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RESEARCH ARTICLE

Evaluating Risk Factors for Early-onset Neonatal Sepsis

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Abstract

Neonatal sepsis is a systemic infection that occurs in infants at 28 days of life and is a significant cause of morbidity and death in newborns. Early-onset neonatal sepsis (EONS) occurs within 72 hours after birth and is often associated with infections contracted before or during childbirth. The study aims to evaluate the risk factors of EONS. The study design was a case-control retrospective observational study that evaluated the medical records of neonates who were admitted to the neonatal care unit of Al Islam Hospital Bandung from January 2020 to December 2022. This study assessed the impact of independent variables such as gestational age, birth weight, premature rupture of membrane (PROM), miconeal amniotic fluid, APGAR score of 5 minutes, and the mother's white blood cell count elevation (>15,000/µl). The logistic regression analyses were employed to analyze the data. The logistic regression analyses were employed to analyze the data. The study included 3,103 neonates, of whom 124 met the inclusion criteria. Thirty-nine patients (31.35%) were diagnosed with sepsis, while 85 patients (68.55%) did not have sepsis. Based on bivariate analysis, EONS was significantly linked to low birth weight (p=0.027, 95% CI=0.184 to 0.902, OR=2.455), PROM (p=0.000, 95% CI=4.359 to 26.582, OR=10.764), and the mother's white blood cell count elevation (p=0.002, 95% CI=1.560 to 7.622, OR=3.448). On multivariate analysis, the risk factors were significantly associated (p<0.05), which had an influence of 38.4% on EONS (Nagelkerke R square=0.384). In conclusion, the risk factors for EONS were low birth weight, PROM, and elevation of white blood cell count in the mother, which increased by 38.4% with EONS.

Keywords: Early-onset neonatal sepsis, risk factors

Introduction

Neonatal sepsis is a clinical condition characterized by a systemic illness accompanied by bacteremia within the first month of a newborn's life.[1] It arises when pathogens invade and proliferate in the bloodstream, causing systemic infection and releasing toxins that can lead to severe health complications and neonatal mortality.[2] Neonatal sepsis is further categorized into early-onset neonatal sepsis (EONS) and late-onset neonatal sepsis (LONS). EONS occurs within 72 hours after birth and is often associated with infections contracted before or during childbirth. On the other hand, LONS typically manifests 72 hours after birth and is commonly attributed to hospital-acquired infections or infections acquired within the community.[1–3]

Neonatal sepsis contributes significantly to morbidity and mortality among newborns, posing a significant health concern.[4] The estimated incidence of early-onset sepsis (EOS) in the United States was between 0.77 and 0.98 cases per 1,000 live births.[1] According to Shane et al.'s[5] study, the incidence of neonatal sepsis varies across different regions. In South Asia, the total incidence of culture-positive sepsis was 15.8 per 1,000 live births,[6] while in sub-Saharan Africa, it ranges from 6–21 cases per 1,000 live births.[7] The Middle East and North Africa region report an incidence of 1.8–12 cases per 1,000 live births, and in the Americas and Caribbean, it is reported as 2.9 cases per 1,000 live births.[7] In specific hospital settings, the incidence of neonatal sepsis can vary. At Dr. Cipto Mangunkusumo National Central General Hospital in Jakarta, from December 2006 to July 2007, neonatal sepsis with positive blood cultures was reported at 6.4%.[8] Similarly, at Sanglah Hospital Bali, from January 2010 to December 2010, neonatal sepsis

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was 5%, with a death rate of 30.4%.[9]

Diagnosing neonatal sepsis can present challenges due to the subtle and varying early signs of sepsis at different gestational ages.[10] Several risk factors contribute to developing neonatal sepsis, such as low birth weight, delivery in unsafe or unclean environments, prolonged rupture of membranes exceeding 18 hours, maternal fever, chorioamnionitis, prolonged labor, and perinatal asphyxia. Clinical symptoms of neonatal sepsis are often nonspecific, and although blood culture is the gold standard for diagnosis, it does not yield immediate results. Additionally, some infants may have received antibiotics before the blood culture, further complicating an early diagnosis.[11] Therefore, timely identification of sepsis in neonates is crucial, as the condition can progress rapidly and sometimes result in fatality.[10] This study aims to identify the risk factors associated with the development of EONS among patients delivered or referred to the neonatal care unit of Al Islam Hospital, Bandung.

