Research Article

Platelet to Lymphocyte Ratio value as Risk Factor for Pediatric Sepsis Mortality

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Abstract

Background: Sepsis is the leading cause of death for newborns and young children. It's critical to identify patients who have a high risk of dying and to correctly predict outcomes early on. In children with sepsis, the platelet-lymphocyte ratio (PLR), a recently developed inflammatory test, indicates a more severe inflammatory response and is a risk factor for mortality.

Objective: The aim of this study is to prove the value of high PLR as a risk factor for pediatric sepsis mortality.

Methodology: This study used an observational analytic research design (retrospective study) with a case-control design conducted at Prof. I G. N. G. Ngoerah General Hospital, Denpasar. The data were collected from medical records of 148 patient with sepsis or shock sepsis admitted in Emergency Room and Pediatric Intensive Care Unit from December 2021 to May 2023. Samples were taken consecutively divided into non survivors and survivors outcome. PLR was calculated as: Platelet count/ Lymphocyte count.

Result: A total of 148 pediatric patients with age range was 1 month–18 years old with a median (IQR) age of 53 month in non-survivor group. The median (IQR) values of PLR in non-survivor groups were 178,3 (292) respectively. Higher PLR valueswere more common in non-survivors group (60,8%). High PLR value as a risk factor for childhood sepsis mortality (OR 3,67; CI 95% 1,85-7,26; p=0,001).

Conclusion: High PLR value as risk factor for pediatric sepsis mortality.

Keywords: Platelet to lymphocyte Ratio, Pediatric sepsis, mortality.

INTRODUCTION

Sepsis as on organ dysfunction, is a life-threatening condition brought on by immunological dysregulation in response to an infection. It is the leading cause of death for new-borns and young children globally, particularly in lower-middle-income nations.[1,2] Accurately predicting the course of events and identifying patients at high risk of mortality are critical in the early stages so that the patient receives appropriate, life-saving care.[3]

One in five deaths overall occurs as a result of sepsis, with the majority occurring in new-borns and children.[4] Regarding its classification, sepsis is a potentially deadly illness with mortality rate that affects approximately 10% of individuals with sepsis and septic shock. Depending on how many organs are malfunctioning, the death rate in children with at least one comorbid condition will rise and eventually reach 76%. The prevalence of severe sepsis in South Korea treated in the Pediatric Intensive Care Unit is approximately 7.3% with a mortality rate of 64.6%. In 2002, 32% of children in developing countries were treated in intensive care with a diagnosis of sepsis and septic shock with a mortality rate of 57.3%.[4]

In Indonesia data from Doctor Sutomo Hospital found 27.08% with severe sepsis were, 14.58% sepsis, and 58,33% sepsis. Sepsis incidence in PICU at Cipto Mangunkusumo Hospital was 19.3% of 502 pediatric septic shock with mortality rate of 54%.[5] Meanwhile, according to the Riskesdas 2007, neonatal sepsis has a high mortality rate of 20.5%. The prevalence of sepsis aged 0-18 years at Sanglah Hospital Denpasar in 2018 was dominated by the infant age category (<2 years) at 57% with septic shock is the most common diagnosis.[4] Sepsis is not only a medical issue but also a global socioeconomic one because it significantly quality of life and increases death rates. Therefore, a precise sepsis prognosis is crucial.

The prognosis of sepsis in children has been assessed using a number of predictors and grading methods, including the PELOD-2 score. However, this necessitates particular tests that establishments with inadequate equipment are unable to carry out.[1] Some other parameters used to predict sepsis mortality are procalcitonin, ferritin, and lactate, but this examination requires quite a long time result, expensive, most not available in rural area. In recent years, the number of platelets and lymphocytes is known to play an important role in the inflammatory process in sepsis.[6] The Platelet to Lymphocyte Ratio has drawn interest as a possible marker of inflammation in a number of illnesses, including sepsis.[7] Research has demonstrated that PLR can be used to identify infants at risk for early sepsis. A high PLR as sepsis mortality risk factor which can be done easily, has a fast turnaround time, can be accessed in areas with limited facilities, and is obtained at a low cost from routine blood tests.[8] Although PLR has been frequently used in diagnosis and prognosis of sepsis in neonates and adults, It has not been studied much in the pediatric population. Some studies have shown non-significant results when using PLR as a predictor for sepsis outcomes.[8]

