S, Hamers RL, Sigaloff K, Osibogun A, et al. The impact of HIV-1 subtypes on virologic and immunologic treatment outcomes at the Lagos University Teaching Hospital: A longitudinal evaluation. Plos One. 2019;15(8):2-6.
25. Ekwaru JP, Campbell J, Malamba S, Moore DM, Were W, Mermin J. The effect of opportunistic illness on HIV RNA viral load and CD4+ T cell count among HIV-positive adults taking antiretroviral therapy. J Int AIDS Soc. 2013;16(1):17355.

Cite this article as: Pratikto BC, Suryana K. Association between neutrophil-lymphocyte ratio and viral load with opportunistic pulmonary infections in human immunodeficiency virus/acquired immunodeficiency syndrome patients. Int J Adv Med 2023;10:596-600.