Methods

The study design was a case-control retrospective observational study that evaluated the medical records of neonates who were admitted to the neonatal care unit of Al Islam Hospital Bandung from January 2020 to December 2022. A purposive sampling technique was used for participant selection. The inclusion criteria were neonates suspected of having bacterial sepsis with a gestational age of >26 weeks. Neonates with significant congenital abnormalities or syndromes (e.g., Down syndrome) and incomplete data were excluded. The data of all neonates diagnosed with suspected sepsis were reviewed, and sample characteristics such as sex, gestational age, birth weight, mode of delivery, parturient, and outcome were collected.

The sample population was divided into two groups: sepsis (proven and probable sepsis) and non-sepsis (suspected infection), which were analyzed between these two groups to assess the impact of independent variables including gestational age (GA), birth weight (BW), premature rupture of membranes (PROM), meconium amniotic fluid, APGAR score of 5 minutes, and the mother's white blood cell count elevation (>15,000/µl). Logistic regression analyses were employed to analyze the data. The collected data were presented in a distribution tabulation, and statistical analysis was performed using a computer-assisted statistical package (SPSS version 12.0). Chi-square and logistic regression analyses were employed to analyze the data. The calculation of risk factors involved calculating odds ratios and 95% confidence intervals. A p-value of less than 0.05 was considered statistically significant.

Diagnosing neonatal sepsis is based on risk factors, clinical findings, and laboratory data. The maternal and neonatal risk factors (EONS) assessed were gestational age <37 weeks, birth weight <2,500 grams, APGAR score <7 on the fifth minute (low APGAR scores), premature rupture of membranes >18 hours before birth, maternal body temperature >38°C intrapartum, the mother's white blood cell count elevations (>15,000/µl), and greenish-thick-and-foulsmelling amniotic fluid in the first 72 hours after birth.

Laboratory examinations include the following: blood cell examination, immature to total RA, value of C-reactive protein, and microbial blood culture. The total white blood cell count was obtained using the Mindray BC 5300 auto hematology analyzer and corrected for nucleated red blood cells. Differential counts were performed on Giemsa smears, and about 200 cells were counted. Hematology sepsis markers confirmed sepsis based on the following: (a) total white blood cell (WBC) count: <5,000/µl, >25,000/µl at birth, >30,000/µl 12–24 h, >21,000/µl day two onwards; (b) platelet count <150,000/µl; (c) immature to a total PMN ratio >0.120; and (d) value of C-reactive protein >6.0 mg/l. Bacteria in blood cultures with clinical and laboratory evidence of sepsis have been proven to have sepsis. Probable sepsis was defined as signs or symptoms of neonatal sepsis supported by two or more septic markers but without evidence of bacteria in the blood culture. Suspected infection was defined as the presence of risk factors for neonatal infection without any signs or symptoms of clinical sepsis.[8]

Results

Based on the data, the number of neonate births at Al Islam Hospital Bandung from January 2020 to December 2022 was 3,103 infants, with the number of neonates who met the inclusion and exclusion criteria in this study being 124 neonates. The diagnosis of sepsis was in 39 patients