Based on several problems described above, it is highly recommended that this examination can provide early information regarding childhood sepsis mortality. This study aims to assess PLR as a risk factor for sepsis mortality in pediatric patients treated in the PICU (Pediatric Intensive Care Unit) and Emergency Unit. This research is expected to improve understanding and outcomes in sepsis patients. Our findings can provide a basis for future research and hopefully reduce the mortality and morbidity rates of sepsis in children.

METHOD

This research is an observational analytical research design (retrospective study) with a case-control design. Dependent variable is sepsis mortality divided to non-survivor group and survivor group taken through medical records. Independent variable is PLR taken from medical record. Confounding variable control by design include malignancy, congenital heart disease, Immunodeficiency, chronic kidney disease. Confounding variable control by analysis is age, gender and nutritional status.

Target population was all pediatric patients with sepsis and septic shock diagnosed by supervisor in charged collected from medical record. The accessible population in this study was pediatric patients aged 1 month – 18 years with a diagnosis of sepsis and septic shock under treatment at the Children's Emergency Room and Pediatric Intensive Care Unit (PICU) at Prof. Dr. I G.N.G. Ngoerah Hospital taken from medical record. Inclusion criteria were sepsis and shock sepsis pediatric patients aged 1 month – 18 years and complete

subject data in the register. Exclusion criteria is malignant disease, congenital heart disease, chronic kidney disease, children with HIV/AIDS.

The research subjects were taken using consecutive sampling until the number of subjects was fulfilled. The sample size was calculated using a formula two proportion independent with effect size 0,24 was used and with minimum sample size is 148 subjects.[9] Some variable in this study included: age, gender, nutritional status, PLR, PELOD-2, organ dysfunction, patient referral, sepsis outcome. The operational definition of variables is as follows:

1. Age presented on a categorical scale by toddler (1-59 month), child (60 -119 month), and teenager (120-216 month).
2. Gender is obtained through patient medical record data. Data is divided into male and female and presented on a nominal data scale.
3. Nutritional status presented in categorical scale divided into well Nourished (Z-score ≥ -2.0 to Z-score ≤ 2.0), wasted (Z-score < -2SD) and overweight (Z-score > 2SD).
4. Platelet to Lymphocyte Ratio is ratio of platelet count divided lymphocytes count obtained from medical record take on day-1, 4 or 7 after diagnosed with sepsis or septic shock. The higest PLR value taken from those day. Cut off point that used in this study is 157, based on study result in Prof. Dr. R. D. Kandou Central General Hospital. The PLR value increases if PLR ≥ 157 and normal if < 157 with a nominal data scale.[10]
5. Sepis or shock sepsis mortality diagnosed by the doctor in charge taken from medial ercord. Mortality sepsis is divided into case (non-survivor) and control (survivor group). Non survivor group is sepsis/shock sepsis child who died within 28 days during hospitalized. Survivor is sepsis/shock sepsis child who survived within 28 days of hospitalization. Data is presented on a nominal data scale.
6. PELOD-2 presented on a numerical scale, and then presented on a categorical data scale PELOD-2 ≥ 7 and PELOD-< 7.
7. Organ dysfunction occurs as a result of sepsis conditions such as failure in the brain, heart, lungs, kidneys, gastrointestinal and microcirculation. Variables are presented on a categorical scale, namely 1 organ, 2 organs and > 2 organs.
8. Referral patients are patients referred by general practitioners or specialist doctors or other health facilities to diagnose or receive further treatment. Variables are presented on a nominal data scale.
9. Malignancy characterized by the growth and spread of abnormal cells in the body like blood cell malignancies (leukaemia) and solid tumors.
10. Congenital heart disease is condition of heart problems in children who have had abnormalities or problems with the structure of their heart since birth.
11. Chronic kidney disease is damage to kidney tissue or a decrease in the glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m2 for 3 months or more with or without kidney damage.

