

PERBANDINGAN RASIO NEUTROFIL LIMFOSIT (RNL) PADA PASIEN TB PARU BTA POSITIF DAN BTA NEGATIF DI RSU ANUTAPURA PALU TAHUN 2017

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ABSTRAK

Latar Belakang : Penyakit Tuberculosis (TB) dapat disebabkan oleh kuman *Mycobacterium tuberculosis*. Berdasarkan hasil pemeriksaan dahak mikroskopis, TB Paru terdiri dari TB paru BTA positif dan TB paru BTA negatif. Salah satu respon imun dari infeksi TB paru dapat ditemukan inflamasi, ditandai dengan adanya peningkatan jumlah hitung neutrofil dan penurunan jumlah hitung limfosit. Diagnosis TB terdiri dari gejala klinik dan pemeriksaan laboratorium. Pemeriksaan penunjang darah rutin untuk mengetahui RNL diharapkan dapat mengetahui derajat virulensi TB paru. Nilai RNL adalah perbandingan jumlah neutrofil absolut terhadap jumlah limfosit absolut.

Tujuan : untuk mengetahui perbandingan RNL pada pasien TB paru BTA positif dan BTA negatif di RSU Anutapura Palu tahun 2017.

Metode Penelitian : Jenis penelitian ini adalah penelitian kuantitatif dengan desain penelitian observasional analitik yang menggunakan pendekatan *cross sectional*. Teknik pengambilan sampelnya menggunakan teknik *total sampling* yang sesuai dengan kriteria inklusi dan eksklusi dengan sampel sebanyak 62 orang.

Hasil Penelitian : Nilai rerata jumlah neutrofil pada TB paru BTA positif sebesar $81,19 \pm 4,12$ lebih tinggi jika dibandingkan pada TB paru BTA negatif sebesar $58,22 \pm 4,14$ ($p:0,000$). nilai rerata jumlah limfosit TB paru BTA positif sebesar $13,35 \pm 5,93$ lebih rendah jika dibandingkan pada TB paru BTA negatif sebesar $20,36 \pm 9,03$ ($p: 0,001$). Nilai RNL pada TB paru BTA positif yaitu $7,60 \pm 3,88$ lebih tinggi dari TB paru BTA negatif, yaitu $3,42 \pm 1,43$ ($p:0,000$)

Kesimpulan : Rasio netrofil limfosit pada TB paru BTA postif lebih tinggi dibandingkan BTA negatif.

Kata Kunci : TB paru, netrofil, limfosit, RNL

**COMPARISON OF NEUTROPHIL LYMPHOCYTE RATIO (NLR) OF PULMONARY
POSITIVE AFB AND NEGATIVE AFB PATIENTS AT GENERAL HOSPITAL
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ABSTRACT

Background : Tuberculosis (TB) is caused by *Mycobacterium tuberculosis*. Based on sputum smear microscopy examination, pulmonary TB consists of positive Acid Fast Bacilli (AFB) and negative AFB. One of immune response of TB infection found inflammatory, marked by the increase of neutrophil count and decrease of lymphocyte count. The diagnosis of tuberculosis consists of clinical symptoms and laboratory examination. Routine blood testing to determine the NLR is expected to determine the degree of virulence of pulmonary tuberculosis. Number of NLR is obtained by dividing neutrophil count over lymphocyte count.

Aim: To determine comparison of NLR of pulmonary TB patients with positive AFB and negative AFB at General Hospital Anutapura Palu in 2017.

Methods : This study used *observational analytic* with *cross-sectional* approach. Samples was taken using *total sampling* with samples is 62 patient.

Results : Average of neutrophil count in positive AFB pulmonary TB is $81,19 \pm 4,12$ higher than negative AFB pulmonary TB $58,22 \pm 4,14$ (p: 0,000). Average of lymphocyte count in positive AFB pulmonary TB is $81,19 \pm 4,12$ lower than negative AFB pulmonary TB is $20,36 \pm 9,03$ (p:0,001). NLR in positive AFB pulmonary TB is $7,60 \pm 3,88$ higher than negative AFB pulmonary TB is $3,42 \pm 1,43$ (p:0,000)

Conclusion : Neutrophil lymphocyte ratio of positive AFB pulmonary TB is higher than negative AFB pulmonary TB.

Keywords : Pulmonary TB, neutrophil, limphocyte, NLR

INTRODUCTION

contagious infection disease that caused by mycobaterium tuberculosis, that can attack various types of organs, especially in the vital organs of the lungs, are called tuberculosis (TB). The mechanism of transmission of Mycobacterium tuberculosis can occur from one individual to another through sprinkling droplets carried by the air such as coughing, phlegm or saliva [1].

