CORRELATION OF NEUTROPHIL LYMPHOCYTE RATIO AND MONOCYTE LYMPHOCYTE RATIO TO THE PELOD-2 SCORE IN CRITICALLY ILL CHILDREN

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Abstract

Critically ill children admitted to the pediatric intensive care unit (PICU) from 75 to 166 per 100,000 children/year including respiratory diseases, infectious diseases, congenital diseases, and perioperative care. Early detection of disease severity in critically ill children uses the PELOD-2 score. Previous studies have shown that neutrophil lymphocyte ratio (NLR) can be used as a predictor of pediatric mortality and monocyte and lymphocyte ratio (MLR) to determine the severity of Klebsiella pneumonia infection. The aim of this study is to determine the correlation of NLR and MLR to PELOD-2 score in critically ill children in the PICU of Haji Adam Malik General Hospital. The research method is cross sectional analytic research from medical records, then documentation of PELOD-2 scores. The subjects were critically ill children from October to December 2022 according to the inclusion and exclusion criteria. Data were analyzed with the Spearman correlation test. **Results**: A total of 59 pediatric patients, the most was female 34 patients (57.6%). The mean age of the children was 6.23 years old. With the most indications was respiratory disease 22 people (37.3%). Spearman correlation test analysis showed that there was no significant correlation between NLR and MLR with PELOD 2 on the first day (p=0.316 and p=0.696) and MLR with PELOD 2 on the third day of treatment (p=0.077). However, a significant correlation was found between NLR and PELOD 2 in critically ill children on the third day of care (p=0.014). **Conclusion**: There was a significant correlation between NLR and PELOD-2 score on the third day of care. However, there was no correlation between first and third day MLR and first day NLR with PELOD-2 score.

Keywords: Critically ill children ; MLR ; NLR ; PELOD-2

Critical illness is a life-threatening condition that requires intensive care, comprehensive observation, and specialized treatment (1). Critically ill children admitted to intensive care units (ICUs) range from 75 to 166 per 100,000 child-years including respiratory diseases, infectious diseases, congenital diseases, and perioperative care are common causes of hospitalization (2). The total number of Pediatric Intensive Care Unit (PICU) patients at Haji Adam Malik Hospital in 2018-2019 was 352 patients (3). One score system that is widely used in pediatric intensive care units is the PELOD-2 score (4,5). PELOD score is a descriptive scoring

system used to determine the presence of organ dysfunction/failure, and severity of illness in critically ill children (6). In addition, the utilization of the PELOD score is also a measure of clinical trial outcomes, severity of illness of treated patients, markers of disease severity in quality assurance and cost of care in the PICU. Based on the scoring test, the results show that PELOD has good sensitivity and specificity with an Area Under The Curve (AUC) of 0.79-0.85 (5).

There have been many studies conducted regarding the Neutrophil-Lymphocyte Ratio (NLR) as a predictor of mortality in pediatric patients. Increased levels of neutrophils and apoptosis of lymphocyte cells are often found in patients with systemic inflammation or disorders that make the NLR increase (7–9). A study by Mathews et al. (2018)(10) stated that a simple and inexpensive marker, such as an increase in NLR helps in predicting PICU mortality comparable to PELOD score 2. A trend towards a decrease in NLR is associated with a shorter length of hospital stay and better survival (10). Very little research has been done on Monocyte-Lymphocyte Ratio (MLR) when compared to NLR against infection. The results of previous studies showed that MLR was not significant as a predictor of sepsis or mortality, but was significant for the severity of patients with Klebsiella pneumonia infection (11–13). Research conducted by Pasaribu et al. (2021) (14) It was found that only NLR (p=0.014) could be used as a predictor of mortality in children with sepsis (11.61+7.39 vs 5.77+4.05) while MLR (p=0.081) was not significantly different between septic (0.60+0.38) and non-septic (0.59+0.72) patients (14). The aim of this study is to determine the correlation of NLR and MLR to PELOD-2 score in critically ill children in the PICU of Haji Adam Malik General Hospital.

