Correlation between nutritional status, leukocyte levels, and neutrophil-lymphocyte ratio to the incidence of respiratory failure in children under five years of age with pneumonia at Abdoel Wahab Sjahranie Hospital, Samarinda

Ainurfaiz Fiqridiyanto[1], Eva Rachmi[2], Annisa Muhyi[3*]

[1]Medical Studies Department, Faculty of Medicine, Universitas Mulawarman;
[2]Department of Physiology, Faculty of Medicine, Universitas Mulawarman;
[3]Department of Child Health, Faculty of Medicine, Universitas Mulawarman.

*Corresponding to:
Annisa Muhyi;
Department of Child Health, Faculty of Medicine, Universitas Mulawarman;
annisa.muhyi@gmail.com

ABSTRACT

Background: The most common infectious infection-related fatality in children under five worldwide is pneumonia, an acute infection of the lung parenchyma. Hypoxemia can induce respiratory failure and pneumonia-related deaths. For children with pneumonia under five years old, several possible predictors, including nutritional status, leukocyte counts, and the neutrophil-lymphocyte ratio (RNL), can be used to forecast respiratory failure. Because these three criteria are common tests that can be employed in basic healthcare institutions, they are promising predictors. This study aims to determine the relationship between nutritional status, leukocyte levels, and RNL on the incidence of respiratory failure in children under five years of age with pneumonia at Abdul Wahab Sjahranie Hospital, Samarinda.

Methods: The research design is case-control. All children with pneumonia under five years old receiving treatment at Abdul Wahab Sjahranie Hospital Samarinda from January to December 2022 made up the study population. Purposive sampling was used to carry out the sampling. The patient's medical record provides the information. Independent T-test and Chi-square test were used to assess the data. Forty patients in all; 20 were case samples, and 20 were control samples.

Results: The results showed that the incidence of respiratory failure was related to nutritional status (OR=0.07; p=0.000; 95% CI 0.01 – 0.35), leukocyte levels (OR=35.28; p=0.000; 95% CI 3.86 – 321.98), and neutrophil-lymphocyte ratio (p=0.036).

Conclusion: Malnutrition and poor nutritional status, high leukocyte levels, and high RNL have the potential to be predictors of respiratory failure in toddlers with pneumonia.

Keywords: leukocytes, neutrophil-lymphocyte ratio, nutritional status, pneumonia, respiratory failure.
Cite This Article: Fiqridiyanto, A., Rachmi, E., Muhyi, A. 2024. Correlation between nutritional status, leukocyte levels, and neutrophil-lymphocyte ratio to the incidence of respiratory failure in children under five years of age with pneumonia at Abdoel Wahab Sjahranie Hospital, Samarinda. *Pediatrics Sciences Journal* 5(1): 1-6. DOI: 10.51559/pedscij.v5i1.63

INTRODUCTION

The most common cause of infectious disease-related mortality in children under five worldwide is pneumonia, an acute respiratory infection that affects the lung parenchyma.[1] In 2020, in the world, there are more than 1,400 cases of pneumonia per 100,000 children, or there is 1 case per 71 children each year.[2]

Numerous studies show that hypoxemia is the primary cause of pneumonia-related deaths. If hypoxemia develops, respiratory failure may result.[3] The majority of hypoxemia-afflicted children under five years old have respiratory failure. The primary cause of this can be an imbalance between perfusion and breathing brought on by untreated hypoxemia.[4] Therefore, it is crucial to identify the predictor of respiratory failure that develops in children with pneumonia under five years old. When a child under five has pneumonia, several possible predictors can be used to determine the likelihood of respiratory failure and death. According to recent studies, in children under five who have pneumonia, nutritional status, leukocyte count, anemia, and severe sepsis can be utilized as predictors of respiratory failure and death.[5,6]

In children under five who have pneumonia, the neutrophil-lymphocyte ratio (RNL) and leukocyte nutritional status are predictive factors of respiratory failure that have not received much attention. Previous research on nutritional status revealed a connection between underweight and the prevalence of respiratory failure in children with pneumonia under the age of five.[6] The number of leukocytes can be used to predict pneumonia severity, but it is a weak predictor.[7] This is different from other studies, which show leukopenia is associated with mortality in pneumonia.[5]

Recent study have shown that the RNL can be used as a determinant of the prognosis of pneumonia patients.[8] Examination at initial hospital admission showed differences in RNL in the outcomes of children with pneumonia. The average RNL was higher in patients with poor outcomes, but no significant differences

were found.[9] These three factors are also promising predictors because they are routine examinations that allow them to be used in primary healthcare facilities.