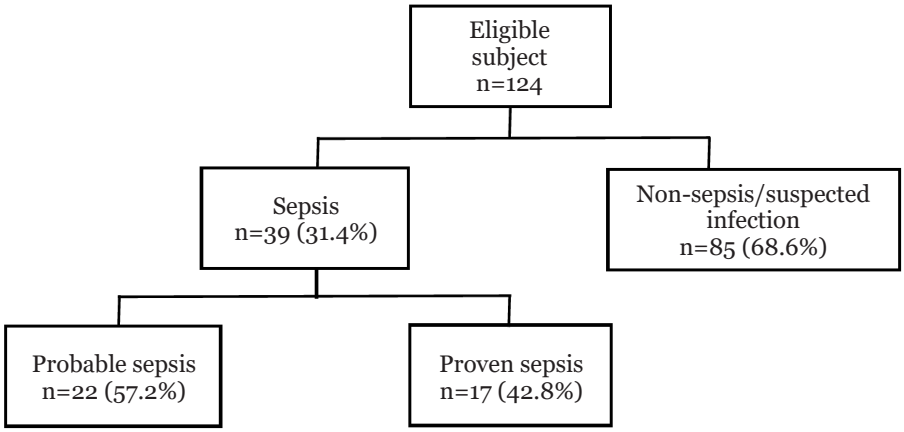

Figure Research Subject Distribution Schema

(50.8%) and no sepsis in 85 patients (49.2%). The incidence of EONS at Al Islam Hospital Bandung during the study was (39/3,103; 1.26%), and the mortality rate during the study was 18/124; 14.5%. Most deliveries were performed spontaneously (79, 63.7%). Most infants had a gestational age over 37 weeks (41, 33.1%) with a mean gestational age of 33.895 (SD=4.213). The birth weight majority were 1,500–2,499 grams (40, 32.25%) and more than 2,500 grams (40, 32.25%), with a mean birth weight of 2,012.22 (SD 884.71) grams—Table 1.

Based on the results of this study (Figure), 39 neonates met the inclusion criteria (sepsis), consisting of probable sepsis 22 (57.2%) and proven sepsis 17 (42.8%). The most common bacteria found were *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*.

Table 2 shows that based on bivariate analysis, the factors that were significantly associated with the occurrence of early-onset sepsis at Al Islam Hospital Bandung were LBW (p=0.027, 95% CI=0.184 to 0.902, OR=2.455), PROM more than 18 hours (p=0.000, 95% CI=4.359 to 26.582, OR=10.764), and the mother's white blood cell count elevation (>15,000/µl, p=0.002, 95% CI=1.560 to 7.622, OR=3.448). Meanwhile, other risk factors did not have a significant influence on the occurrence of EOS, such as gestational age <37 weeks (p=0.094, 95% CI=0.892 to 4.326, OR=1.964), meconium amniotic fluid (p=0.111, 95% CI=0.853 to 4.688, OR=2.000), and a 5-minute APGAR score <7 (p=0.372, 95% CI=0.578 to 4.341; OR=1.583).

Multivariate analysis results are shown in Table 3. The maternal factors significantly associated with bacterial EONS were premature rupture of membranes >18 hours (OR=0.096, 95% CI=0.036 to 0.255, p=0.000) and leukocytosis in the mother >15,000 (OR=0.283, 95% CI=0.112 to 0.718, p=0.008). The neonatal factors associated with bacterial EONS were BW (OR=1.358, 95% CI=0.196 to 9.427, p=0.757) and GA (OR=1.493, 95% CI=0.213 to 10.460, p=0.687). We decided on multivariate analysis that the risk factors were significantly associated (p-value<0.05), where all risk factors had an influence of 38.4% (Nagelkerke's R square=0.384) on early-onset neonatal sepsis.

Discussion

This research shows that the incidence of EONS at Al Islam Hospital Bandung is 1.26% of cases from 3,103 subjects. This incidence rate is higher than the report by Lusyati and Sauer[13] at Harapan Kita Hospital, Jakarta, around 1.4 cases per 1000 population, but still lower than the research by Suwarna et al.[14] at Dr. Hasan Sadikin General Hospital, Bandung, where the incidence of early-onset neonatal sepsis in 2018–2019 was 8.1% from 5,224 subjects. In our study, 17/124 (42.8%) subjects had bacterial-positive blood cultures, and 22/124 (57.2%) had probable sepsis. This research shows that positive blood cultures are higher than the research by Fitriana et al.[12] at Mohamad Hossein Hospital Palembang (42.8% vs 9.3%), but still lower than the research by Sianturi et al.[15] at Adam Malik Hospital, Medan (42.8% vs 66.1%). Meanwhile, Giannoni et al.,[16] in a previous study, identified blood culture-proven sepsis, 20% of whom had EONS and 62%