1. Methods

This study used a cross-sectional analytic analytic design. The population was pediatric patients who were admitted to the pediatric intensive care unit of Haji Adam Malik Hospital Medan during October to December 2022. The inclusion criteria in this study is pediatric patients admitted to the pediatric intensive care unit. Exclusion criteria used in this study were pediatric patients with immune system disorders, malnutrition, on chemotherapy treatment and incomplete patient data from medical records. Patient data was recorded including age, gender, diagnosis, and patient outcomes (survive/dead). Complete blood collection data of patients and recording the PELOD-2 score during PICU treatment. Data was recorded, collected and analyzed statistically. Bivariate analysis using the Paired T test or Wilcoxon test. To analyze whether there is a correlation between NLR and MLR on the PELOD-2 score on the first and third day of treatment, the Spearman correlation test is used. NLR and MLR values on the first treatment day were correlated with Pelod-2 Score on the first day, NLR and MLR values on the third treatment day were correlated with Pelod-2 Score on the third day.

2. Results

This study was attended by 59 critically ill children who were admitted to the PICU of Haji Adam Malik Hospital Medan during October 2022 to December 2022. There were 34 female children (57.6%). The mean age of the children was 6.23 years with the youngest being 1 month old and the oldest being 17.5 years old. The mean weight and height of the children were 18.86 kg and 101.22 cm, respectively. The most common indication was respiration, totaling 22 (37.3%) (Table 1). Hematologic characteristics of critically ill pediatric patients on day one and day three of treatment are shown in tables 2 and 3.

Table 1. Demographic Characteristics of Critically Ill Pediatric Patients.

Demographic Characteristics	n = 59
Sex, n (%)	
- Male	25 (42,4)
- Female	34 (57,6)
Age, years	
- Mean (SD)	6,23 (6,08)
- Median (Min-Max)	4 (0,08 – 17,5)
Weight, kg	
- Mean (SD)	18,86 (15,99)
- Median (Min-Max)	11,1 (1,7 – 62)
Height, cm	
- Mean (SD)	101,22 (38,01)
- Median (Min-Max)	93 (45 – 171)
Indication for hospitalization in PICU, n (%)	
- Respiration	22 (37,3)
- Cardiovascular	8 (13,6)
- Central Nervous System	11 (18,6)
- Shock	6 (10,2)
- Nephrology	5 (8,5)
- Post-Surgery	7 (11,9)

Table 2. Hematologic Characteristics of Critically Ill Pediatric Patients on First Day Care.

Hematologic Characteristics	Mean (SD)	Median (Min – Max)	p*
Hemoglobin, g/dL	9,99 (3,01)	9,6 (2,2 – 20)	0,200
Erythrocytes, million/µL	3,77 (1,08)	3,78 (0,44 – 6,32)	0,200
Leukocytes, thousand/µL	17,55 (11,82)	15,93 (4,57 – 89,28)	0,006
Hematocrit, %	30,93 (9,34)	30,1 (7,5 – 68,1)	0,200
Platelets, thousand/µL	336,41 (189,27)	387 (40 – 867)	0,023
MCV	82,01 (16,48)	81 (23 – 171)	<0,001
MCH	27,07 (4,57)	26,9 (16,1 – 50)	0,022
MCHC	32,84 (5,67)	32,3 (26,2 – 72)	<0,001
Neutrophils, %	72,63 (14,87)	77,8 (40,8 – 94,1)	0,003
Lymphocytes, %	18,36 (13,27)	14,5 (3,19 – 73,8)	0,010
Monocytes, %	7,73 (4,02)	6,7 (1,8 – 20,6)	0,019
Eosinophils, %	0,97 (2,91)	0,3 (0 – 22,1)	<0,001
Basophils, %	0,21 (0,17)	0,2 (0 – 1)	<0,001
NLR	7,44 (6,22)	5,4 (0,24 – 27,7)	0,002
MLR	0,77 (0,78)	0,6 (0,09 – 3,8)	<0,001
CRP	1,4 (0,94)	1,2 (0 – 3,6)	<0,001
PCT	7,01 (16,11)	0,64 (0,02 – 98)	<0,001
PELOD 2	3,56 (2,62)	*3 (0 – 9)	0,001

Table 3. Hematologic Characteristics of Critically Ill Pediatric Patients on Third Day Care.