Based on this description, pneumonia is a health problem that needs attention in Samarinda. To increase the effectiveness of pneumonia treatment, it is necessary to explore predictors of pneumonia respiratory failure, such as nutritional status, leukocytes, and RNL in children under five years of age with pneumonia in Samarinda. Abdul Wahab Sjahranie Hospital was chosen as the research location because it is a referral hospital that treats children under five years of age with pneumonia in Samarinda. Therefore researchers are interested in examining the relationship between nutritional status, leukocyte count, and RNL on the incidence of respiratory failure in children under five years of age with pneumonia at Abdul Wahab Sjahranie Hospital, Samarinda.

METHODS

This study, conducted at Abdoel Wahab Sjahranie Hospital in Samarinda, uses an observational analytic approach with a case-control study design to investigate the association between nutritional status, leukocyte count, and red blood cell count (RNL) and the incidence of respiratory failure in children with pneumonia under the age of five. This study had four factors: respiratory failure was the dependent variable, and nutritional status, leukocyte count, and NLR were the independent variables. Purposive sampling was the approach used for the sampling process. From January 2022 to December 2022, medical records at Abdul Wahab Sjahranie Hospital Samarinda provided the research

data. The inclusion criteria were: 1) All children under five years of age with pneumonia diagnosed in the medical record. 2) Children under five years of age with pneumonia aged ≥ 12 months – 59 months. 3) Infants with pneumonia with complete data such as weight, height/length, leukocyte levels, neutrophil, and lymphocyte counts. Exclusion criteria were: 1) Infants with pneumonia who suffer from immune system disorders, such as HIV/AIDS or malignancy. 2) Children under five years of age with pneumonia who suffer from heart defects, cystic fibrosis, pulmonary tuberculosis, and asthma. 3) Children under five

years of age with pneumonia who have incomplete medical record data. Bivariate analysis using Chi-square statistical test and Independent T-test. The results are significant if p-value <0.05 with all data analyzed using SPSS 26.0 software

RESULT

The sample of this study consisted of 2 groups, namely children under five years of age with pneumonia who experienced respiratory failure as the case group and children under five years of age with pneumonia who did not have respiratory failure as the control group. The number of children under five years of age with

Table 1. Characteristics of respondent

Characteristic	Total (n)	Percentage (%)
Age (years)		
1	18	45
2	14	35
3	6	15
4	2	5
Gender		
Male	17	42.5
Female	23	57.5
Outcome status		
Improvement	22	55
Death	18	45
Incidence of Respiratory Failure		
Respiratory Failure	20	50
Without Respiratory Failure	20	50
Nutritional Status		
Severely Wasted	4	10
Wasted	13	32.5
Normal	20	50
Overweight	3	7.5
Leukocytes Count		
Low	1	2.5
Normal	14	35
High	25	62.5
Total	40	100

Table 2. Analysis of the correlation between nutritional status and leukocyte count with incidence of respiratory failure

Variable	Incidence of Respiratory Failure				Total n	P-value	Odd Ratio (95% CI)
	Respiratory Failure		Without Respiratory Failure				
	n	%	n	%			
Nutritional Status							
Severe Wasted and Wasted	14	35	3	7.5	17	0.00	0.07 (0.01-0.35)
Normal and Overweight	6	15	17	42.5	23		
Leukocytes Count							
Low and Normal	1	2.5	14	35	15	0.00	35.28 (3.86 –321.98)
High	19	47.5	6	15	25		
Total	20	50	20	50	40		

Table 3. Analysis of the correlation between neutrophil-limphocyte ratio with incidence of respiratory failure

	Neutrophil-Lymphocyte Ratio			P-value
	N	Mean	Std. Deviation	
Respiratory Failure	20	4.76	2.45	0.036
Without Respiratory Failure	20	1.78	1.11	

pneumonia who experienced respiratory failure in the period January 2022 - December 2022 was 34 patients. Several patients were excluded, namely, 10 patients aged less than 1 year and 4 patients with co-morbidities, congenital heart disease (2 patients), asthma (1 patient), and tuberculosis (1 patient), so the final number of cases was 20 patients. The number of children under five years of age with pneumonia who did not experience respiratory failure for the period January 2022 - December 2022 was 99 patients, which were then randomly taken as many as 20 patients as the control group.

