

Relation of NLR Value and Mortality Rate in Neonatal Sepsis

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ABSTRACT

Introduction: Neonatal sepsis is a significant issue for newborns everywhere and causes a large amount of morbidity and mortality. Various indicators of newborn sepsis are expensive and occasionally unavailable in peripheral hospitals. The neutrophil-lymphocyte ratio (NLR), which is affordable, is a component of complete blood counts and does not call for further testing. This study intended to investigate the neutrophil-to-lymphocyte ratio (NLR) as a predictor of neonatal mortality rate in the local hospital in rural locations.

Methods: This study sampled newborns with sepsis in the perinatal room of dr. Soebandi Hospital Jember for this cross-sectional study, from January 2021 to June 2022. NLR is calculated by manually dividing the number of neutrophils by the actual number of lymphocytes. Our neutrophil and lymphocyte data were obtained from the patient's lab results. This study analyzed neonatal sepsis NLR data using Spearman analysis to find the relation between NLR value and mortality rate of neonatal sepsis.

Results: This study obtained 43 data on neonatal sepsis in the perinatology ward during this period. The data found to show that 37 neonatal sepsis survived and 6 died. The collected data analysis found that the lowest NLR neonatal sepsis is 0.4, the highest NLR neonatal sepsis is 25.6 and the mean value for NLR neonatal sepsis in perinatology was 3.88. This study found no correlation between the NLR value of the sepsis neonate and the neonatal mortality rate Sig. (2-tailed) 0.662.

Conclusion: In this study demonstrated no correlation between the NLR value of the sepsis neonates and the neonatal mortality rate.

Keywords: lymphocytes; mortality; neonatal sepsis; neutrophils

INTRODUCTION

Neonatal sepsis is a significant issue for newborns everywhere and causes a large amount of morbidity and mortality (term and preterm), particularly in underdeveloped nations ^{1,2}. Neonatal sepsis, a clinical syndrome that affects newborns in their first month of life, is characterized by blood pathogen isolation and systemic infections (bacteremia) ³. In neonatal with sepsis, clinical signs may quickly worsen from minor symptoms to mortality in less than 24 hours, having a variety of manifestations, including vomiting, respiratory distress (tachypnea), suckling refusal, diarrhea, hyperthermia or hypothermia, hyperglycemia or hypoglycemia, lethargy, jaundice, irritability, prominent fontanelle, shock, and convulsions, to disseminated intravascular coagulopathy (DIC). Early diagnosis and immediate treatment are required to enhance outcomes and prevent mortality because these symptoms can occasionally be fairly mild in the early stages of the condition ⁴. Each year, infections cause up to 1.6 million neonatal deaths, 60% of which take place in developing nations ⁵. In wealthy countries, the incidence of neonatal sepsis is 1–5 per 1000 live births; in developing countries, the rate is greater (10–50 per 1000 live births) ⁶. Various indicators of newborn sepsis have different diagnostic values,

including immature/total neutrophil (I/T) ratio, C-reactive protein (CRP), total leukocyte count, and absolute neutrophil count (ANC). A specific bacterial infection marker called procalcitonin is expensive and occasionally unavailable in hospitals, specifically in rural areas ⁷. The neutrophil-lymphocyte ratio (NLR), which is affordable, is a component of complete blood counts and does not call for further testing ⁷. There is a report that has ever described normal NLR levels in healthy newborn or pediatric populations, with an average NLR value of 0.52-0.91 ⁸. Nearly two times as many septic newborns with NLR 2.12 had positive blood culture study approach ⁹. When newborns with neonatal sepsis were first admitted, the survival rate was high, and as the length of admission grew, the cumulative death rate also rose ¹⁰. Therefore, this study wants to test whether there is an effect of NLR values on septic neonates as a preliminary predictor of neonatal sepsis mortality that can be applied in places with limited resources.