Hematologic Characteristics	Mean (SD)	Median (Min – Max)	p*
Hemoglobin, g/dL	9,84 (2,26)	10 (2,3 – 13,1)	0,200
Erythrocytes, million/µL	5,49 (6,57)	3,82 (0,45 – 30,3)	<0,001
Leukocytes, thousand/µL	14,73 (7,13)	13,17 (1,9 – 34,84)	0,001
Hematocrit, %	30,47 (7,26)	30,5 (6,8 – 42)	0,066
Platelets, thousand/µL	304,27 (200,78)	262 (36 – 880)	0,051
MCV	84,53 (12,45)	82 (70 – 151)	0,002
MCH	27,3 (4,65)	27,1 (19,2 – 51,1)	0,004
MCHC	32,08 (2,04)	32 (26,9 – 37)	0,200
Neutrophils, %	73,75 (14,81)	74,8 (40,4 – 96,3)	0,200
Lymphocytes, %	18,18 (11,25)	17 (3,1 – 48,4)	0,035
Monocytes, %	7,41 (4,33)	7 (0,8 – 24,8)	0,001
Eosinophils, %	1,07 (2,1)	0,2 (0 – 8,7)	<0,001
Basophils, %	0,26 (0,37)	0,2 (0 – 2,7)	<0,001
NLR	8,23 (9,64)	4,4 (0,45 – 45,8)	<0,001
MLR	0,71 (0,75)	0,53 (0,06 – 3,8)	<0,001
CRP	0,83 (0,68)	0,6 (0,1 – 2,8)	<0,001
PCT	13,31 (29,49)	0,8 (0,02 – 100)	<0,001
PELOD 2	3,73 (2,46)	3 (0 – 9)	<0,001

*Kolmogorov Smirnov

No significant differences were found for most hematological parameters of critically ill pediatric patients ($p>0.05$). The only three parameters that differed significantly between the examination on the first day of treatment and the third day were: leukocytes ($p=0.003$), MCV ($p=0.011$) and CRP ($p<0.001$) (Table 4).

Table 4. Differences in Hematologic Characteristics of Critically Ill Pediatric Patients on the First and Third Day of Treatment.

Hematologic Characteristics	First Day	Third Day	p*
Hemoglobin, g/dL	9,99 (3,01)	9,84 (2,26)	0,717[a]
Erythrocytes, million/µL	3,77 (1,08)	3,82 (0,45 – 30,3)	0,328[b]
Leukocytes, thousand/µL	15,93 (4,57 – 89,28)	13,17 (1,9 – 34,84)	0,003[b]
Hematocrit, %	30,93 (9,34)	30,47 (7,26)	0,685[a]
Platelets, thousand/µL	387 (40 – 867)	304,27 (200,78)	0,053[b]
MCV	81 (23 – 171)	82 (70 – 151)	0,011[b]
MCH	26,9 (16,1 – 50)	27,1 (19,2 – 51,1)	0,243[b]
MCHC	32,3 (26,2 – 72)	32,08 (2,04)	0,422[b]
Neutrophils, %	77,8 (40,8 – 94,1)	73,75 (14,81)	0,683[b]
Lymphocytes, %	14,5 (3,19 – 73,8)	17 (3,1 – 48,4)	0,413[b]
Monocytes, %	6,7 (1,8 – 20,6)	7 (0,8 – 24,8)	0,291[b]
Eosinophils, %	0,3 (0 – 22,1)	0,2 (0 – 8,7)	0,744[b]
Basophils, %	0,2 (0 – 1)	0,2 (0 – 2,7)	0,328[b]
NLR	5,4 (0,24 – 27,7)	4,4 (0,45 – 45,8)	0,872[b]

MLR	0,6 (0,09 – 3,8)	0,53 (0,06 – 3,8)	0,279[b]
CRP	1,2 (0 – 3,6)	0,6 (0,1 – 2,8)	<0,001[b]
PCT	0,64 (0,02 – 98)	0,8 (0,02 – 100)	0,484[b]
PELOD 2	3 (0 – 9)	3 (0 – 9)	0,368[b]