Table 1 Shows the age of majority is 1 year old patient with 18 patients (45%). Most respondents were female, with 23 patients (57.5%). Most toddler pneumonia patients undergoing hospitalization had a living status when they left the hospital, namely 22 respondents (55%). The highest distribution was found in respondents with normal nutritional status, namely 20 respondents (50%). The highest distribution was found in respondents with high leukocytes, namely 25 respondents (62.5%)

Table 2 presents the results of the Chi-square test used to analyze the relationship between nutritional status and the incidence of respiratory failure. The test yielded a p-value of less than 0.05, indicating a relationship between the two variables. The odds ratio in this study was 0.07 (95% CI 0.01 – 0.35), indicating a negative correlation between the occurrence of respiratory failure and nutritional status. Analysis of the relationship between leukocyte levels and the incidence of respiratory failure was carried out using the Chi-square test, which showed a p-value <0.05, so it can be concluded that there is a relationship between leukocyte levels and the incidence of respiratory failure. In this study, the Odds ratio was 35.28 (3.86 – 321.98), which means that leukocyte levels had a positive relationship to the incidence of

respiratory failure. High leukocyte levels have a risk of 35.28 times experiencing respiratory failure.

There is a correlation between RNL and the incidence of respiratory failure, according to Table 3's analysis of the relationship between the neutrophil-lymphocyte ratio and the incidence of respiratory failure using an independent T-test, which revealed a significance value of 0.036 (p-value < 0.05).

DISCUSSION

The study's distribution pattern for age, sex, nutritional status, leukocyte counts, and RNL was comparable to numerous other Indonesian locations. According to the study's findings, the bulk of respondents—up to 18 respondents, or 45%—are only one year old. The findings of this investigation are consistent with Lailla's 2020 study carried out at the Zainoel Abidin Hospital in Banda Aceh, which found that children under five in the age range of one to less than two years get pneumonia at a rate of 33.7%.[10]

The study's findings indicated that 23 (57.5%) of the patients had the highest distribution of sex. The findings of this investigation are consistent with Hasanah's research from 2021, which reports that 34 children under the age of five (51.5%) are female and account for the bulk of pneumonia cases in children under five.[11] The findings of this study contradict those of Wasita's 2019 study, which was carried out at Wangaya Hospital in Denpasar and revealed that 22 patients, or 55% of the total, were male and suffered from toddler pneumonia.[12]

The results of this study showed that the highest distribution of nutritional status in children under five years of age with pneumonia was normal nutritional status, namely 20 respondents (50%). Normal nutritional status also dominates 91% of pneumonia cases in the hospital. Dr. M. Djamil Padang, 70% of cases in

Wangaya-Denpasar Hospital, and 60% of cases in Cibodasari Health Center, Tangerang.[11,13,14]

The results of this study indicate that the highest distribution of leukocyte levels was found in respondents with high leukocytes, namely 25 respondents (62.5%). High leukocyte levels also dominate cases of toddler pneumonia, with an average of 12.850 /dL in Wangaya-Denpasar Hospital, and 14.720 /dL in children with very severe pneumonia and 12.970 /dL in severe pneumonia in Sanglah Hospital, Denpasar.[12,15] The results of this study indicate that the average sample has an RNL of 3.2. This study's results align with Katleya's research in 2015 with an average RNL of 3.42 in pneumonia children with poor outcomes.[9]

This study found a significant connection (p = 0.000, p <0.05) between nutritional status and the incidence of respiratory failure in children under five years old who have pneumonia. This study supports the findings of Nurnajiah's (2016) investigation, which similarly showed a p-value of 0.001 correlation between the incidence of pneumonia in children under five years old at Dr. M. Djamil Padang Hospital and nutritional status.[13] Respiratory failure affected 10 respondents or 76.9% of the study's total malnourished respondents. Similar findings were found in a 2016 study conducted by Shaima in Dhaka, Bangladesh, which indicated a correlation between underweight and the prevalence of respiratory failure in children with pneumonia under five years old.[6]

