



## NEUTROPHIL LYMPHOCYTES RATIO AS A PREDICTOR OF BACTEREMIA IN CHILDREN

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### ABSTRACT

Bacterial infections are an important problem in the world. Early and accurate diagnosis to detect infection is very important in order to reduce mortality. Many bacterial infections that cause leukocytes are circulating and are characterized by increased neutrophils and decreased lymphocytes, this is caused by the inflammatory process. The neutrophil lymphocyte ratio (NLR) is one of the infection markers currently being investigated because it is easy to do, simple with relatively low cost so that it can be used in daily practice. Research with a cross-sectional retrospective design on children performed blood culture at H. Adam Malik Hospital in 2017. Sampling was done in total population and a sample of 506 children who met the inclusion and exclusion criteria was obtained. Data analysis used the chi squared test ( $p < 0.05$ ). This study looked at the 5 most bacteria, namely *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Escherichia coli*, *Staphylococcus haemolyticus*. The neutrophil lymphocyte ratio is better for determining bacteremia with sensitivity of 80.5%, specificity of 26.9%, positive predictive value of 33% and negative predictive value of 74% and cut off 1.3 but cannot be used as a guide because the relationship between blood culture and NLR is not significant with ( $p = 0.1$ ) and ( $OR = 1.4$ )

**KEYWORDS :** bacterial infection; blood culture; marker of infection; neutrophil lymphocyte ratio; predictor.

### 1. INTRODUCTION

Bacterial infection is an important problem in a world where mortality in developed countries is 20% with the largest number in children aged 1-4 years. Early and accurate diagnosis of infection in children is very important to reduce mortality. [1]

The human body is at risk of infection by various types of pathogenic microorganisms. Before causing an infection, microorganisms must come into contact with the host and then form the focus of infection. [2] Bacterial infections that reach blood are called bacteremia. [3] Cases of bacteremia can be established through culture testing and drug sensitivity which is the gold standard examination. [4]

Bacteremia can cause death with a mortality of 30% where high mortality is associated with the establishment of inaccurate and late diagnoses. [4-5] Bacterial infections causing leukocytes are widely circulated and are characterized by increased neutrophils and lower lymphocytes, this is caused by an inflammatory process. [6]

The neutrophil lymphocyte ratio (NLR) is one of the infection markers currently being investigated and from the results of previous studies in the Netherlands in 2001 stated that RNL was better as a predictor of bacteremia compared to C-reactive protein (CRP), total leukocytes, and neutrophils. [7] The same was stated in Turkey in 2015 where the neutrophil lymphocyte ratio could be used as an inflammatory biomarker in acute exacerbation of bronchiectasis in children due to the physiological response of leukocyte circulation in the human body due to increased neutrophils and decreased lymphocytes. [8] Increased neutrophils occur during systemic inflammation caused by delayed apoptosis and stem cell stimulation by growth hormone and decreased lymphocytes due to redistribution of lymphocytes to the lymphatic system accompanied by accelerated apoptosis. [7,9-10]

Research that assesses NLR begins in adults but still few in children where several studies report that an increase in NLR is associated with poor prognosis and ideal cut-off still varies with grades 3 to 5.4. Therefore, research is needed to assess NLR in children because NLR is easy, simple with a relatively low cost so that it can be used in daily practice. [5,11-12] This study aims to determine whether NLR can be used as a predictor of bacteremia.

### 2. METHODS

Research with a cross-sectional retrospective design on children performed blood culture at H. Adam Malik Hospital in 2017. Sampling was done in total population and a sample of 506 children who met the inclusion and exclusion criteria was obtained. Data analysis used the chi squared test ( $p < 0.05$ ). Inclusion Criteria: 1. Patients aged 0 days - 18 years (before the 18th birthday), 2. Patients treated in January 2017 to December 2017, 3. Blood cultures are examined, 4. There are data on neutrophils and lymphocytes. Exclusion Criteria: Secondary data from medical records are incomplete (examination of blood culture and complete blood, especially neutrophils and lymphocytes is not available).

This research was conducted 6 months after obtaining approval from the Health Ethics Committee from the Faculty of Medicine, Universitas North Sumatra/RSUPH. Adam Malik.

### 3. RESULT

This research was conducted at H. Adam Malik General Hospital Medan in 2018. Samples were taken from the medical records of pediatric patients who carried out blood culture examinations in 2017. The total sample was 511 people but 6 people did not meet the inclusion criteria totaling 505 people. The flow of research results can be seen in figure 1.

