Correlation between the neutrophil-lymphocyte count ratio and bacterial infection in patient with human immunodeficiency virus

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Abstract. Parameters for starting antibiotic therapy such as CRP andleukocytosis are considered non-specific. Previous studies have shown the Neutrophil-Lymphocyte Count Ratio (NLCR) can serve as the basis of bacterial infection, the level of infection, and the basis of antibiotic therapy. Compared with the Procalcitonin parameter, this NLCR is rapid, an inexpensive and requires no additional sampling. To determine the correlation between The Neutrophil-LymphocyteCount Ratio to bacterial infection in HIV patients. This study was a cross-sectional observational approach to HIV subject at Wahidin Sudirohusodo and Hasanuddin University Hospital. The subjects performed routine blood, microbiology test,and blood Procalcitonin levels tests. Then performed NLCR calculations based on routine blood results. The subjects then grouped the presence or absence of bacterial infection.In 146 study subjects, there were 78 (53.4%) with bacterial infections and 68 (46.6%) without bacterial infection as controls. Subjects with bacterial infections had higher total neutrophils (84.83) compared with non-bacterial infections. Subjects with bacterial infections had total lymphocytes with an average of 8.51 lower than non-bacterial infections. Subjects with bacterial infections had higher NLCR values with an average of 12.80. The Neutrophil-Lymphocyte Count Ratio can become a marker of bacterial infection in HIV patients.

1. Introduction

Human immunodeficiency virus (HIV) is a typical lymphotropic retrovirus that infecting cells from the immune system, destroy or damage specific white blood cells called T-helper lymphocytes or T4 factor carrier lymphocytes (CD4).[1] CD4 T- lymphocytes remain becomes an important parameter. The declining of CD4 cell count is a progress indicator of HIV. The lower number of CD4 T-lymphocytes in HIV patients will be positively correlated with the incidence of infection.[2]

In HIV-infected patients, sepsis rates continue to increase every year. The level of sepsis in this population also depends on the level of immunity. Data compared in the pre HAART (highly active antiretroviral therapy) era, many HIV-infected patients went into the Intensive Care Unit (ICU) with sepsis and eventually died. The latest data from the United States estimates about 13.7% of those who enter the ICU, and a mortality rate is about 42%.[3]

The high number of deceased which caused by sepsis due to bacterial infection causes a lot of research that can be used as a marker of antibiotic therapy in the early stage. On the other hand, the

exact confirmation of bacterial infection through microbiological examination becomes difficult to do in all health facilities, especially the results of aculture that sometimes give negative results, and the duration of the results of this culture examination. Inflammation markers are like C-reactive protein (CRP) or leukocyte values are considered less specific for bacterial infections. Other markers such as tumor necrosis factor (TNF-α), interleukin (IL) -1β, IL-6, and Procalcitonin. Procalcitonin over 0.5 ug/L is considered a very specific marker for bacterial infections. However, those infection indicator is not often found in the general health care centers.[4]

The Neutrophil-Lymphocyte Count Ratio (NLCR) is the result of dividing total neutrophils with total lymphocytes.[5] The Neutrophil-Lymphocyte Count Ratio is often used to determinethelevel of inflammation in malignancy, cardiovascular disease, and also used as a marker of bacterial infection. The Neutrophil-Lymphocyte Count Ratio has been accepted as an independent predictor of the patient's life expectancy in that case.[6] Furthermore, NLCR can be used as a parameter in predicting the level of bacteremia in emergencies.[3]

The purpose of this study is to find the correlation of NLCR with abacterial infection in HIV patients and to find out that NLCR can be used as a basis for administration of antibiotics in suspected bacterial infection cases in this demographic.

2. Subject and Research Method

The study population was all HIV-infected inpatient and outpatient at WahidinSudirohusodo Hospital and Hasanuddin University Hospital in Makassar. The samples of the study were from the population that met the inclusion criteria, i.e., culture results found bacteria or Procalcitonin exceeded normal values, no other viral coinfection found, no malignancy comorbidity and ACS, and patients were willing to follow the study. The study was conducted from January to December 2016 until the number of samples was reached (146 subjects). The research design was observational withthecross-sectional design.

The study was screened HIV-infected patients according to the inclusion criteria. Blood sample and microbiological test were taken to those who met the inclusion criteria then collected data were analyzed throughacomputer by using the program Statistical Package for the Social Sciences (SPSS) version 22. The statistical testwas by using Chi-Square, Independent T,andANOVA test. Statistical test results are significant if the value of $p < 0.05$. The results are in narrative form with tables and graphs.

3. Research Result

From the total of 146 subjects in this study, 94 subjects are male, and 52 subjects are female. Subjects age between 18-70 years, 38 subjects age less than 30 years, 70 subjects age between 30-39 years, 22 subjects age between 40-49 years, and there are 16 subjects age ≥ 50 years. Research subjects had two groups, i.e., subjects with bacterial infections amounted to 78 subjects (53.4%) and subjects without bacterial infection amounted to 68 subjects (46.6%).