Research Procedure

This research uses secondary data in the form of patient medical record. Cases that meet the inclusion criteria included as research subjects using consecutive sampling until the sample size is reached. Data collection was carried out by recording characteristic data, clinical data, and what was needed in the research. The collected data is then analysed using a computer program.

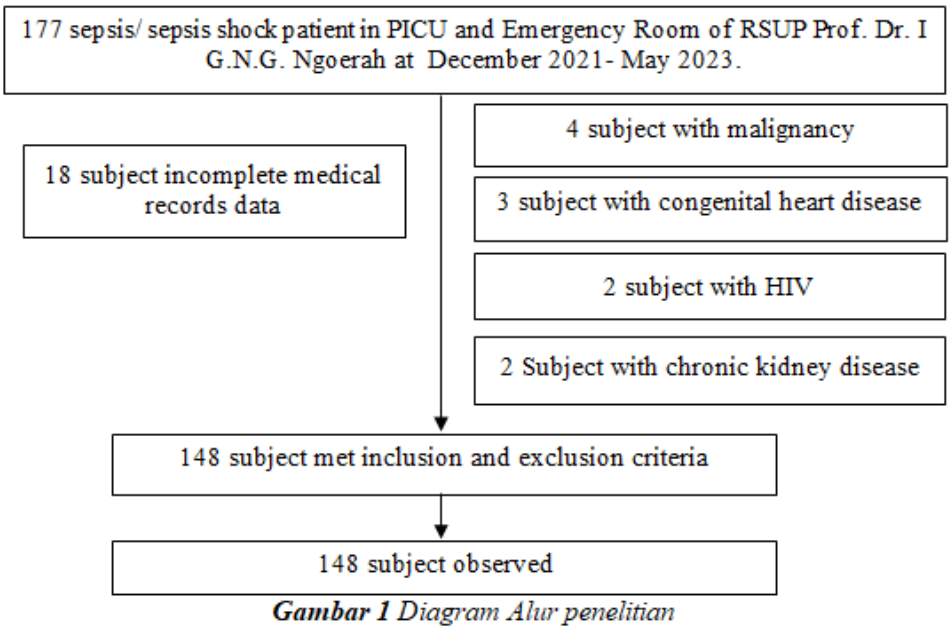
Statistical analysis

Descriptive analysis of numerical data, normality of data distribution is determined by carrying out the Kolmogorov-Smirnov test (if $p > 0.05$). If numerical data with a normal distribution is presented in the form of mean and SD, while numerical data with a non-normal distribution is presented in the form of median and interquartile range (IQR). Numerical data with a normal distribution is carried out by the t test and if the data is not normally distributed then the Mann-Whitney test is carried out.

Bivariate test of the independent variable on a categorical scale with the dependent variable on a categorical scale uses a logistic regression test to obtain the Odds Ratio value. Multivariate analysis is carried out by controlling confounding variables if these variables are significantly related to the dependent variable. The level of significance used is if the P value is <0.05.

RESULT

This research was carried out at RSUP Prof. Dr. I G.N.G. Ngoerah from December 2021 to May 2023. The research flow diagram presented in **Figure 1** shows 177 patients with septic shock/sepsis that treated in the PICU and pediatric emergency room. Total 148 subjects who met the inclusion and exclusion criteria were then studied.