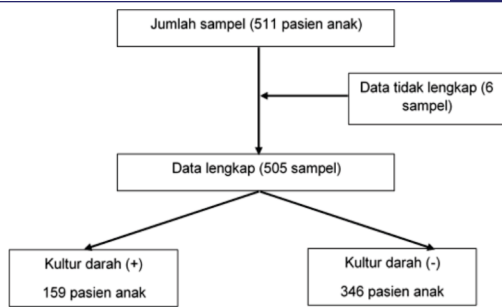


Fig 1. Flow of Research Results Characteristic data

Characteristic data, n (%)	n= 505
Gender, n(%)	
• Boys	293 (58)
• Girls	212 (42)
Age, n (%)	
• < 1 year	174 (34,4)
• 1-4 year	107 (21,2)
• 5-10 year	103 (20,4)
• > 10 year	121 (24,0)
Neutrofil, mean (SD)	
• < 1 year	62,9 (17,7)
• 1-4 year	57,6 (25,1)
• 5-10 year	57,5 (27,7)
• > 10 year	70,6 (24,3)
Limfosit, mean (SD)	
• < 1 year	25,4 (15,2)
• 1-4 year	31,0 (22,9)
• 5-10 year	29,3 (23,9)
• > 10 year	18,5 (18,6)
Leukosit, mean (SD)	
• < 1 year	14.583 (9.319)
• 1-4 year	19.456 (28.948)
• 5-10 year	12.288 (9.416)
• > 10 year	20.760 (52.457)
C-Reactive Protein	
• Positif	159 (31,4)
• Negatif	70 (13,9)
• Not inspected	276 (54,7)
Procalcitonin	
• Positif	134 (26,5)
• Negatif	136 (26,9)
• Not inspected	235 (46,5)
IT Ratio	
• Positif	1 (2)
• Negatif	43 (8,5)
• Not inspected	461 (91,3)

4. DISCUSSION

This study found the types of bacteria that appeared in blood cultures and found 5 most types of bacteria, namely *Klebsiella pneumonia*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Escherichia coli* and *Staphylococcus haemolyticus*. This is different from the findings of a retrospective study in the United Kingdom in 2014 in 1954 of patients with bacteremia with age > 17 years with the discovery of *Escherichia coli* as the most bacteria followed by *Streptococcus spp* and *Staphylococcus spp*. [13] This difference was influenced by different germ patterns in each hospital. In Australia, *Haemophilus Influenza* was found as the most bacteria found in 2001 to 2010. [14] This is different from this study where *Haemophilus influenza* was fastidious and thus was not detected in this study.[15]

Research in Africa said that the most bacteria found in the study were *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumonia* and *Acinetobacter baumannii*. [16] The bacteria found in this study were in line with the five largest

bacteria in our study, the 5 most germs only had a sequence different. Possibly caused by the two studies carried out in developing countries, with the type of bacteria that circulates similarly.

The neutrophil lymphocyte ratio is one of the infection markers that can be used as a predictor of bacterial infection. This occurs because delayed apoptosis and growth hormones are stimulated by stem cells resulting in an increase in neutrophils and accelerated apoptosis accompanied by redistribution of lymphocytes so that neutrophils increase. [7,9-10] Retrospective studies in Spain obtained NLR results >7 and eosinopenia as markers of mortality in bacteremia and prospective studies in the Czech Republic obtained NLR >6.2 as a diagnostic bacteremia. While in this study the cut-off of NLR ≥ 1.3.[17-18] This difference in NLR cut-off may be due to the different ages in each of these studies.

Our study is a retrospective cross sectional study with the results of the study found NLR sensitivity of 80.5% with specificity of 26.9%, positive predictive value of 33% and negative predictive value of 74%. In a retrospective study in England in 2014 in 1954 patients with bacteremia with age were found starting 17 years with results of sensitivity and specificity of 70%, positive predictive value of 20% and negative predictive value of 92% and prospective studies in Czech 2012 in 87 adult bacterial infections with 91% sensitivity and 96% specificity.<sup>13,18</sup> If the three studies are compared then we can see that these three studies have high sensitivity but our study has low specificity. High sensitivity and specificity produce low levels of diagnostic errors. [19] Sensitivity and specificity and cut-off are related to the number of patients.

In this study, we analyzed the cut-off of NLR with gram-positive and gram-negative bacteria. Gram positive bacteria have a cut off of 1.4 with a sensitivity of 81.1% and specificity of 26.3%. Gram negative bacteria have a cut off of 1.3 with a sensitivity of 80.2% and specificity of 24.8%. The purpose of this analysis is to predict what bacteria will appear when a blood culture examination is carried out so that we can provide antibiotics that might be suitable for the bacteria.

In this study, it was found that NLR was better for determining bacterial infections than procalcitonin, CRP and IT ratio but could not be used as a guide because the relationship between NLR and blood culture was not significant. This is in line with Zahorec's research, et al., Who said that NLR compared to CRP total leukocytes and neutrophils had better results for determining bacteremia. [7] The study by Holub, et al. Stated that NLR is a good parameter for predicting bacterial infections compared to WBC, CRP and the number of neutrophils. [19] Other researchers, Kristiani, et al., stated that NLR is associated with inflammation so that it can be used as a parameter to diagnose neonatal infection. [20] Research by Mentis found results of NLR and CSF neutrophil count useful for distinguishing bacterial infections from viruses. [21] Several other studies that obtained different results, namely the study by Hamiel U, et al., Obtained CRP results as the best single marker for acute infection in febrile infants, absolute neutrophil count best for invasive bacterial infections and NLR and absolute neutrophils play a role in evaluating bacterial infections.[22]

Our research has benefits and advantages because we can use NLR as a predictor of bacterial infections as an alternative examination, especially on health facilities that are limited to cheap and simple costs and we can give antibiotics immediately while waiting for the results of blood cultures so that patients can be treated more fast and on target.

The limitation of our study is that this study was conducted using a retrospective cross-sectional design, incomplete data,

medical records so that it can cause information bias so that further prospective research is needed to ascertain whether this NLR can properly be a predictor of bacterial infections so that it can be applied daily . The absence of fastidious bacteria is likely due to non-existent inspection facilities.

## 5. CONCLUSION

The ratio of neutrophil lymphocytes not yet used as a predictor of bacteremia in children.

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