

Relationship Between Albumin Levels and Leukocyte Counts in The Incident of Neonatal Sepsis

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ABSTRACT

Background: Sepsis can affect all age, but is most common in young infants and neonates. Young infants and neonates are more susceptible to infection because their immune systems are immature, unable to localize infections, and lack the IgM needed to protect the body against bacterial infections. When experiencing neonatal sepsis, there is often an increase in leukocytes in response to infection and inflammation, where inflammation can also cause a decrease in albumin in the blood. Objective: This study aims to analyze the relationship between albumin levels and leukocyte counts in the incidence of neonatal sepsis. Methods: The research method used analytic correlation with a cross sectional approach. A sample of 31 patients with neonatal sepsis who were treated at Waluyo Jati hospital, Probolinggo Regency in December 2022 - April 2023 were sampled using saturation sampling method. Results: The results of the study on neonatal sepsis based on laboratory examinations mostly occurred in conditions of leukocytosis (45.2%) and hypoalbuminemia (77.4%), while the results of the study based on Pearson correlation test analysis obtained a significant value (p) of 0.737 ($\alpha=0.05$). Conclusion: there is no relationship between albumin levels and leukocyte counts in neonatal sepsis.

INTRODUCTION

Sepsis is a life-threatening condition in which the body's organs do not function normally, caused by the body's inability to respond to infection (Irvan, 2018). Sepsis can affect all age, but is most common in young infants and neonates. Young infants and neonates are more susceptible to infection because their immune systems are immature, unable to localize infections, and lack the IgM needed to protect the body against bacterial infections (Kyle & Carman, 2013).

According to UNICEF (2022), around 670.000 newborns die from sepsis each year. Data from WHO (2018) states that neonatal sepsis accounts for 15% of neonatal mortality globally. Data from the Probolinggo Regency Health Office in 2020, that the direct cause of infant mortality is sepsis, which is 1.36% (Dinas Kesehatan, 2021). Information obtained from RSUD Waluyo Jati, Probolinggo Regency in 2021, from 711 neonate patients there were 72 (10.13%) incidents of neonatal sepsis, 50% of them died with a diagnosis of sepsis.

Sepsis can become septic shock when there is an exaggerated systemic response to infection, caused by bacteria (most commonly), fungi, parasites or viruses, low blood flow, resulting in hypotension and multi-system organ failure (Kyle & Carman, 2013). An increase in leukocytes (leukocytosis) is common during sepsis, followed by a decrease in leukocytes (leukopenia) as the patient's prognosis worsens due to bone marrow suppression (Fitriani et al., 2019). In most cases, leukocytosis (neutrophilia) is caused by infection, especially infection with *Streptococcus pneumoniae* and *Staphylococci*, while some types are caused by inflammation, acute stress, tissue damage, or necrosis (Kiswari, 2014). Leukocyte count is an examination to determine whether there is an increase or decrease in the number of leukocytes, which is a sign of infection or to see the progression of the disease (Nugraha, 2017).

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Neonatal sepsis is also one of the risk factors for decreased albumin levels in neonates (Darmawan, 2021). In sepsis, macrophages release proinflammatory cytokines with their mediators, then several types of cells are activated, causing endothelial cells to be damaged. Damage to endothelial cells will stimulate leukocyte migration and the formation of micro thrombin, causing damage to organs. The occurrence of inflammation in endothelial cells results in vasodilation of smooth muscle, and can increase vascular permeability and cause capillary leakage. This leakage can lead to the diffusion of albumin from the inside to the outside of the vasculature, which can lead to a decrease in albumin in the blood (Wowor et al., 2013). Albumin, a single protein consisting of 610 or more amino acids (Nugraha, 2017), is the most abundant protein in the human body (55-60% of all plasma proteins). Serum albumin levels are determined by a function of the rate of albumin synthesis and degradation, and the distribution between vascular compartments (intravascular and extravascular). Low albumin (hypoalbuminemia) can slow down the body's immune response to infection (Susanti & Firdayanti, 2021).

Based on the results of research by Wowor et al. (2013), a description of the results of albumin examination in 38 patients, of 16 neonatal sepsis patients there were 75% experiencing hypoalbuminemia and 25% with normal albumin levels, 22 non-sepsis patients 22.7% experienced hypoalbuminemia and 77.3% with normal albumin levels. In the research journal Lorencia et al. (2019), found the results of 76.1% hypoalbuminemia and 23.9% with normal albumin levels in neonatal sepsis patients. Research by Güneş et al., (2021), obtained albumin results of 2.5-3.1 mg/dL in Gram Negative bacterial sepsis neonate patients, and albumin results of 2.8-3.1 mg/dL in Gram Positive bacterial sepsis neonate patients. Leukocyte research on neonatal sepsis was conducted by Yustika et al. (2020), namely 98.70% of neonates had leukocytosis and 1.30% did not have leukocytosis. Previous research related to the number of leukocytes in infants suspected of sepsis by Romadhoni & Sinaga, (2022), was also obtained with the results of 3% low leukocyte count, 19% high leukocyte count, and 78% normal leukocyte count. Likewise, the results of research by Siahaan et al. (2021), on neonatal sepsis at RSUD Dr. Pirngadi Medan, namely 76.4% of leukocytes increased, 22.2% of normal leukocytes, and 1.4% of leukocytes decreased. The same research was also related to albumin and leukocytes in relation to early predictive factors for sepsis conducted by Zharfan et al. (2019) at Dr. Soetomo Surabaya Hospital, namely the results of albumin levels <3.5 g/dL ($p: 0.029$) and leukocyte counts $> 12,000/\mu\text{L}$ ($p: 0.049$), with the conclusion that low albumin levels and high leukocytes are considered independent predictors of mortality in adult sepsis patients.