***Gambar 1** Diagram Alur penelitian*

Figure 1. Study Flow Chart

Based on **Table 1**, the median age in the case group is 53 months and the control group is 22 months with a range of 1-215 months. Nutritional status was divided into 3 categories wasted, well-nourished and overweight, with the majority in the case group being wasted (73.3%) than in the control group (37.8%). Overweight found 8.1% and in the control group 6.3%. Median (IQR) PELOD-2 in the case group 11.5 (6.2) and 6.0 (6.3) in the control group. Most organ dysfunction was found with more than 2 organs in the case group 74.0% and in the control group with 2 organ dysfunction is 58.1% and 29.7% in the control. The number of referrals in the case group 59.5%, higher than in the control group (54.1%). The median (IQR) of PLRvalue was 178.3 (292) in the case group and 64.4 (151.1) in the control group.

Table 1 Characteristic of subject based on case and control group

Variable	Group	
	Non- survivor	Survivor
Age (month), median (IQR)	53 (125,5)	22 (70)
Gender, n (%)		
-Male	43 (58,1)	39 (52,7)
-Female	31 (41,9)	35 (47,3)
Nutritional Status		
-Well-nourished	13 (17,6)	40 (54,8)
- Wasted	55 (73,3)	28 (37,8)
- Overweight	6 (8,1)	6 (8,2)
PELOD-2 score, median (IQR)	11,5 (6,2)	6,0 (6,3)
Organ Dysfunction, n (%)		
- One	4 (5,4)	9 (12,2)
- Two	12 (16,2)	43 (58,1)
- More than 2	58 (74,0)	22 (29,7)
Referral, n (%)		
- Yes	44 (59,5)	40 (54,1)
- No	30 (40,5)	34 (45,9)
Platelet to Lymphocyte Count, median (IQR)	178,3 (292)	64,4 (151,1)
Platelet count (IQR)	271(125)	221 (136)
Lymphocyte Count (IQR)	2,2 (1,87)	2,6 (3,07)
Outcome, n (%)	74 (50)	74 (50)

In **Table 2**, male 58,1% in the case group, higher than in the control group (52.7%). Female in the case group was 41.9%, lower than in the control group (47.3%). There was no difference in gender proportion between the case and control groups and the value was not statistically significant (OR 1.24; 95% CI 0.65-2.38; p=0.508). Based on age, toddler in the case group 52.7% and in the control group is 74.3%. Child in case group found 17,6%, higher than in controlled group 9,5%. Teenager in case group is higher 31,1% than in controlled group 16,2%. Age is associated death in childhood sepsis (p=0.015).

Nutritional status is divided into wasted, well-nourished and overweight. Wasted condition in the case group is 73.3% and higher than the control group 37.8%. There was a difference in the proportion of wasted in the case group which was significantly higher than the control group with an OR of 6.0. Wasted is a risk factor for pediatric sepsis mortality (OR 6.0; 95% CI 2.79-13.10; p=0.001). Subjects with overweight status were 8.1% in the case group and 8.2% in the control group. There were no differences in proportions between the case and control groups (OR 0.32; 95% CI 0.08-1.18; p=0.08).

Table 2 Bivariate Variable Risk Factor Risk Pediatric Sepsis Mortality

Variable	Group n(%)		OR (95% CI)	p
	Non-survivor	Survivor		
Gender				
Male	43 (58,1)	39 (52,7)	1,24 (0,65-2,38)	0,508
Female	31 (41,9)	35 (47,3)		
Age				
Toddler	38 (51,4)	55 (74,3)		0,015*
Child	13 (17,6)	7 (9,5)		
Teenager	23 (31,1)	12 (16,2)		
Nutritional status				
Well nourished	13 (17,6)	40 (54,8)	Reff	Reff
Wasted	55 (73,3)	28 (37,8)	6,0 (2,79-13,10)	0,001*
Overweight	6 (8,1)	6 (8,2)	0,32 (0,08-1,18)	0,08
PELOD-2 score				
≥7	64 (86,5)	31 (41,9)	8,88 (3,95-19,97)	0.001*
<7	10 (13,5)	43 (58,1)		
Referral				
Yes	44 (59,5)	40 (54,1)	1,247 (0,65-2,39)	0,507
No	30 (40,5)	34 (45,9)		
Platelet to Lymphocyte Ratio				
High	45 (60,8)	22 (29,7)	3,67 (1,85-7,26)	0,001*
Normal	29 (39,2)	52 (70,3)		
Outcome	74 (50,0)	74 (50,0)		