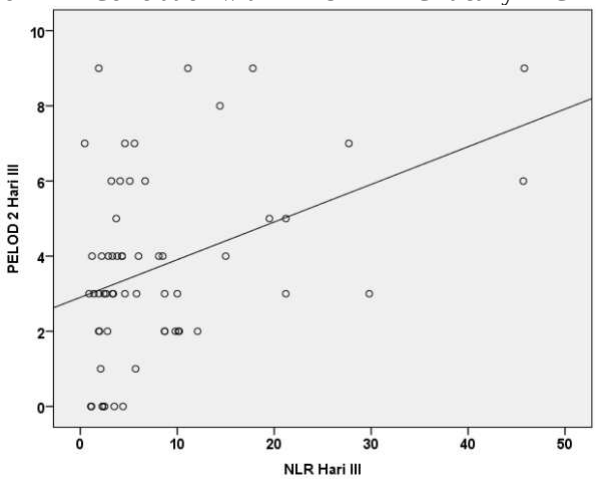
The data shown are mean (SD), Median (Min-Max), [a]Paired T, [b]Wilcoxon

Using the Spearman correlation test showed that there was no significant correlation between NLR and MLR with PELOD 2 in critically ill children on the first day of care. Likewise, for MLR with PELOD 2 on the third day of treatment (p=0.077). However, a significant relationship was found between NLR and PELOD 2 in critically ill children on the third day of treatment (p=0.014). The correlation value obtained was 0.319. The positive correlation indicates that the relationship between NLR and PELOD 2 is directly proportional, which means that an increase in NLR value will be followed by an increase in PELOD 2. The strength of the resulting correlation is weak strength (r>0.2-0.4) (Table 5 ; Figure 1).

Table 5. Correlation of NLR and MLR with PELOD 2 in Critically Ill Children on the First and Third Day of Care.

Treatment	Variable	PELOD 2	
		p*	r
First Day	NLR	0,316	0,133
	MLR	0,696	-0,052
Third Day	NLR	0,014	0,319
	MLR	0,564	0,077

Figure 1. Scatterplot Graph of NLR Correlation with PELOD 2 in Critically Ill Children on Day 3 Treatment.



3. Discussion

The role of NLR and MLR is still being explored as parameters or markers of inflammation, considering that they are basically a comparison between two cells with different progenitor origins. Although both are derived from the same stem cell, the multipotential hematopoetic stem cell, neutrophils and monocytes are

derived from myeloid progenitors, while lymphocytes are derived from lymphoid progenitors (15,16). Thus, developing a ratio involving two cell types from different progenitors is expected to help clinicians determine the type of infection a patient is experiencing. For example, high neutrophil counts are closely associated with bacterial (especially non-tuberculous) infections, high monocytes are associated with innate responses of the immune system, while high lymphocyte values correlate with an individual's adaptive immunity (17,18).

Theoretically, the more severe the bacterial infection, the higher the NLR (increased neutrophils with fixed/decreased lymphocytes). In that regard, infection-related NLR or MLR markers may be related to the degree of organ damage/dysfunction that occurs (19,20). In the pediatric population, there is a scoring system called PELOD-2 (described in the previous section). This organ dysfunction scoring method consists of 5 main variables (neurological, cardiovascular, renal, respiratory, and hematological) that adequately represent the severity of ongoing dysfunction (21). This study aims to elaborate on the correlation between NLR/MLR values and PELOD-2 by analyzing whether there is a positive/negative correlation between the two based on the Spearmann test.

The population analyzed in this study itself is quite representative of the critically ill conditions encountered by researchers during clinical practice, with a percentage of 57.6% being female (mean age 6.23 ± 6.08 years). Diseases related to the pulmonary and respiratory systems were the most common causes of critical illness experienced by the pediatric population in this study. Researchers also conducted a thorough examination of the laboratory aspects of all 59 children included in the study, although the main focus was to determine the correlation between NLR/MLR values and PELOD-2. Assessment of all these variables was done on the first and third day post-treatment. On the first day, it was found: NLR (7.44 ± 6.22); MLR (0.77 ± 0.78); and PELOD-2 (3.56 ± 2.62). Furthermore, on the third day, we found: NLR (8.23 ± 9.64); MLR (0.71 ± 0.75); and PELOD-2 (3.73 ± 2.46). The researcher also attached the data of the three variables in the form of medians (min-max). The differences in laboratory results from the first and third days were also not statistically significant (P>0.05), which partially indicated that the three variables were consistent enough to be tested by the Spearmann method.