The results of a preliminary survey in October 2022 at RSUD Waluyo Jati, Probolinggo Regency, there were 6 patients with a diagnosis of neonatal sepsis, 50% of whom experienced death, 83% experienced leukocytosis, and 50% experienced hypoalbuminemia.

Based on the background description and preliminary survey, the author considers it important to examine the correlation or relationship between albumin levels and leukocyte counts in the incidence of neonatal sepsis at RSUD Waluyo Jati, Probolinggo Regency. Another consideration is that there are still cases of sepsis in RSUD Waluyo Jati Probolinggo Regency, especially in neonates, and this research has never been done in RSUD Waluyo Jati Probolinggo Regency or even in Indonesia before.

This study aims to analyze the relationship between albumin levels and leukocyte counts in the incidence of neonatal sepsis.

MATERIALS/METHOD

This study used analytic correlation research with a cross sectional approach. The sample amounted to 31 neonate patients (age ≤ 30 days) with a diagnosis of neonatal sepsis who were treated in the NICU and Neonatology room of RSUD Waluyo Jati Probolinggo Regency in December 2022 - April 2023, which was collected by saturation sampling method.

The research data was in the form of primary data, which was obtained from the examination of blood specimens of neonatal sepsis patients who were examined for leukocyte counts using the automatic haematology analyzer Sysmex XN-L 350 and blood albumin levels using the clinical chemistry analyzer Cobas Integra 400 Plus. The data obtained were analyzed using the Pearson correlation parametric test ($\alpha: 0.05$).

This study has also met the research rules based on the ethical feasibility certificate No. EA/1535/KEPK-Poltekkes_Sby/V/2023 issued by the Health Research Ethics Commission of the Surabaya Ministry of Health Polytechnic on March 25, 2023.

RESULTS AND DISCUSSION

The results of research conducted in December 2022 - April 2023 obtained a sample of 31 neonatal sepsis patients who were treated in the Neonatal Intensive Care Unit (NICU) and Neonatology room of RSUD Waluyo Jati, Probolinggo Regency. The research data are presented based on the characteristics of the respondents in table 1.

Table 1. Frequency Distribution of Respondent Characteristics

Respondent Characteristics	Frequency	Percentage (%)
Gender (n=31)		
Male	15	48,4
Female	16	51,6
Age of Neonates (n=31)		
≤ 7 days	14	45,2
> 7 days	17	54,8
Albumin examination (n=31)		
Hipoalbuminemia	24	77,4
Albumin Normal	7	22,6
Leukocyte examination (n=31)		
Leukopenia	6	19,3
Normal leukocyte	11	35,5
Leukocytosis	14	45,2

Sources: Primary Data

Based on table 1, the majority of respondents were female, as many as 16 out of 31 patients (51.5%), respondents at the age of neonate > 7 days, as many as 17 out of 31 patients (54.8%). While based on the results of the albumin examination, the majority of respondents were in the hypoalbuminemia category, namely 24 of 31 respondents (77.4%) and the most respondents in the results of the leukocyte examination were leukocytosis, namely 14 of 31 respondents (45.2%).

Based on the age distribution of neonates, there were more patients with age > 7 days (54.8%) than those with age ≤ 7 days (45.2%). There are several factors in infants that affect the occurrence of sepsis in infants > 7 days of age, namely frequent treatment in the neonatal intensive care unit, premature infants who experience a long treatment period, intravenous nutrition that lasts a long time, infections originating from treatment equipment, infections that occur in the hospital or occur crosswise from other patients or medical personnel (nurses), which include nosocomial infections or horizontal transmission infections, commonly referred to as Late-Onset Neonatal Sepsis (LOS) (Rahmawati & Rahman, 2018). According to Sisay et al. (2022), the duration of hospitalization was found to be a predictor of the incidence of neonatal sepsis, prolonged hospitalization can increase the likelihood of developing new infections. This study is in line with research conducted by Rahmawati dan Rahman (2018) at Dr. M. Djamil Hospital in Padang, with the results of 53.1% LOS. Likewise with the research of Novita et al. (2015), where the incidence of LOS was the highest incidence, namely 80%.