*p<0,05

Pediatric logistic organ dysfunction-2 (PELOD-2) ≥7, 86,5% in the case group, higher than the control group 41.9%. There was a difference in the proportion of PELOD-2 ≥7 in the case group which was significantly higher than the control group with an OR of 8.88. PELOD-2 ≥7 is a risk factor for pediatric sepsis mortality (OR 8.88; CI95% 3.95-19.97; p=0.001). The number of referrals in the case group was higher (59.5%), compared to the control group (54.1%). However, there was no statistically significant difference (OR 1.25; 95% CI 0.65-2.39; p=0.507).

Based on **Table 2**, in the case group found 60.8% had high PLR values. In the control group, 29.7% had a high PLR. There was a significant difference in the proportion of PLR in the case group compared to the control group with an OR of 3.67. High PLR is a risk factor for pediatric sepsis mortality (OR 3.67; 95% CI 1.85-7.26; p=0.001).

Tabel 3 Multivariate Analysis PLR value as risk factor pediatric sepsis mortality after controlled confounding factor

Variable	Adjusted OR (ExpB)	95% CI	p
Platelet to Lymphocyte Ratio (high)	5,60	2,12-14,78	0,001*
PELOD-2>7	11,6	4,13-32,61	0,001*
Wasted	5,85	2,54-13,43	0,001*

*p<0,05

Multivariate analysis with logistic regression was carried out on all variables and obtained high PLR values (aOR 5,6; 95%CI 2,12-14,78; p=0.001) and wasted status (aOR 5,85; 95% CI 2,54-13,43; p=0.001) which is an independent factor of several variables studied which are associated with childhood sepsis mortality. PELOD-2 >7 as risk factor of child sepsis mortality (aOR 11,6; 95% CI 4,13-32,61; p=0.001). Based on

multiple logistic regression analysis, the PLR value as a risk factor for pediatric sepsis mortality after controlling for confounding variables, the result presented in **Table 3**.

DISCUSSION

Sepsis is a life-threatening condition with the death rate increasing every year.[4] From all patients treated in the PICU and emergency room, it was found that 36% were patients with sepsis and septic shock, higher than data from previous research at the same location in 2019, namely 35.7%. RSUP Prof. Dr. I G.N.G. Ngoerah is a type A hospital belonging to the Ministry of Health located in Bali. As a referral hospital for Bali and Nusa Tenggara, this causes a high number of patients diagnosed with sepsis and septic shock who are treated at this hospital.

This research was conducted on data from medical record with 177 patients who were treated with a diagnosis of sepsis/septic shock in the PICU and pediatric emergency room at Prof. Hospital. Dr. I G.N.G. Ngoerah in August 2021- October 2023 (Figure 1). The results of this study showed that the male gender who died (58.1%) was higher than those who lived (52,7%). Female gender in the case group was 41.9% lower than in the control group 47.3%. In this study, there was no difference between male or female gender as a risk factor for sepsis mortality, but it was found that the number of male in the sepsis group who died was higher than in the sepsis group who survived. Research by Botan et al., conducted in the PICU for 5 years, obtained the same result that from 2,781 children, 53.4% of the children who died were male. Accordance with a study of 1919 pediatric patients in PICU for 6 years with the result that 60.5% of children who died were male.[11] Male more often experience more severe conditions due to increased pro-inflammatory mediators such as TNF, IL-6, IL-10 causing dysfunction and even organ failure which causes a high risk of death. While female sex hormones naturally guard against inflammation, male sex hormones depress the immune system.[10,12]