Table 1 Characteristics of Subjects

Variables	Sepsis		Non-sepsis		Total	
	n=39	50.8%	n=85	49.2%	n=124	100%
Gender						
Male	19	48.7	29	34.1	48	38.7
Female	20	51.3	56	65.9	76	61.3
Type of pregnancy						
Singleton	37	94.9	77	90.6	114	91.9
Gemeli	2	5.1	8	9.4	10	8.1
Mode of delivery						
Spontaneous	25	64.1	54	63.5	79	63.7
Caesarian section	13	33.3	30	35.3	43	34.7
Vacuum extraction	1	1.6	1	1.2	2	1.6
Birth weight (grams)						
Means (SD)	2,012.22 (884.71)					
<1,000 (extremely low BW)	6	15.4	8	9.4	14	11.3
1,000–1,499 (very low BW)	7	17.9	23	27.1	30	24.2
1,500–2,499 (low BW)	8	20.5	32	37.6	30	32.25
≥2,500	18	46.2	22	25.9	40	32.25
Gestational age (weeks)						
Means (SD)	33.895 (4.213)					
26–29+6 (very early preterm)	8	20.5	18	21.2	26	21.0
30–33+6 (early preterm)	6	15.4	28	32.9	34	27.4
34–36+6 (late preterm)	8	20.5	15	17.6	23	18.5
≥37 (term)	17	43.6	24	28.2	41	33.1
Parturient						
Primipara	15	38.5	27	31.8	42	33.9
Multipara	24	61.5	58	68.2	82	66.1
Mortalitas						
Dead	18	46.2	18	21.2	36	29.0
Alive	21	53.8	67	78.8	88	71.0

of whom had late-onset neonatal sepsis.

The mortality rate for neonatal sepsis in this study was 14.5%, much higher than other studies such as those by Lim et al.[17] at Chang Gung Memorial Hospital, China, where the case fatality rate in neonatal sepsis patients was 7.0% (11/158). In Indonesia, RSCM Jakarta reported that neonatal sepsis mortality was 14.18%.[9] Similar results were reported at Moewardi Hospital Surakarta, which found that the neonatal sepsis mortality rate was 40%.[18] Various factors can explain differences in mortality rates in neonatal sepsis between countries. Including economic, geographic, and social-racial factors, using ventilators and incubators, and exposure to different microorganisms and antibiotics.[4] While advancements in neonatal intensive care have decreased the impact of EONS among full-term infants, the risk of EONS and its consequences remains high for preterm infants. Additionally, very-low-birth-weight (VLBW) infants are susceptible to late-onset (healthcare-associated) sepsis.[4] Among infants born at 37 weeks gestation or more, the incidence of EONS is approximately 0.53 cases per 1,000 live births. However, in the preterm population, the incidence is significantly higher at 3.7 cases per 1,000 live births (seven times higher). Among VLBW infants, the incidence escalates to approximately 11 cases per 1,000 live births (20 times higher).[1]

Birth weight and mortality showed significant differences in the characteristics of the sepsis and non-septic groups. Neonates with birth weight <2,500 grams were found in 36 patients (57.14%) with a p-value of 0.003, similar to research by Suwarna et al.[14] at Dr. Hasan Sadikin General Hospital, Bandung, where there was a significant relationship between birth weight <2,500 grams

Table 2 Risk Factors for Early-onset Sepsis (Bivariate Test)