The correlation analysis between NLR/MLR and PELOD-2 was relatively clinically insignificant, although on the third day of treatment a weak positive correlation was found between NLR and PELOD-2 values (r=0.319). These results indicate the possibility that an increase in NLR value can be a predictor of an increase in PELOD-2 value despite its statistically weak capacity. On the other hand, NLR values on the first day and MLR values on both monitoring days did not show any significance in their correlation with PELOD-2 (P>0.05). This finding is also supported by the scatter plot analysis graph that shows a linear correlation between the NLR and PELOD-2 values on the third day. Theoretically, the correlation is based on the possibility of higher potential organ dysfunction if the neutrophil/lymphocyte ratio increases, considering that an increase in neutrophils can be interpreted as an acute inflammatory response to a massive infection.

The effectiveness of PELOD-2 in predicting pediatric mortality has also been described several times in the literature. Matthew et al. in 2019 mentioned the PELOD-2 score mortality rate at PELOD-2 values >10 and >20 was 39.1% and 46.4%, respectively. These findings indicate the severity of organ dysfunction is almost certainly directly proportional to the risk of patient death. The same study also mentioned an increase in NLR values was also associated with mortality events in the pediatric intensive therapy service-based study (10). The stratification of PELOD-2 scores against mortality percentage by Deshmukh et al. in their study consecutively mentioned: scores 0-4 (1.6%); 5-9 (14.8%); 10-14 (50.0%); and >15 (66.6%). Desmukh et al. also compared the area under the curve (AUC) value in the study with other findings around the world with almost similar results to each other (AUC in Desmukh et al.'s study was 0.87; the range of AUC found was 0.78-0.91) (22). A study with a similar design as this study conducted by Dewi and Imanillah at Cipto Mangunkusumo Hospital, Jakarta, Indonesia, found no significant correlation between NLR and PELOD-2 (P>0.05; r=0.021) (7). The results of the study correlated with the researchers' findings on the first day of critical care that there was no significant correlation between the two variables.

The role of NLR itself has also been mentioned several times as a predictor of organ dysfunction, one of which is by using qSOFA or guidelines set by the International Pediatric Sepsis Consensus Conference as a

method of assessing pediatric sepsis conditions. Zhong et al. in their study mentioned the NLR value in pediatric patients with sepsis was higher than the control (Median; 6.03 vs. 3.03). The same study also mentioned that NLR is a fairly accurate predictor in predicting pediatric sepsis with an AUC value of 0.715 ($P<0.05$) (23). Li et al. reported that, in accordance with theory, pediatric patients who experienced mortality due to sepsis would have had significantly higher NLR and SOFA values than patients who were still alive at the end of the study. In addition, the combination of NLR and SOFA in Li et al. was also shown to be an important predictor of mortality in this study. Therefore, combining NLR/MLR with PELOD-2 in predicting the degree of mortality may be a suggestion and recommendation for future studies (24).

The study by Yuliarto et al. in Indonesia mentioned that there was a statistically significant correlation between NLR and qSOFA, suggesting they may have a linear correlation in their assessment. More specifically, Yuliarto et al. focused on the assessment of NLR values on the first day with the results of qSOFA assessment on the third day which showed a moderate degree of correlation ($P<0.05$; $R=0.407$) (19). Pasaribu et al. in their study that focused on determining the correlation between NLR/MLR and the incidence of sepsis mentioned that NLR can act as a predictor, but not MLR. Based on the report of the study, the following results were found in the sepsis and non-sepsis groups respectively: NLR, 8.99 ± 6.73 vs. 4.80 ± 5.30 ($P<0.05$) and MLR, 0.60 ± 0.38 vs. 0.59 ± 0.72 ($P>0.05$). These findings indicate that NLR is a fairly effective parameter in predicting sepsis, but not MLR (14).