Age is classified according to minister of health of the republic of Indonesia, presented as toddler (1-59 month), child (60 -119 month), and teenager (120-216 month). Median (IQR) was 53 months (125.5). Research conducted at RSUP Prof. IG.N.G. Ngoerah in 2018 received a median (IQR) of 10.5 months (6.48).[4] At the Prof. R.D. Kandou Hospital in Manado, North Sulawesi, another study with a similar outcome was carried out from February to August 2020. The mean age of the survivors was 50 months, while the mean age of the deceased was 59.62 months.[10]

In this study, toddler died in the sepsis group 52.7% and 74.3% survived in the sepsis group. In child group 17,6% case in non-survivor group higher than in survivor group about 9,5%. In teenager group there 31,1% higher than in survivor group 16,2%. We found a relationship between age and sepsis mortality in children with a P value <0.05 (p=0.015). These results are in accordance with the Southeast Asia Infectious Disease Clinical Research Network study which reported that the toddler age group was the group most frequently diagnosed with septic shock. Reasearch in Turkey with a total of 2,781 critically ill children in the PICU found an average age of 64 months or less than 6 months.[11] Hermon et al.'s research, conducted in PICU for 10 years, stated that the incidence of sepsis in children less than 6 years old was more than 70%.[13] In this study found, child and teenager group with higher mortality in sepsis than in toddler group. This condition can

caused by malnutrition happened most case in child and teenager group that caused higher risk of mortality in those patient. That could be caused the primary diagnosed more severe in child and teenager group that caused PELOD-2 score higher and more disfunction organ can happened that increased of mortality case.

Nutritional status was divided into 3 categories wasted, well-nourished and overweight with the majority in the case group being 73.3% is wasted. The wasted status in the case group (73.3%) was found to be higher than the control group (37.8%). There was a difference in the proportion of wasted in the case group which was significantly higher than the control group with an OR of 6.0. Wasted is a risk factor for pediatric sepsis mortality (OR 6.0; 95% CI 2.79-13.10; p=0.001). Subjects with overweight status 8.1% in the case group and 8.2% in the control group. There was no difference in proportions in the case and control groups (OR 0.32; 95% CI 0.08-1.18; p=0.08). This condition is in accordance with research found that 51.7% of critically ill patients experienced malnutrition with the risk factor for poor nutritional status on sepsis mortality was 3.06 times after controlled all confounding facto. Nutritional disorders that occur in patients are caused by changes in anabolism and catabolism status.[14] These results are in accordance with research conducted by Irving et al. based on an analysis of 417 patients aged less than 18 years treated with severe sepsis in 128 PICUs throughout the world, where based on BMI the majority, 67%, were classified as wasted or overweight.[15]

Malnutrition with care in the PICU room is associated with increased mortality rates, length of stay, longer use of ventilators and increased risk of infection during care. The stress response to critical illness is characterized by protein breakdown, providing free amino acids in the anti-inflammatory process and tissue repair. The inflammatory response to infection releases inflammatory mediators by reducing appetite, increasing skeletal catabolism and inhibiting the body's ability to store energy. Protein loss in severe and long-term illnesses will have a negative impact on lean body mass. Infants and children with minimal fat reserves are very susceptible to the adverse effects of this phenomenon.[16]

In this study, the median (IQR) PELOD-2 in the case group was 11.5 (6.2) and in the control group 6.0 (6.3). Then, if it is categorized into high and low PELOD-2 values with a cut-off value of 7, it is obtained that PELOD-2 ≥7 in the sepsis group died higher (86.5%) than the control group (41.9%). There was a difference in the proportion of PELOD-2 ≥7 in the case group significantly higher than the control group with an OR of 8.88. PELOD-2 ≥7 is a risk factor for mortality in pediatric sepsis (OR 8.88; CI95% 3.95-19.97; p=0.001). Accordance with research conducted in the PICU in Cipto Mangunkusumo Hospital with subjects who survived had an average PELOD-2 score of 7.59 ± 3.025, while those who died had an average score of 13.9 ± 4.564.[17] Study at Dr. Mohammad Hoesin Palembang showed that the PELOD-2 score was significantly different in PICU patients who managed to improve and patients who died. Mean in survivor group with PELOD-2 score of 2.58 ± 1.41, while patients who died is 10.23 ± 4.53.[18] The research at Dr. Moewardi Surakarta obtained a PELOD-2 score >20 with a 7.75 times greater risk of mortality compared to patients with a PELOD-2 score <20. A PELOD score of 20 has a probability of death of around 50%, and the higher the PELOD score, the higher the probability of death in a child (sensitivity 54.5%; specificity 80.9%; p < 0.5).[19] Another study evaluated PELOD-2 scores based on median values and interquartile ranges. It was found that PICU patients