METHODS

This cross-sectional study sampled newborns with sepsis at the perinatology Soebandi General Hospital Jember between January 2021 and June 2022. Sepsis Neonate samples were taken from neonates diagnosed with sepsis by a pediatrician based on clinical symptoms and leukocytosis without bacterial culture. NLR is calculated by manually dividing the absolute number of neutrophils from lymphocytes. Neutrophil and lymphocyte data were obtained from the patient's lab results. This study obtained 43 data on neonatal sepsis in the perinatology ward during this period. Spearman analysis is used to find the relation between NLR value and mortality rate in neonatal sepsis. This research was approved by the Ethics Committee of the Faculty of Medicine, Jember University with registration number 1703/H25.1.11/KE/2023

RESULTS

This study analyzed 43 samples of neonatal sepsis in perinatology. The data found from outcome show that 37 neonatal sepsis survived and 6 died; from weight of newborn there were 21 neonates with normal birth weight, 19 neonates with low birth weight, and 3 neonates with very low birth weight; from gestational age this study found 23 neonatal with normal gestational age, and 20 neonatal with premature; and from sex this study found 25 male and 18 female neonatal (Table. 1). From the collected data analysis found that the lowest NLR neonatal sepsis is 0.4, the highest NLR neonatal sepsis is 25.6 and the mean value for NLR neonatal sepsis in perinatology was 3.88 (Figure. 1). Of all the collected neonatal sepsis NLR data along with neonatal data that survived and died were analyzed using Spearman's analysis, it was found that no correlation between the NLR value of the sepsis neonate and the neonatal mortality rate Sig. (2-tailed) 0.662.

Table 1. Characteristic of the subject

| Characteristic | n | % |
|-----------------------|----|-------|
| Gestational Age | | |
| Normal | 23 | 53,49 |
| Premature | 20 | 46,51 |
| Outcome | | |
| Die | 7 | 16,28 |
| Survived | 36 | 83,72 |
| Weight of Newborn | | |
| Normal Birth Weight | 21 | 48,84 |
| Low Birth Weight | 19 | 44,19 |
| Very Low Birth Weight | 3 | 6,97 |
| Sex | | |
| Male | 25 | 58,14 |
| Female | 18 | 41,86 |

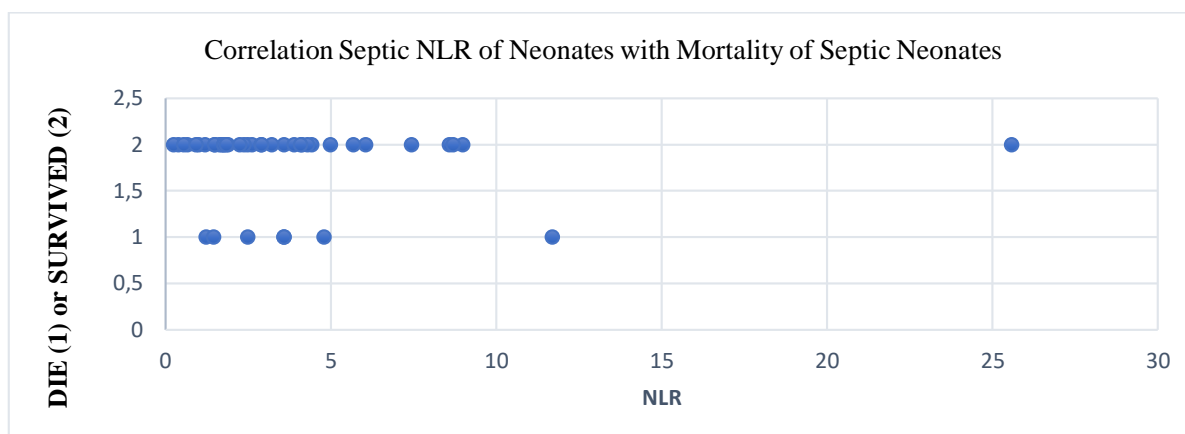


Figure 1. Data NLR Value of Septic Neonates with Mortality Rate

DISCUSSION

The results of this study found no correlation, possibly due to not taking into account other factors other than neonatal sepsis and NLR such as neonatal birth weight and gestational age, therefore further research is needed with data that takes these factors into account. Adonis, et al.¹¹ identified primiparity and very low birth weight as independent risk factors for mortality in neonatal sepsis. Xin, et al.¹² suggest that the NLR is a helpful indicator for the diagnosis of early neonatal sepsis, but it still needs to be combined with other laboratory tests and specific clinical manifestations. This study took samples of NLR at the time of arrival of patients with various conditions of neonatal sepsis with the hypothesis from various studies of NLR as a predictor of sepsis but found no correlation between the NLR value of the sepsis neonate and the neonatal mortality rate.