The odds ratio in this study for the association between nutritional status and the incidence of respiratory failure in children under five who had pneumonia was 0.07 (95% CI 0.01 – 0.35), indicating that children with moderate and underweight nutritional status are protected against respiratory failure, respectively. The findings of this study are consistent with that of Kirolos' study from 2021, which found that, for extremely thin respondents, the OR of pneumonia-related death was 5.3 (95% CI 3.9 - 7.4) prior to 2000 and remained high at 4.1 (95% CI 3.0 - 6.0) following that year. Within the range of 19.6% to 66.3%, the prevalence of wasting children hospitalized for

pneumonia varied in that research, with a median value of 40.2%.[16]

Malnutrition continues to be a serious issue for world health. Low protein energy intake causes underweight, wasting, and stunting.[17] Protein deficiency will cause atrophy in the thymus, resulting in decreased T-cell production. This results in decreased immunity so that infections occur more easily. Malnutrition also results in decreased IgA secretion. IgA functions to protect the respiratory tract from infection by pathogens. Decreased IgA can exacerbate the degree of pneumonia infection.[18]

Children with poor nutritional status tend to experience vitamin A deficiency. Vitamin A has an important role in the maintenance of epithelial cells. The role of vitamin A in the non-specific immune system is seen in the integrity of the epithelial mucosa. The study's results revealed that children deficient in vitamin A were at risk of suffering from respiratory tract disease and experiencing severity.[19]

In impoverished nations, stunting affects nearly one-third of children and increases the number of fatalities from pneumonia and diarrhea. Malnourished children who die from illness may have weakened immune memories against common infections. Malnutrition affects innate and adaptive immunity, resulting in decreased complement proteins, fewer circulating dendritic cells, decreased granulocyte microbicidal activity, and impaired skin and intestinal epithelial barrier function. Defects in adaptive immune function in children with C include lower levels of soluble IgA in tears and saliva, lymphocyte hyporesponsiveness to phytohemagglutinin, atrophy of lymphoid organs, a decreased delayed-type hypersensitivity response, fewer B cells in circulation, and a shift in cytokines from Th1- to Th2-associated. Such immunoparalysis can make malnutrition-related immunodeficiency worse. After acute systemic exposure to proinflammatory stimuli, the condition known as immunoparalysis is characterized by immunosuppression and is linked to elevated rates of subsequent infections, including sepsis.[20]

This study found a significant connection (p = 0.000, p <0.05) between leukocyte counts and the incidence of respiratory failure in children under five years old who had pneumonia. The findings of this study indicate a positive correlation between leukocyte counts and the occurrence of respiratory failure, with an odds ratio of 35.28 (3.86 – 321.98). This study contradicts studies published in 2016 by Araya, who found a link between leukopenia and pneumonia patient death.[21]

Leukocyte levels will increase due to inflammation of the lung parenchyma. Infection and damage to lung parenchymal tissue can cause stimulation of the immune system in circulation. Leukocytosis is a systemic inflammatory response to infection due to the stimulation of proinflammatory cytokines and the presence of endotoxinemia; therefore, the number of leukocytes will align with the release of proinflammatory cytokines. Lung parenchymal infection causes the release of proinflammatory cytokines such as IL-1, IL-6, and tumor necrotizing factor-α. The release of these cytokines is in accordance with the damage to the lung parenchyma that occurs so that it will correlate with the severity of the pneumonia.[22]

This study is not in line with Atwa's study in 2015, which was conducted at a tertiary hospital in Egypt and showed leukopenia was associated with mortality in pneumonia. In that study, leukopenia was considered a predictor of the course of fatal pneumonia. Leukopenia in pneumonia was associated with sepsis (P: 0.001; OR 1.931; 95%CI 1.431–3.215) and death (P: 0.01; OR 2.119; 95%CI 1.322–3.102).[5]

Leukocytosis can occur depending on the examination time since the onset of pneumonia. Initially, the body responds by releasing excessive amounts of leukocytes, but if therapy is inadequate or the progression of pneumonia increases, the number of leukocytes will decrease.[23] This is thought to be why there are different theories regarding leukocytosis and leukopenia regarding the incidence of respiratory failure in pneumonia.