The World Health Organization 2018 reports that, in 2017 there were around 10 million people suffering from TB including 5.8 million male, 3.2 million female and 1 million children. Participants in pulmonary TB in Indonesia ranked third in the world after India and China [2]. The number of pulmonary TB sufferers from year to year in Indonesia continues to increase. Pulmonary TB can affect anyone and anywhere. Every year, there are 250,000 new cases of TB and around 140,000 deaths occur each year caused by pulmonary TB [3].

Based on data from the Palu City Health Office [4], there were 256 new cases and 5,912 were suspected of finding Acid-fast bacilli (AFB) of 451 cases examined from 100,000 residents. Data from Anapapura Hospital [5], there were 217 patients with positive AFB tuberculosis with no TB bacterial culture, including 130 male patients and 87 female patients with 188 out of life and 29 patients out of life.

The physiological immune response of pulmonary TB infection can be found that leukocytes circulating against various inflammatory stress conditions are characterized by an increase in neutrophil count and a decrease in lymphocyte count has long been known. Lymphocytes Neutrophil Ratio (LNR) is one of the laboratory tests used to evaluate or as a marker of inflammation [6]. Lymphocytes Neutrophil Ratio (LNR) is a good parameter in predicting bacteremia. Based on Yoon's research [7] states that LNR is a marker that can distinguish between tuberculosis and pneumonia [8]. The value of LNR is obtained from the number of neutrophils divided by the number of lymphocytes. LNR is said to be physiological if its value is <5 and is said to be pathological if it has an increase of > 6 , such as severe infection or Systemic Inflammatory Response Syndrome (SIRS) [9]. This check can be done easily, cheaply and quickly [8].

The value of the Lymphocytes Neutrophil Ratio (LNR) is to divide absolute neutrophil counts to absolute lymphocyte counts. The leukocyte count (diff count) only shows the relative number of each cell type. To get the absolute number of each cell type, the relative value (%) multiplied by the total leukocyte count (cell / μL). The normal value of absolute neutrophils counts are 3000-7000 μL (60-70%). The normal values of absolute lymphocyte counts are 1000-4000 μL (25-33%) [9].

In general there is a close relationship between laboratory values especially neutrophils and lymphocytes as an inflammatory marker for diagnosing pulmonary TB. Therefore, researchers are interested in conducting a study on how to compare the Lymphocytes Neutrophil Ratio (LNR) in pulmonary TB patients in Anapapura Palu Hospital in 2017.

METHOD

This type of research is quantitative research with descriptive analytic research design that used a cross sectional approach. The sampling technique used total sampling techniques that were in accordance with inclusion and exclusion criteria. This research was conducted in the Medical Record section of Anutapura Hospital in December 2018.

RESULTS

From the research that has been done in Anutapura General Hospital, Central Sulawesi Province, the medical record data for the period of December 2017 obtained as many as 217 people with pulmonary tuberculosis. Out of the 217 people, there were 62 people who met the inclusion criteria. The characteristics of the research subjects included age, gender, number of neutrophils, lymphocytes and LNR presented in table 4.1 below.

Table 4.1. Characteristics of Research Subjects

Tabel 4.1. Karakteristik Subyek Penelitian

Characteristics		AFB positive		AFB negative		Total	
		(n = 31)		(n = 31)		(n = 62)	
		n	(%)	n	(%)	n	(%)
Age	17-25 years	5	(16,1)	7	(22,5)	12	(19,3)
	26-35 years	9	(29,0)	9	(29,0)	18	(29,0)
	36-45 years	13	(41,9)	11	(35,4)	24	(38,7)
	46-55 years	4	(12,9)	4	(12,9)	8	(12,9)
Gender	Male	19	(61,3)	18	(58,1)	37	(59,7)
	Female	12	(38,7)	13	(41,9)	25	(40,3)
Neutrophils (mean ±SD)		81,19 ±4,12		58,22 ±4,14			
Lymphocytes (mean ±SD)		13,35 ±5,93		20,36 ±9,03			
Neutrophils		7,60±3,88		3,42±1,43			
Lymphocytes							
Ratio							
(mean±SD)							

Description: Acid-fast bacilli (AFB)

This study received 62 subjects, with 31 people (50%) of pulmonary TB patients with AFB positive and 31 people (50%) of pulmonary TB patients with AFB negative. At the ages of 17 until 25 years in pulmonary TB patients with AFB positive were 5 people (16.1%) and in pulmonary TB patients with AFB negative were 7 people (22.5%). Furthermore, at the ages of 26 until 35 years in pulmonary TB patients with AFB positive were 9 people (29.0%) and pulmonary TB patients with AFB negative were 9 people (29.0%). Furthermore, at the age of 36