To date, very few studies have focused on assessing the function of MLR as a predictor of sepsis or organ dysfunction. Therefore, this study is expected to serve as a basis or one of the main bases in determining whether MLR really has clinical significance in laboratory studies, especially in critically ill pediatric patients. From the hematology point of view, the role of monocytes is quite relevant but versatile, and has certain roles in inflammatory and infectious processes. For example, monocytosis (high monocyte count which may be followed by increased MLR value) is associated with several systemic inflammatory disorders, especially those related to autoimmunity such as systemic lupus erythematosus (SLE), sarcoidosis, and rheumatoid arthritis (RA). Monocytes also play an important role in immune responses due to mycobacterial or varicella-zoster virus (VZV) infections. In fact, there are reports that monocytosis can occur in cases of myocardial infarction and is associated with increased serum creatinine kinase (25,26).

However, this study could not find a significant correlation between MLR and PELOD-2 values as a representative of organ failure in the pediatric population. This is thought to stem from the basic characteristics of monocytes that are not strongly related to the etiology of critical illness experienced by the population, in contrast to NLR which has a weak degree of correlation with PELOD-2 although its significance is only seen on the third day of treatment. We suggest a study with a larger sample size, longer follow-up period, and more varied inflammatory/laboratory variables; especially to determine if there is an association between the three previously analyzed variables and the mortality rate of pediatric patients in future studies.

4. Conclusion

There was a significant correlation between NLR on the third day and PELOD-2 score, but there was no significant correlation between MLR (first and third day) and NLR (first day). There was a linear correlation between NLR values and PELOD-2 on the third day with a weak degree of correlation.

5. References

1. IDAI. Buku panduan pelayanan emergensi, rawat intermediet dan rawat intensif anak. Latief A, Pudjiadi A, Kushartono H, Malisie R, editors. Jakarta: Badan Penerbit Ikatan Dokter Anak Indonesia; 2016. 3–4 p.
2. Park E, Park H, Kang D, Chung CR, Yang JH, Jeon K, et al. Health disparities of critically ill children

according to poverty: the Korean population-based retrospective cohort study. BMC Public Health. 2021;21(1):1–9.