In this study, RNL and the incidence of respiratory failure in children under five years of age with pneumonia proved to have a significant relationship, namely p = 0.036 (p <0.05). This study is in line with a study conducted by Jager in 2012, which stated that patients who had a poor prognosis or who entered the Intensive Care Unit had an RNL value with a cut-off≥10.0.[22] The study conducted by Katleya in 2016 also stated that there was a difference in RNL with outcomes of children with pneumonia. A higher mean RNL was found in patients with poor outcomes.[9]

Circulating leukocytes undergo a drop in lymphocyte count and an increase in neutrophils during different stages of the physiological stress response. Demargination of neutrophils, postponing neutrophil death, and growth factors stimulating stem cells are the causes of neutrophilia. The three main mechanisms of lymphocytopenia are lymphocyte redistribution, rapid apoptosis, and lymphocyte margination. Patients with community-acquired pneumonia (CAP) also have lymphocytopenia. There is a decrease in peripheral blood T cell counts in CAP patients.[22]

The inflammatory process that appears as the body's response in recognizing and fighting against incoming pathogens, especially in cases of pneumonia, is an important clinical marker. RNL is a laboratory examination item obtained from the results of comparing the absolute neutrophil count with the absolute lymphocyte count, and this parameter can be used as a marker of inflammation. This examination has been widely used in addition to assisting in diagnosis, this examination is also widely used to predict the prognosis and severity of pneumonia patients better than other inflammatory markers.[22]

Through their ability to chemotact, phagocytose, emit reactive oxygen species (ROS) granule proteins, produce and release cytokines, and other mechanisms, neutrophils are the first line of defense against pathogens. In order to exert their effects, neutrophils first activate and prime other immune cells to secrete a range of cytokines and chemokines that are proinflammatory and immunomodulatory. Moreover, neutrophils are the primary effector cells in the systemic inflammatory response (SIRS) and are crucial for adaptive

immunity. SIRS is linked to the innate response's inhibition of neutrophil death. One of the most frequent causes of sepsis, which can result in patient death and morbidity, is pneumonia.[24,25]

The degree of illness and the rate at which lung function is declining correlate with the quantity of neutrophils seen in sputum and bronchial biopsy specimens. Serine proteases secreted by neutrophils cause damage to the alveoli. Since neutrophils are efficient inducers of mucus secretion, which may result in airflow restriction, airway neutrophilia is linked to mucus hypersecretion.[26]

Tissue invasion by neutrophils frequently results in harm to host cells. In numerous clinical situations, including acute lung injury, excessive neutrophil infiltration is linked to tissue damage. The generation and release of cytotoxic granule proteins, ROS (reactive oxygen species), and neutrophil extracellular traps (NET) can all result in this additional harm. NETs, DNA constructs accompanied by nuclear, granule, and cytosolic proteins, can capture bacteria, viruses, and fungi, among other microbes. An immune response out of balance may cause NETs to release irregularly, worsening inflammation and injury to host tissue while outperforming their antibacterial action. As a result, NETs are known to cause cytotoxicity in a variety of tissues and contribute to several disorders.[27]

For individuals with pneumonia, lymphocytopenia and death are substantially correlated. According to several studies, people who experience a viral infection and are seriously and critically ill have lower lymphocyte counts than patients who are well, have minimal symptoms, or have recovered.[28]

The intensity of the viral infection is correlated with the lymphocyte count. This happens due to modifications to the lympho-hematopoietic system, including hemophagocytosis, apoptosis brought on by viruses, and depletion of lymphocytes. Since T cells are essential for virus-specific adaptive immunological responses, lymphocytopenia may seriously impair the body's defenses against infection. TNF-α can cause T cells to undergo apoptosis and is also a proinflammatory cytokine. Reduced lymphocyte proliferation and differentiation leads to lymphocytopenia, mediated by IL-6, IL-10, TNF-α, IFN, and other cytokines and chemokines.[28]

The limitation of this research is that several factors besides those listed in the study's variables such as immunization status and environmental, were not examined. Those factors could theoretically affect respiratory failure in children under five years of age with pneumonia. Immunization status and environmental factors cannot be controlled because they are not listed in the medical record, which can lead to a risk of bias.