Table 1. The distribution of biological and laboratory characteristic (n=146).

Variable	Category	N	%
Gender	Male	94	64.4
	Female	52	35.6
Age	<30 years	38	26.0
	30-39 years	70	47.9
	40-49 years	22	15.1
	>=50 years	16	11.0
Bacterial infection	Yes	78	53.4
	No	68	46.6

Table 2 shows the ratio of neutrophils, lymphocytes, and NLCR based on bacterial infection. Neutrophil count was significantly higher in subjects with bacterial infections compared with non-bacterial infections, 84.83 with 59.38 ($p < 0.001$). While the number of lymphocytes was significantly lower in subjects with bacterial infections than subjects, not bacterial infections, i.e., 8.51 with 28.61 ($p < 0.001$). The Neutrophil-Lymphocyte Count Ratio was significantly higher in subjects with bacterial infections than subjects, not bacterial infections, i.e., 12.80 with 2.40 ($p < 0.001$).

Table 2. The ratio between neutrophil, lymphocyte, and NLCR according to infection.

Variable	Infection	N	Mean	SD	P
Neutrophil	Yes	78	84.83	4.89	<0.001
	No	68	59.38	10.66	
Lymphocyte	Yes	78	8.51	3.84	<0.001
	No	68	28.61	8.97	
NLCR	Yes	78	12.80	9.19	<0.001
	No	68	2.40	1.16	

4. Discussion

Various factors play a role in the decline in CD4 T lymphocyte cell numbers that cause patients with HIV to be particularly vulnerable to infection. These factors are the direct cytopathic effects of HIV against CD4 lymphocyte cells and their progenitors, the induction of apoptosis through immune activation, stem cell destruction and bone marrow stromal cells, cytotoxicity cytokine, lymphoid tissue destruction including the thymus gland so that new cell production does not occur. Destruction of stem cells and bone marrow stroma can have an impact on function and neutrophil count. Neutrophil dysfunction can cause a person susceptible to bacterial infection.[3]

Of the 146 HIV-infected subjects, significant neutrophil counts were higher in the subjects group with bacterial infection than in the subject group without bacterial infection ($p < 0.001$). In this study also found the number of lymphocytes significantly lower in subjects with bacterial infections than subjects without bacterial infection ($p < 0.001$). Neutrophil changes occur very quickly even in the early stages of an inflammatory response. Neutrophilia will usually be accompanied by lymphocytopenia, which is also a good predictor of bacteremia.[7,8]

The study also showed that the ratio of lymphocyte neutrophils higher in subjects with bacterial infection than subjects without bacterial infection ($p < 0.001$). The ratio's ability to predict bacteremia compared with traditional parameters in emergency patients with community pneumonia. It has been investigated by Jager et al. The study concludes that NLCR is a better predictor compared with leukocyte count, count neutrophil, or serum C-Reactive Protein (CRP). The Neutrophil-Lymphocyte Count Ratio is assumed to be able to differentiate infectious agents of a patient whether caused by bacterial or non-bacterial infection, e.g. virus.[9] Zahorec also evaluated NLCR in oncologist patients who had sepsis in the ICU and found that NLCR associated with severity of the disease.[5]

The diagnostic markers for determining a bacterial etiology are not always usable. Also, the often-used markers in clinical practice usually require a higher cost and are not always available. In contrast, NLCR is an easy and affordable parameter to obtain because it does not require specific equipment.[8]

5. Conclusion

The Neutrophil-Lymphocyte Count Ratio can become a marker of bacterial infection in HIV-infected patients.

References

[1] Brooks G F B J S and M S A 2005 *Mikrobiologi kedokteran* (Jakarta: Salemba Medika) pp 317-27

[2] Fasakin K, Omisakin C, Esan A, *et al.* 2014 Total and CD4+ T-lymphocyte count correlation in

newly diagnosed HIV patients in resource-limited setting *J. Med. Lab. Diagn.* **5(2)** 22–8
[3] Mayr F B Y S and A D C 2014 Epidemiology of severe sepsis *Virulence* **5(4)** 11
[4] Schuetz P AW and M B 2011 Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future *BMC Med.* **107(9)** 1–9
[5] Zahorec R 2011 Ratio of neutrophil to lymphocyte counts--rapid and simple parameter of systemic inflammation and stress in critically ill *Bratisl. Lek. List.* **102(5)** 14
[6] Kumar R, Geuna E, Michalarea V, *et al.* 2015 The neutrophil-lymphocyte ratio and its utilization for the management of cancer patients in early clinical trials *Brit. J. Cancer* **112(1157)** 65
[7] Liu X, Shen Y, Wang H, *et al.* 2016 Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: a prospective observational study *Hindawi Publ. Corp.* 1–8
[8] Holub M, Beran O, Kasprikova N, *et al.* 2012 Neutrophil to lymphocyte count ratio as a biomarker of bacterial infections *Cent. Eur. J. Med.* **7(2)** 258–61
[9] Jager C D, Wever P, Gemen E, *et al.* 2012 The neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia *PLoS ONE* **10(7)** 461–5