3. Adilla NR, Lubis AD. Hubungan Prokalsitonin dan Rasio Neutrofil Limfosit dengan Mortalitas Pneumonia di Ruang Rawat Intensif Anak Rumah Sakit Umum Pusat Haji Adam Malik Medan. Sari Pediatr. 2022;23(6):390.
4. El-Nawawy A, Mohsen AA, Abdel-Malik M, Taman SO. Performance of the pediatric logistic organ dysfunction (PELOD) and (PELOD-2) scores in a pediatric intensive care unit of a developing country. Eur J Pediatr. 2017;176(7):849–55.
5. Gulla K, Sachdev A. Illness severity and organ dysfunction scoring in Pediatric Intensive Care Unit. Indian J Crit Care Med. 2016;20(1):27–35.
6. Wulandari A, Martuti S, Kaswadi P. Perkembangan diagnosis sepsis pada anak. Sari Pediatr. 2018;19(4):237.
7. Rismala Dewi, Risa Imanillah. Hubungan Antara Nilai Leukosit, Rasio Jumlah Neutrofil-limfosit (NLR), C-Reactive Protein (CRP) dan Prokalsitonin dengan Skor Pediatric Logistic Organ Dysfunction (PELOD-2) sebagai Prediktor Derajat Keparahan Penyakit pada Anak Sakit Kritis. J Indones Med Assoc. 2021;71(1):30–5.
8. Lubis N. Rasio Neutrofil Limfosit Sebagai Prediktor Infeksi Bakteri pada Anak. Repos USU. 2019;
9. Adilla NR. Hubungan Prokalsitonin dan Rasio Neutrofil Limfosit dengan Angka Mortalitas Pasien Pneumonia Anak di PICU RSUP Haji Adam Malik Medan Tahun 2018-2019. Repos USU. 2021;
10. Mathews S, Rajan A, Soans S. Prognostic value of rise in neutrophil to lymphocyte ratio and platelet to lymphocyte ratio in predicting the mortality in pediatric intensive care. J Pediatr Crit Care. 2018;5(8):71.
11. Djordjevic D, Rondovic G, Surbatovic M, Stanojevic I, Udovicic I, Andjelic T, et al. Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Mean Platelet Volume-to-Platelet Count Ratio as Biomarkers in Critically Ill and Injured Patients: Which Ratio to Choose to Predict Outcome and Nature of Bacte. Mediators Inflamm. 2018;2018.
12. Wang JL, Lu XY, Xu XH, Zhang KJ, Gong H, Lv D, et al. Predictive role of monocyte-to-lymphocyte ratio in patients with Klebsiella pneumonia infection: A single-center experience. Med (United States). 2019;98(38).
13. BG S, Gosavi S, Rao AA, Shastry S, Raj SC, Sharma A, et al. Neutrophil-to-Lymphocyte, Lymphocyte-to-Monocyte, and Platelet-to-Lymphocyte Ratios: Prognostic Significance in COVID-19. Cureus [Internet]. 2021 Jan 11 [cited 2023 Jan 9];13(1). Available from: https://www.cureus.com/articles/48272-neutrophil-to-lymphocyte-lymphocyte-to-monocyte-and-platelet-to-lymphocyte-ratios-prognostic-significance-in-covid-19
14. Pasaribu FM, Setyaningtyas A, Andarsini MR. Neutrophil to lymphocyte ratio, monocyte to lymphocyte ratio, platelet to lymphocyte ratio, mean platelet volume as a predictor of sepsis mortality in children at dr. Soetomo general hospital. Crit Care Shock. 2021;24(2):65–71.
15. Faria SS, Fernandes PC, Silva MJB, Lima VC, Fontes W, Freitas R, et al. The neutrophil-to-lymphocyte ratio: A narrative review. Ecancermedicalscience. 2016;10:1–12.
16. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? BMC Res Notes. 2017;10(1):1–4.
17. Naess A, Nilssen SS, Mo R, Eide GE, Sjursen H. Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. Infection. 2017;45(3):299–307.
18. Cheng HR, Song JY, Zhang YN, Chen Y Bin, Lin GQ, Huang GQ, et al. High Monocyte-To-Lymphocyte Ratio Is Associated With Stroke-Associated Pneumonia. Front Neurol. 2020;11(October):4–7.
19. Yuliarto S, Kadafi KT, Maharani D, Ratridewi I, Winaputri SL. Paediatrica Indonesiana.

2023;63(01):14–20.
20. Qin ZJ, Wu QY, Deng Y, Li X, Wei X Di, Tang CJ, et al. Association between high-sensitivity troponin t on admission and organ dysfunction during hospitalization in patients aged 80 years and older with hip fracture: A single-centered prospective cohort study. Clin Interv Aging. 2021;16:583–91.
21. Dewi R, Christie CD, Wardhana A, Fadhilah R, Pardede SO. Pediatric logistic organ dysfunction-2 (PELOD-2) score as a model for predicting mortality in pediatric burn injury | Score "pediatric logistic organ dysfunction 2 (PELOD 2)" et prédiction de mortalité chez l'enfant brûlé. Ann Burns Fire Disasters. 2019;32(2):135–42.
22. Deshmukh T, Varma A, Damke S, Meshram R. Predictive efficacy of pediatric logistic organ dysfunction-2 score in pediatric intensive care unit of rural hospital. Indian J Crit Care Med. 2020;24(8):701–4.
23. Zhong X, Ma A, Zhang Z, Liu Y, Liang G. Neutrophil-to-lymphocyte ratio as a predictive marker for severe pediatric sepsis. Transl Pediatr. 2021;10(3):657–65.
24. Li Y, Wang J, Wei B, Zhang X, Hu L, Ye X. Value of Neutrophil:Lymphocyte Ratio Combined with Sequential Organ Failure Assessment Score in Assessing the Prognosis of Sepsis Patients. Int J Gen Med. 2022;15(February):1901–8.
25. Ginhoux F, Mildner A, Gautier EL, Schlitzer A, Jakubzick C, Varol C, et al. Editorial: Monocyte Heterogeneity and Function. Front Immunol. 2021;11(January):1–4.
26. Espinoza VE, Emmady PD. Histology-Monocytes. StatPearls. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022.