CONCLUSION

It was concluded that nutritional status, leukocyte levels, and RNL were associated with the incidence of respiratory failure in children under five years of age with pneumonia at Abdul Wahab Sjahranie Samarinda Hospital.

ETHICAL CLEARANCE

This research has passed the ethical feasibility test by the health research ethics committee of Abdul Wahab Sjahranie Samarinda Hospital.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest in the publication of this article.

FUNDING

This research has no source of funding, grants, or third-party support.

AUTHOR CONTRIBUTIONS

All authors contributed to all processes in this research in the form of concept, design, monitoring, data collection and analysis, preparation, and approval for publication of this manuscript.

REFERENCE

1. World Health Organization. Pneumonia. 2019; 2 August. Available from URL: https://www.who.int/news-room/fact-sheets/detail/pneumonia.

2. United Nations Children's Fund. Pneumonia. 2020 October. Available from URL: https://www.unicef.org/media/64701/file/Every-childs-right-to-survive-pneumonia-2020.pdf.

3. Chisti C, Jobayer M, Salam MA, Smith JH, Ahmed T, Pietroni MAC. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: An open, randomised controlled trial. The Lancet. 2015; 386(9998), 1057–65. Available from URL: https://pubmed.ncbi.nlm.nih.gov/26296950/.

4. West JB, Luks AM. Respiratory Physiology: The Essentials. In Physical Therapy 10th ed. 2015; Vol. 55, Issue 5.

5. Atwa ZT. Usefulness of gender and abnormal blood count for predicting pneumonia outcome in children. Egyptian Journal of Chest Diseases and Tuberculosis. 2015; 64(1), 169–74.

6. Shaima SN, Alam, T, Shahid, ASMS, Shahrin L, Sarmin M, Afroze F. Prevalence, Predictive Factors, and Outcomes of Respiratory Failure in Children With Pneumonia Admitted in a Developing Country. Frontiers in Pediatrics. 2022; 10: 1–7. Available from URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9115563/.

7. Dean P, Florin TA. Factors Associated With Pneumonia Severity in Children: A Systematic Review. J Pediatric Infect Dis Soc. 2018. Available from URL: https://pubmed.ncbi.nlm.nih.gov/29850828/.

8. Lagunas-Rangel FA. Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. Medical Virology. 2020. Available from URL: https://pubmed.ncbi.nlm.nih.gov/32242950/.

9. Katleya F, Anam M, Dadiyanto DW. Rasio Jumlah Neutrofil-Limfosit pada Awal Masuk Rawat sebagai Faktor Risiko Luaran Pneumonia Anak. Sari Pediatri. 2016; 17(1): 47.

10. Lailla A, Andayani H., Ismy J, Bakhtiar B, Salawati L. Hubungan Imunisasi Dasar Lengkap dengan Kejadian Pneumonia pada Balita di RS Zainoel Abidin Banda Aceh.Jurnal Kedokteran Nanggroe Medika. 2020; 3 (1). Available from URL: https://api.semanticscholar.org/CorpusID:230613082.

11. Hasanah, U., Santik, Y.D.P. Faktor Intrinsik dan Ekstrinsik yang Berhubungan dengan Kejadian Pneumonia di Wilayah Puskesmas Rembang. Jurnal Kesehatan Masyarakat Indonesia. 2021; 16 (2).

12. Wasita, IKS, Setiawan PA. Perbedaan rasio neutrofil-limfosit terhadap lama rawat anak dengan pneumonia di Ruang Kaswari , RSUD Wangaya , Denpasar , Bali , Indonesia. 2019; 10(3), 851–7. Available from URL: https://api.semanticscholar.org/CorpusID:254813092.

13. Nurnajiah M, Rusdi, R, Desmawati D. Hubungan Status Gizi dengan Derajat Pneumonia pada Balita di RS. Dr. M. Djamil Padang. Jurnal Kesehatan Andalas. 2016; 5(1).