- 45 years in pulmonary TB patients with AFB positive were 13 people (41.9%) and in pulmonary TB patients with AFB negative were 11 people (35.4%). Furthermore, at the age of 46-55 years in pulmonary TB patients with AFB positive were 4 people (12.9%) and in pulmonary TB patients with AFB negative were 4 people (12.9%) with a total of 12 people (19.3%) pulmonary TB aged 17 -25 years, 18 people (29.0%) pulmonary TB aged 26-35 years, 24 people (38.7%) pulmonary TB aged 36-45 years, and 8 people (12.9%) pulmonary TB aged 46-55 years. Based on the gender, this study found male were 37 people (59.7%) and female were 25 people (40.3%). In pulmonary TB patients with AFB positive, the number of male were 19 people (61.3%) and female were 12 people (38.7%). In pulmonary TB patients with AFB negative, the number of male were 18 people (58.1%) and female were 13 people (41.9%). The mean value of neutrophils in pulmonary TB with AFB positive were 81.19 higher when compared to pulmonary TB with AFB negative at 58.22. Lymphocyte counts in pulmonary TB with AFB positive were 13.35 lower when compared to pulmonary TB with AFB negative of 20.36 and the number of LNR in pulmonary TB with AFB positive were 7.60 and in pulmonary TB with AFB negative were 3.42.

Comparison of Lymphocytes Neutrophil Ratio in pulmonary TB

The patients of pulmonary TB were 62, of which 31 people (50%) of pulmonary TB with AFB positive and 31 people (50%) of pulmonary TB with AFB negative. If looking at the value of neutrophils and lymphocytes from the overall data, the number of neutrophils in pulmonary TB with AFB positive were 81.19 higher when compared with pulmonary TB with AFB negative at 58.22. Lymphocyte counts in pulmonary TB with AFB positive were 13.35 lower when compared to pulmonary TB with AFB negative at 20.36, and the number of LNR in pulmonary TB with AFB positive were 7.60 and in pulmonary TB with AFB negative were 3.42. The first test used was the One-Sample Kolmogorov-Smirnov (K-S Test) normality test to show whether the data was normally distributed or not, and the results were the data distributed normally. Furthermore, the independent t-test was used to find out there were significant mean differences between the 2 free groups with data interval or ratio scale. The two free groups referred to here were two groups that were not in pairs, meaning that the data source comes from a different subject. The results obtained in the test were significant differences in neutrophils ($p = 0,000$), lymphocytes ($p = 0,001$) and LNR ($p = 0,000$) which means if sig- (2-tailed) $< 0,05$ then H_0 was rejected and H_1 was accepted. The results of the significance analysis were presented in table 4.2.

Table 4.2 Bivariate analysis of comparison of Lymphocytes Neutrophil Ratio in pulmonary TB with AFB positive and AFB

	AFB positive	AFB negative	P*
Neutrophils	81,19 ±4,12	58,22 ±4,14	0,000
Lymphocytes	13,35 ±5,93	20,36 ±9,03	0,001
LNR**	7,60±3,88	3,42±1,43	0,000

*) p: the value of the T-independent test was significant if (<0.05)

***) LNR : Lymphocytes Neutrophil Ratio

DISCUSSION

From the results of the study it was found that the majority of pulmonary tuberculosis patients were in the age group of 36-45 years which amounted to 38.7% followed by the age group of 26-35 years which amounted to 29.0% then followed by the age group of 17-25 years which amounted 19,3% and followed by the age group 46-55 years which were 12.9%. This was in accordance with Herlana's research (2014) [10] which stated that most TB patients were in late adulthood, which was 36-45 years old, amounted to 8 people (26.7%). This was because at that age more susceptible to various disease problems because at that time humans would experience a period of change, namely aging, which caused the body's immune system began to decrease and at that age someone's desire to make good changes has begun to decline. It could be concluded that in the late adulthood, a person's immunological system decreased causing susceptibility to disease, including one of them was pulmonary TB disease.

Based on the results of the study found that male as many as 36 people (58.1%) and female as many as 26 people (41.9%). In pulmonary TB with AFB Positive, the number of male were 19 people (61.3%) and female were 12 people (38.7%). In pulmonary TB with AFB negative, there were 17 male (54.8%) and 14 female (45.2%). This was consistent with the Dotulong study [11] stating that male were at greater risk of developing pulmonary TB disease compared to women. Because more men who smoking and drinking alcohol compared to women, smoking and alcohol could reduce body immunity so that it was more susceptible to pulmonary TB disease.