Variables	EOS		No EOS		OR	95% CI		p
	n=39	%	n=85	%				
Gestational age (weeks)								
<37	22	58.4	61	66.9	1.964	0.892	4.326	0.094
≥37	17	43.6	24	33.1				
Birth weight (grams)								
<2,500	21	53.8	63	74.1	2.455	0.184	0.902	0.027*
≥2,500	18	46.2	22	25.9				
Premature rupture of membranes (hours)								
<18	15	38.5	74	87.1	10.764	4.359	26.582	0.000*
≥18	24	61.5	11	12.9				
Meconeal amniotic fluid								
No	26	66.7	68	80.0	2.000	0.853	4.688	0.111
Yes	13	33.3	17	20.0				
APGAR score 5 minutes								
>7	6	15.4	19	22.4	1.583	0.578	4.341	0.372
≤7	33	84.6	66	77.6				
Mother's white blood cell (/µl)								
<15,000	14	35.9	56	65.9	3.448	0.156	7.622	0.002*
≥15,000	15	64.1	29	34.1				

Note: EOS: early-onset sepsis, *significance p<0.05

and the incidence of neonatal sepsis (p-value 0.001). Neonates weighing <2,500 grams have a 1.42 times higher risk of experiencing neonatal sepsis compared to babies weighing the same or more than 2,500 grams. This is because babies with low birth weight are mostly born prematurely, have difficulty eating, lose heat quickly, have low glucose levels, and are at greater risk of experiencing hypoglycemia. Apart from physiological factors, neonates with low birth weight are closely related to other risk factors for neonatal sepsis, such as a history of maternal infection, premature rupture of membranes >24 hours, prematurity, and asphyxia.[1,4]

Based on bivariate analysis in this study, the following were significantly associated with the occurrence of EONS: LBW (p=0.027, 95% CI=0.184 to 0.902, OR=2.455), PROM (p=0.000, 95% CI=4.359 to 26.582, OR=10.764), and the mother's white blood cell count elevation (p=0.002, 95% CI=1.560 to 7.622, OR=3.448), with a multivariate analysis, with an influence of 38.4%. A case-control study in Tanzania found the following maternal risk factors to be associated with bacterial EONS: chorioamnionitis (OR=1.9), HIV (OR=2.9), premature rupture of membranes >18 hours (OR=2.8), cloudy amniotic fluid (OR=3.2), foul-smelling amniotic fluid (OR=4.2), and vaginal examination during the delivery process (OR=5.9). The neonatal risk factors associated with EONS were <37 weeks gestational age (OR=1.5), newborn weight risk (OR=1.5),

Table 3 Risk Factors for Early-onset Sepsis (Multivariate Test)

Variables	B	S.E	Wald	OR	95%CI		p
BW	0.306	0.988	0.096	1.358	0.196 to	9.427	0.757
GA	0.401	0.993	0.163	1.493	0.213 to	10.460	0.687
PROM	−2.344	0.498	22.121	0.096	0.036 to	0.255	0.000
Leukocytosis	−1.262	0.475	7.060	0.283	0.112 to	0.718	0.008
Constant	1.738	0.510	11.604	5.683			0.001

Note: EOS: early-onset sepsis, *significance p<0.05

fetal distress (OR=1.6), and perinatal asphyxia (OR=6.7).[19] In Utomo's[20] study, it was found that risk factors with a significant relationship included low birth weight, premature gestational age, SC birth, and meconium amniotic fluid p-value <0.05. Babies with low birth weight and premature birth are at risk of immunodeficiency, thereby predisposing them to sepsis. LBW and premature conditions also tend to require invasive procedures and close monitoring, so there is a risk of nosocomial infections, which can lead to sepsis.