Frequency distribution of infant age ≤ 7 days was 45.2%. In neonatal sepsis patients with age ≤ 7 days, infection can occur due to infections and diseases experienced by the mother during pregnancy and during labor, or vertical transmission infections, these infections are commonly referred to as Early Onset Neonatal Sepsis (EOS). The risk of EOS can occur from maternal factors, which occurs in the condition of the labor process of the birth of a premature baby, labor with action, affected by chorioamnionitis, rupture of membranes for more than 18 hours, urinary tract infection (UTI), maternal fever with a temperature of more than 38.4° C, socioeconomic factors and maternal nutrition. While the risk of infant factors can occur in conditions of asphyxia, low birth weight (LBW), babies born prematurely, congenital abnormalities and invasive procedures (Rahmawati & Rahman, 2018). Different research results were obtained by Yustika et al. (2020), with the incidence of EOS as much as 80%. Likewise with the research of Prawesti et al. (2018) with the results of the incidence of EOS as much as 59.78%.

Based on the distribution of leukocyte examination, neonatorum sepsis patients with leukocytosis category were more (48.4%) than those with normal leukocytes (41.9%) and leukopenia (9.7%). This is in line with research conducted by Siahaan et al. (2021) on neonatal sepsis at RSUD Dr. Pirngadi Medan, namely 76.4% of leukocytes increased, 22.2% of normal leukocytes, and 1.4% of leukocytes decreased. The same thing was also obtained from the research of Yustika et al. (2020), namely 76 (98.7%) neonates diagnosed with neonatal sepsis had leukocytosis and the rest were not leukocytosis.

In sepsis infants, infection occurs due to viruses, bacteria, or fungi that take place in the blood, which causes an inflammatory response. The presence of an inflammatory process in the body is characterized by an increase in white blood cells (leukocytosis), which is a response to inflammation or infection in the body (Yustika et al., 2020). In patients with neonatal sepsis, leukocytosis or leukopenia (decreased white blood cells)

may occur. Leukopenia can also occur due to an increased need for leukocytes, decreased bone marrow production, viral infection and decreased lymphoid production (Siahaan et al., 2021).

Based on the distribution of albumin examination, the hypoalbuminemia category in neonatal sepsis patients, which is 74.2%, is more than the normal albumin category (25.8%). This is in line with research conducted by Wowor et al. (2013) at Prof. Dr. R. D. Kandou Manado Hospital, with a description of the results of albumin examination of 16 neonatorium sepsis patients, 75% had hypoalbuminemia and 25% with normal albumin levels, and showed there was a relationship between albumin levels and neonatorium sepsis (p: 0.001). Likewise, research conducted by Lorencia et al. (2019) on neonatal sepsis patients, with the results of 76.1% hypoalbuminemia and 23.9% with normal albumin levels.

During sepsis, the transfer of albumin from intravascular to extravascular increases, resulting in altered rates of protein synthesis and degradation, which will slowly decrease albumin levels and remain decreased until the healing stage of the disease. Sepsis also results in changes in albumin formation. If there is an acute response to inflammation, CRP will increase, IL-6 and TNF- α , which play a role in reducing albumin gene transcription, will be released, resulting in decreased albumin synthesis (Wowor et al., 2013).

Table 2. Data Analysis

Variable	Kadar	P-value
Leukocyte (*10 ³ /mm ³)	18.7 \pm 10.7	0.737
Albumin (g/dL)	2.9 \pm 0.8	

Source: Primary Data

Based on data analysis (table 2), the pearson correlation parametric correlation test results obtained a significant value (p) of 0.737. this value is greater than $\alpha = 0.05$, which means that there is no relationship between albumin levels and leukocyte counts in neonatal sepsis patients.

An increased leukocyte count (leukocytosis) often occurs at the beginning of sepsis and will then decrease (leukopenia) due to continuous bone marrow suppression as the patient's condition worsens (Fitriani et al., 2019). According to Yasa (2014), that one third of infants infected with bacteria (bacteremia) have normal leukocyte values, especially in the first 48 hours. While serum albumin levels decrease in the acute phase of infection (Yang et al., 2016). When viruses, bacteria, fungi and bacterial toxins enter the body, they are responded to by the innate immune system. Innate immunity is a humoral and cellular mechanism that acts automatically against attacks and causes inflammation (Chen & Shi, 2019). Inflammatory factors play an important role in the pathophysiology of neonatal sepsis (Alifia Kurnia Wulansari, 2017). The intensity of the inflammatory response to infection in critical patients is associated with low albumin levels (Yang et al., 2016). The continuous inflammatory response can result in albumin synthesis being disrupted for a long time. Increased vascular permeability, increased albumin degradation, decreased albumin synthesis and decreased albumin gene transcription also affect albumin levels in neonatal sepsis (Wowor et al., 2013). This study is in line with previous research conducted by Yang et al. (2016), which states that there is no relationship between albumin levels and leukocyte counts in infected infants (neonatal sepsis), with a significance (p) of 0.236.

CONCLUSIONS

Based on the results of the study, it can be concluded that there is no relationship between albumin levels and the number of leukocytes in the incidence of neonatal sepsis.

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