who successfully experienced improvement had a median PELOD-2 score of 5 (3-6.25), while patients who died during treatment had a median PELOD-2 score of 9 (6-13).[20]

A tool used to assess the severity of organ dysfunction in children in critical condition is the PELOD-2 score. Subjects with organ dysfunction were divided into dysfunction in 1 organ, 2 organs, and more than 2 organs. Organ dysfunction was most commonly found with more than 2 organs in the deceased sepsis group (74.0%) compared to the living sepsis group with 2 organ dysfunction (58.1%). In the case group, the number of organ dysfunction was >2, which was the largest number of cases, namely 68 (77.3%) and in the control group, the majority had dysfunction of 2 organs with 52 cases (63.1%). Organ dysfunction is a risk factor for death in childhood sepsis (p=0.001). Accordance with research conducted by Wati et al., with the highest number of patients dying based on organ involvement, which was found to be the majority with involvement of 3 organs at 58.3%.[4] The number of referral cases in the dead sepsis group was higher, namely 59.5%, compared to the live sepsis group, namely 54.1. However, no risk factors were found for referral cases to increase sepsis mortality in children (OR 1.25; 95% CI 0.65-2, 39; p=0.507).

In this study, it was found that a high PLR was an independent risk factor for pediatric sepsis mortality. The median (IQR) value of PLR was 178.3 (292) in non-survivor (case) group. This result found higher than cut off point that used in this study is 157 that devided case and controlled group taken from study result in Prof. Dr. R. D. Kandou Central General Hospital. The total of high PLR in this study found 45%. This is higher than effect size that used in this study 24%.[9] In non-survivor group was found to be 60.8% with a high PLR value. In survivor group was found to be 29.7% with a high PLR value. There was a significant difference in the proportion of PLR in the non-survivor group compared to survivor group with an OR of 3.67. A high PLR value is a risk factor for pediatric sepsis mortality (OR 3.67; 95% CI 1.85-7.26; p=0.001). In the multivariate analysis, it was found that high PLR was an independent variable as a risk factor pediatric sepsis mortality after controlling confounding variables analytically (aOR 5,6; 95% CI 2.12-14,78; p=0.001). Apart from these risk factors, this research also found that characteristics such wasted as risk factors for pediatric sepsis motility (aOR 5,85; 95% CI 2,54-13,43; p=0.001) and PELOD-2 >7 as risk factors for pediatric sepsis motility (aOR 11,6; 95% CI 4,13-32,615; p=0.001)

This result in line with meta-analysis study consist of 16 studies comprising 2403 septic patients which found that PLR levels were significantly higher in no survivors than in survivors. This findings support PLR to be a promising biomarker in prediction and prevention of sepsis mortality.[21] We also discovered that the PICU at Prof. Dr. R. D. Kandou Central General Hospital in Manado had similar results, with increased PLR in non-survivor group. The same outcomes were shown in study, where the mean PLR for those who survived sepsis was 77.53 and 157.2 in non- survivor group. This suggests a substantial correlation between PLR and death.[11] In adults, a study showed that the PLR in adult sepsis patients who survived was 111 and 209 in non-survivor group.[22] Study in adult patients with total 5537 sepsis patient using SOFA score calculated within 24 hours of ICU admission, showed that a high PLR value >200 was significantly related to mortality.[6]