Premature rupture of membranes carries the risk of "prolonged leakage" of amniotic fluid, thereby increasing the risk of ascending bacterial infection from the urinary tract, proven by the presence of leukocytosis. Microorganisms from the vagina can infect the amniotic sac ascendingly, resulting in infection of the baby in utero.[21,22] The results of this study are similar to the research of Shifera et al.,[22] where it was found that PROM had a significant relationship with neonatal sepsis, especially in PROM >18 hours; the incidence of sepsis was five times higher. Meanwhile, in Fitriana et al.'s[12] study at Mohamad Hossein Hospital Palembang, Suwarna et al.'s[14] study at Hasan Sadikin General Hospital Bandung, and Wilar et al.'s[23] study at Kandau Hospital Manado, premature rupture membranes >18 hours were significantly associated with bacterial early onset sepsis (OR=4.46, 95% CI=1.35 to 14.71, p=0.008), (OR=1.69, 95% CI=1.27 to 2.25, p=0.001), and (OR=1.41, 95% CI=1.24 to 1.59, p=0.002), respectively. However, in Utomo's[20] study, there was no correlation between premature membrane rupture and sepsis. Some factors may contribute to this finding, such as the patient's history and the fact that there was no correlation between premature rupture of the membrane and sepsis. Some factors may contribute to this finding, such as the patient's history and the fact that the patient didn't remember when the membrane ruptured. This condition also indicates that the post-delivery antibiotic always given in the PROM neonate as a standard procedure can decrease the risk of neonatal sepsis.[1]

Our study found that the mother's white blood cell count elevation (>15,000/µl) had a significant relationship with a 3.4 times higher incidence of EONS (OR=3.448, 95% CI=1.560 to 7.622, p=0.002). Meanwhile, Fitriana et al.'s[12] study at Mohamad Hossein Hospital Palembang had no significant relationship to EONS (OR=1.74, 95% CI=0.53 to 5.73, p=0.357).8 The cause of early-onset sepsis in this study was *Staphylococcus epidermidis* and *Staphylococcus haemolyticus*. According to Juniatiningsih et al.'s[8] study at Dr. Cipto Mangunkusumo National Central General Hospital Jakarta and Sianturi et al.'s[15] study at Adam Malik Hospital Medan, the cause of EONS were generally Gram-negative bacteria, 80.5%, and 54,5%, respectively, such as *Acinetobacter calcoaceticus*, *Enterobacter aerogenes*, *Pseudomonas* sp., *Escherichia coli*.[8] and *Staphylococcus epidermidis*, *Pseudomonas* sp.[15] Meanwhile Hafidz et al.'s[24] study at Hasan Sadikin General Hospital Bandung, blood cultures were obtained *Staphylococcus hemolytic*, *Staphylococcus aureus*, *Staphylococcus hominis*, and *Klebsiella pneumoniae*.

Conclusions

There was a significant bivariate relationship between LBW, PROM, and the mother's white blood cell count elevation. Simultaneously, there was a significant relationship between the risk factors for the incidence of EONS, with an effect of 38.4%.

Conflict of Interest

All authors stated that this study had no conflict of interest.

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References

1. Gomella TL, Eyal FG, Bany-Mohammed F, editors. Gomella's neonatology: Management, procedures, on-call problems, diseases, and drugs. 8th edition. New York: McGraw-Hill Education; 2020.
2. Kuzniewicz MW, Mukhopadhyay S, Li S, Walsh EM, Puopolo KM. Time to positivity of neonatal blood cultures for early-onset sepsis. Pediatr Infect Dis J. 2020;39(7):634–40.
3. Kucova P, Kantor L, Fiserova K, Lasak J,