14. Sangadji NW, Vernanda LO, Muda CA. Hubungan Jenis Kelamin, Status Imunisasi Dan Status Gizi Dengan Kejadian Pneumonia Pada Balita (0-59 Bulan) di Puskesmas Cibodasari Tahun 2021. Health Science. 2022; 2 (2). Available from URL: https://digilib.esaunggul.ac.id/hubungan-jenis-kelamin-status-imunisasi-dan-status-gizi-dengan-kejadian-pneumonia-pada-balita-059-bulan-di-puskesmas-cibodasari-tahun-2021-29233.html.

15. Pramana KP, Subanada IB. Hubungan Jumlah Leukosit Serta Kadar C-Reaktif Protein dengan Derajat Keparahan Pneumonia pada Anak. Medicina. 2015; 46 (2). Available from URL: https://ojs.unud.ac.id/index.php/medicina/article/download/18084/11736.

16. Kirolos A, Blacow RM, Parajuli A. The impact of childhood malnutrition on mortality from pneumonia: a systematic review and network meta-analysis. BMJ Glob Health. 2021; 6 (11). Available from URL: https://pubmed.ncbi.nlm.nih.gov/34848440/.

17. Savino W, Durães J, Maldonado-Galdeano C, Perdigon G, Mendes-da-Cruz DA, Cuervo P. Thymus, undernutrition, and infection: Approaching cellular and molecular interactions. Front Nutr. 2020. Available from URL: https://pubmed.ncbi.nlm.nih.gov/36225882/.

18. Olofin I, McDonald CM, Ezzati M, Flaxman S, Black RE, Fawzi WW. Associations of suboptimal growth with all-cause and cause-specific mortality in children under five years: a pbourkeled analysis of ten prospective studies. PLoS One. 2013;8(5). Available from URL: https://pubmed.ncbi.nlm.nih.gov/23734210/.

19. Siswanto S, Budisetyawati B, Ernawati. Peran Beberapa Zat Gizi Mikro Dalam Sistem Imunitas. 2013; 6(1), 57–64.

20. Bourke CD, Berkley JA, Prendergast AJ. Immune Dysfunction as a Cause and Consequence of Malnutrition. Trends Immunol. 2016; 37(6):386. Available from URL: https://pubmed.ncbi.nlm.nih.gov/27237815/.

21. Araya S, Lovera D, Zarate C. Application of a prognostic scale to estimate the mortality of children hospitalized with community-acquired pneumonia. Pediatr Infect Dis J. 2016; 35:369–73. Available from URL: https://pubmed.ncbi.nlm.nih.gov/26629871/.

22. Jager CPC, Wever PC, Gemen EFA, Kusters R, Lafeber AB, Poll T, Laheij RJF. The Neutrophil-Lymphocyte Count Ratio in Patients with Community-Acquired Pneumonia. PLoS ONE, 2012; 7(10), 4–11. Available from URL: https://pubmed.ncbi.nlm.nih.gov/23049706/.

23. Muller, B., Harbarth, S., Stolz, D., Bingisser, R., Mueller, C., & Leuppi, J. Diagnostic and Prognostic Accuracy of Clinical and Laboratory Parameters in Community-Acquired Pneumonia. 2007; 7, 1–10. Available from URL: https://pubmed.ncbi.nlm.nih.gov/17335562/.

24. Singh RP, Kashyap AK, Puri S, Whig J. Pulmonary manifestations in HIV seropositive patients and their correlation with cd4 counts in a tertiary care centre of north India. JK Science India. 2013;15:140-4.

25. Buonacera A, Stancanelli B, Colaci M, Malatino L. Neutrophil to Lymphocyte Ratio: An Emerging Marker of the Relationships between the Immune System and Diseases. Int J Mol Sci. 2022 .

26. Sun, W., Luo, Z., Jin, J. The Neutrophil/Lymphocyte Ratio Could Predict Noninvasive Mechanical Ventilation Failure in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Retrospective Observational Study. International Journal of Chronic Obstructive Pulmonary Disease. 2021.

27. Hidalgo A, Libby P, Soehnlein O, Aramburu IV, Papayannopoulos V, Silvestre-Roig C. Neutrophil extracellular traps: from physiology to pathology. Cardiovasc Res. 2022.

28. Guo Z, Zhang Z, Prajapati M, Li Y. Lymphopenia Caused by Virus Infections and the Mechanisms Beyond. Viruses. 2021 ;13(9):1876.