A condition known as sepsis is characterized by an uncontrollably high level of systemic inflammation, which is then followed by inflammatory mediator-induced increased vascular permeability and plasma protein leakage. These events have the potential to cause hypotension, shock, multiorgan dysfunction syndrome (MODS), and even death.[22] During inflammation, platelets and neutrophils interact, causing responses on the surface of the endothelium.[23] Chemotaxis is the process by which platelets actively stimulate neutrophils and monocytes to move to the site of tissue damage. Moreover, platelets indirectly stimulate the contact between monocytes and neutrophils by a number of methods, such as by activating TREM-1 in neutrophils, which in turn triggers a variety of pro-inflammatory reactions.[24] By producing lymphocyte apoptotic products, lymphocytes can stimulate anti-inflammatory responses. The immune system is weakened by an overabundance of apoptotic lymphocytes in sepsis, which typically results in septic shock, immunological paralysis, and eventually death.[25]

The haemostatic system is impaired in sepsis, and platelets are essential for haemostasis as well as the immune system's reaction to various assaults. Following pathogen invasion, the body's coagulation system is triggered at the infection site, and local capillaries create thrombus as a defensive measure to keep the infection contained to the lesions. These localized reactions spread throughout the body during sepsis, and disseminated intravascular coagulation (DIC) and MODS are the results of an uncontrolled "inflammation-coagulation" process.[26] Patients with high platelet counts experience more substantial inflammation as a result of the thromboxane's and other mediators secreted by platelets.[27]

Apoptosis-induced lymphopenia is frequent during sepsis, and its duration and intensity are related to worse clinical outcomes, including increased mortality rates and prior infections. One of the most plausible causes of injury-related lymphopenia is apoptosis, which also contributes both directly and indirectly to injury-induced immunoparalysis. Because active cells travel to inflammatory sites, lymphocyte apoptosis increases, resulting in a decrease in lymphocyte count that can last for up to 28 days.[28] Significant inflammation is indicated by a high platelet count, whereas a low lymphocyte count points to a poor immune response to infection. Increased platelet to lymphocyte ratio and low lymphocyte counts were the results of this disorder. Consequently, elevated PLR levels have been associated to significant systemic inflammation and have the potential to exacerbate sepsis and other illnesses.[6]

In children, PLR studies have been limited to an overall critical patient condition. A high PLR value implies a more severe inflammatory response. Clinical worsening, a worse prognosis, and mortality could result from more severe inflammation. Our study indicated that PLR levels among sepsis non-survivors are significantly higher than the survivors and high PLR value as risk factor of pediatric sepsis mortality. Therefore, PLR is a low-cost, easily perform and straightforward potential clinical predictor that can be used in regions with limited facilities settings.

Platelet Lymphocyte Ratio research in children has been restricted to a general critical patient state. A higher degree of inflammation is implied by a higher PLR value. More severe inflammation may lead to worsening clinical symptoms, a worse prognosis, and mortality. According to our research, PLR levels are

considerably higher in non-survivors of sepsis than in survivors, and a high PLR value is associated with a higher risk of pediatric sepsis mortality. Therefore PLR is simple, low cost, routine examination that can used in limited facilities.

This study has weaknesses, including this study did not examine other factors that might influence sepsis mortality in pediatric. Wasted as another factor influencing childhood sepsis mortality needs to be studied further to prove a significant relationship.

CONCLUSSION

Platelet Lymphocyte Ratio as risk factor pediatric sepsis mortality. High PLR increased risk of mortality 5,6 times compared with normal PLR value. Therefore, a high PLR is a risk factor for determining pediatric sepsis mortality with low cost, fast results, and is easy to perform so it can be used in areas with limited facilities. Apart from these risk factors, this research also found that characteristics such nutritional status (wasted) were significant risk factors for sepsis motility.

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