Röderova M, Kolar M. Bacterial pathogens and evaluation of a cut-off for defining early and late neonatal infection. Antibiotics (Basel). 2021;10(3):278.
4. Poupolo KM. Bacterial and fungal infection. In: Eichenwald EC, Hansen AR, Martin CR, Stark AR, Jain N, editors. Cloherty and Stark's manual of neonatal care. South Asian edition. New Delhi: Wolters Kluwer; 2021. p. 743–76.
5. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017;390(10104):1770–80.
6. Li J, Shen L, Qian K. Global, regional, and national incidence and mortality of neonatal sepsis and other neonatal infections, 1990–2019. Front Public Health. 2023;11:1139832.
7. Stoll BJ. Neonatal infections: a global perspective. In: Remington JS, Klein JO, editors. Infectious diseases of the fetus and newborn infant. 5th edition. Philadelphia: Elsevier Saunders; 2001. p. 141.
8. Juniatiningsih A, Aminullah A, Firmansyah A. Profil mikroorganisme penyebab sepsis neonatorum di Departemen Ilmu Kesehatan Anak Rumah Sakit Cipto Mangunkusumo Jakarta. Sari Pediatri. 2008;10(1):60–5.
9. Putra PJ. Insiden dan faktor-faktor yang berhubungan dengan sepsis neonatus di RSUP Sanglah Denpasar. Sari Pediatri. 2012;14(3):205–10.
10. Narasimha A, Harendra Kumar ML. Significance of hematological scoring system (HSS) in early diagnosis of neonatal sepsis. Indian J Hematol Blood Transfus. 2011;27(1):14–7.
11. Yadav P, Kumar Yadav S. Progress in diagnosis and treatment of neonatal sepsis: a review article. J Nepal Med Assoc. 2022;60(247):318–24.
12. Fitriana L, Ramadanti A, Indrayady I. Scoring model to predict early-onset bacterial sepsis at Dr. Mohammad Hoesin Hospital, Palembang. Paediatr Indones. 2023;63(1):29–36.
13. Lusyati S, Sauer PJJ. Sepsis neonatal di NICU RSAB Harapan Kita Jakarta. Sari Pediatri. 2007;9(3):173–7.
14. Suwarna NO, Yuniati T, Cahyadi AI, Achmad TH, Agustian D. Faktor risiko kejadian sepsis neonatorum awitan dini di RSUP Dr. Hasan Sadikin Bandung. Sari Pediatri. 2022;24(2):99–105.
15. Sianturi P, Hasibuan BS, Lubis BM, Azlin E, Tjipta GD. Profil sepsis neonatus di Unit Perawatan Neonatus RSUP H Adam Malik Medan tahun 2008–2010. Sari Pediatri. 2012;14(2):67–72.
16. Giannoni E, Agyeman PKA, Stocker M, Posfay-Barbe KM, Heininger U, Spycher BD, et al.; Swiss Pediatric Sepsis Study. Neonatal sepsis of early onset, and hospital-acquired and community-acquired late onset: a prospective population-based cohort study. J Pediatr. 2018;201:106–114.e4.
17. Lim WH, Lien R, Huang YC, Chiang MC, Fu RH, Chu SM, et al. Prevalence and pathogen distribution of neonatal sepsis among very-low-birth-weight infants. Pediatr Neonatol. 2012;53(4):228–34.
18. Hafidh Y, Hidayah D, Sunyataningkamto S. Factors affecting mortality of neonatal sepsis in Moewardi Hospital, Surakarta. Paediatr Indones. 2007;47(2):74–7.
19. Masanja PP, Kibusi SM, Mkhoi ML. Predictors of early onset neonatal sepsis among neonates in Dodoma, Tanzania: a case control study. J Trop Pediatr. 2020;66(3):257–66.
20. Utomo MT. Risk factors of neonatal sepsis: a preliminary study in Dr. Soetomo Hospital. IJTID. 2010;1(1):23–6.
21. Joseph CJ, Lian WB, Yeo CL. Nosocomial infections (late onset sepsis) in the neonatal intensive care unit (NICU). Proc Singap Healthc. 2012;21(4):238–44.
22. Shifera N, Dejenie F, Mesafint G, Yosef T. Risk factors for neonatal sepsis among neonates in the neonatal intensive care unit at Hawassa University Comprehensive Specialized Hospital and Adare General Hospital in Hawassa City, Ethiopia. Front Pediatr. 2023;11:1092671.
23. Wilar R, Kumalasari E, Suryanto DY, Gunawan S. Faktor risiko sepsis awitan dini. Sari Pediatri. 2010;12(4):265–9.
24. Hafidz A, Yuniati T, Solek P. Neopterin serum as early predictor of poor outcome in neonatal sepsis. GMHC. 2017;5(3):241–6.