In neonatal with sepsis, clinical signs may quickly worsen from minor symptoms to mortality in less than 24 hours, having a variety of manifestations, including vomiting, respiratory distress (tachypnea), suckling refusal, diarrhea, hyperthermia or hypothermia, hyperglycemia or hypoglycemia, lethargy, jaundice, irritability, prominent fontanelle, shock, and convulsions, to disseminated intravascular coagulopathy (DIC). Early diagnosis and immediate treatment are required to enhance outcomes and prevent mortality because these symptoms can occasionally be fairly mild in the early stages of the condition⁴. The gold standard is blood culture; however, it can take up to 48 hours to get results. Additionally, blood cultures are insensitive and susceptible to a variety of influences, including contamination, insufficient blood volume, and maternal antibiotic therapy¹³. Neonatal sepsis is a syndrome of systemic inflammation reaction brought on by the entrance of particular or suspected microorganisms into the circulation and ongoing toxin reproduction. Along with it, organ system failure and pathological inflammation occur¹⁴. Inflammatory, regulatory, and chemokine-releasing neutrophils are a crucial component of the innate immune response in sepsis. Through the use of various antimicrobial peptides, proteases, and oxidants, neutrophils can also ingest and kill pathogens that are invading the body¹⁵. The discovery of neutrophil extracellular traps (NETs) in recent years has revealed a new resource in the immune system's inventory against pathogen infection¹⁶. On the other hand, excessive inflammatory and tissue damage are also a result of the formation of NET and increased inflammatory cytokine production.¹⁷ However, lymphocytes participate in the immune response to bacterial and viral infections. Antigen-presenting cells identified microbial antigens during pathogen infection and presented them to T cells. In the following stage, CD4⁺ T cells release cytokines that benefit phagocytotic cells in eliminating intracellular microorganisms¹⁸. However, apoptosis caused by

sepsis causes a considerable decrease in lymphocyte numbers. This decrease in immune function is expected to have a significant impact on the immunosuppressive condition that makes patients vulnerable to acquiring new infections.¹⁹ Leukocyte counts, both total and differential, were as affordable, easily accessible biomarkers of the inflammatory response. Neutrophil and lymphocyte numbers are reflected in NLR. Recently, the NLR has drawn a lot of interest as a potential risk factor that could aid in sepsis diagnosis. Sepsis patients may have a greater NLR level because the pathogenic microorganisms that cause the condition could raise neutrophil levels while lowering lymphocyte counts²⁰. NLR can be used as a predictive of neonatal sepsis in resource limited settings. A value of more than 2.25 of neutrophil to lymphocyte ratio is highly predictive of neonatal sepsis.²¹ Meta-analyses and several researches have shown that NLR may be a useful sepsis predictor and that patients with greater NLR may have worse outcomes. The research conducted by Liu et al included that Adult sepsis patients' NLR assessed at entry was a reliable predictor of in-hospital mortality²². However, the majority of studies investigating the link between sepsis and NLR have been undertaken on adults. From a study that stated that a high NLR value gave a poor outcome, this study tried to prove the relationship between NLR and the mortality rate of sepsis neonates. When newborns with neonatal sepsis were first admitted, the survival rate was high, and as the length of admission grew, the cumulative death rate also risen¹⁰.

This study has several limitations. First, this study is cross-sectional and single-center, which means it is unable to predict the future and may be biased. Second, clinical signs rather than a positive blood culture were used to identify newborn sepsis. Third, NLR was never measured more than once and do not pay attention to other factors such as neonatal birth weight and gestational age. It would be helpful to further investigate the dynamic link between NLR and the change in newborn sepsis using serial measures, which would give additional details on their relationship.

CONCLUSION

This study demonstrated no correlation between the NLR value of the sepsis neonates and the neonatal mortality rate.

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For this investigation, no funding was provided.

CONFLICT OF INTEREST

The authors reported no potential competing interests.

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