On neutrophil counts, the mean neutrophil count on pulmonary TB with AFB Positive were 81.19 ± 4.12 higher when compared to pulmonary TB with AFB negative were 58.22 ± 4.14 . Based on this study, an increase in neutrophil counts was seen to be quite significant in pulmonary TB with AFB positive. This was in accordance with the theory of Robert [12] that neutrophils were cells that first act in the host's defense against pathogens that attack, neutrophil reactions aimed to attack pathogens but could cause lung tissue damage, therefore the presence of neutrophils played a role in pathological formation rather than protection the host. Neutrophils in sputum and bronchialveolar fluid in patients with active TB shows signs of M. Tuberculosis bacteria replication.

Based on this, it could be concluded that neutrophils had poor anti-mycobacterial activity and even hide M. Tuberculosis from macrophages and allowed M. Tuberculosis to replicate in it. So that during active disease neutrophils were increasing and could cause poor pathology. The large number of neutrophils in bronchialveolar fluid was associated with lung tissue activity and cavitation. Neutrophils were believed to contribute to disease progression by multiplying local inflammatory reactions and mediating tissue damage.

On the number of lymphocytes, the mean lymphocytes count of pulmonary TB with AFB positive amounted to 13.35 ± 5.93 was lower than pulmonary TB with AFB negative at 20.36 ± 9.03 . In this study, the number of lymphocytes specifically pulmonary TB with AFB positive has decreased and the AFB negative has a slight increased and the rest in the reference value limit, lymphopenia (decreased in lymphocytes) could relatively occur due to a shift in the left leukocyte count (shift to the left), namely there was an increase in immature neutrophil cells [13], because when neutrophils were infected then dendritic cells were immediately infected with the lungs. Dendritic cells infected with M. Tuberculosis in the lungs could reduce the movement of dendritic cells to the mediastinal KGB. This event caused delayed T cell antigen activation

and proliferation. These observations provided clues to a neutrophil mechanism triggering the adaptive immune response in TB. Mycobacterium tuberculosis which lived in phagocytes in the lungs and prevented the maturation of phagosomes in order to survive and replicate [12].

In pulmonary TB patients with AFB positive obtained a mean RNL value of 7.60 ± 3.88 higher than negative pulmonary TB which was 3.42 ± 1.43 . In this study, the results of the t-independent test found that the ratio of neutrophil lymphocytes in patients with pulmonary TB of AFB positive and negative ($p = 0,000$) was significant if ($p < 0.05$). From these results it could be concluded that there were significant comparisons for neutrophil lymphocyte ratio values in AFB positive and negative, which was the value of RNL in AFB positive was higher than the value of RNL in AFB negative. This was in accordance with Sorimin's theory [14] namely physiological immune response from pulmonary TB infection could be found that leukocytes circulating against various inflammatory stress conditions were characterized by an increase in neutrophil count and decreased lymphocyte count. Jilma [15] stated that a decrease in the number of lymphocyte counts and an increase in neutrophils by 85% after 4-6 hours of exposure to endotoxemia in healthy volunteers.

Neutrophils were the first cells to be deployed to where bacteria enter and most of the leukocytes in circulation while lymphocytes in peripheral blood were small cells with a small diameter of 10 μm which played a role in the cellular specific immune system was the main mediator of immune defense against M. TB. The lymphocyte neutrophil ratio has a role as a predictor of bacteremia. Several studies have been conducted that increase the lymphocyte neutrophil ratio to predict the condition of bacterial infections. Yoon [7] stated that the role of the lymphocyte neutrophil ratio (AUC: 0.95) was useful and better than CRP (AUC: 0.83) in distinguishing microorganisms that caused community pneumonia whether caused by bacteria or pulmonary TB.

The weakness of this study, the data taken did not pay attention to the duration of drug used and the type of drug used in these patients that could affect the value of neutrophil lymphocytes in pulmonary TB patients, and this study did not see the severity of symptoms and duration of disease.

CONCLUSIONS AND RECOMMENDATIONS

Based on the results of research that has been obtained, researchers could conclude the following:

1. The value of neutrophils in AFB positive was 81.19 ± 4.12 higher when compared to pulmonary TB with AFB negative of 58.22 ± 4.14 and mean lymphocytes in pulmonary TB with AFB positive were 13.35 ± 5.93 lower if compared to pulmonary TB with AFB negative were 20.36 ± 9.03 .
2. There were significant differences in the meaningful Lymphocyte Neutrophil Ratio (LNR) in pulmonary TB with AFB positive and negative ($p = 0,000$).
3. The Lymphocyte Neutrophil Ratio in Pulmonary Tb with AFB positive was higher than AFB negative.

The suggestions from this study were as follows:

1. The researcher expects further research on the comparison of Lymphocyte Neutrophil Ratio in pulmonary TB patients by examining other variables.
2. It was better for the next researcher to use the sample by paying attention to the factors that could influence changes in the Lymphocyte Neutrophil Ratio value and correct the weaknesses found in this study.

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