


Bacterial Patterns and Sensitivity to Antibiotics in Neonatorum Sepsis Patients at Dr. M. Djamil Padang General Hospital in the Period 2018–2021

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Article Info	ABSTRACT
<p>Keywords: Neonatal Sepsis, bacteria, sensitivity test</p>	<p>Neonatal sepsis is one of the leading causes of morbidity and mortality in neonates. Bacteria are the most common cause of neonatal sepsis. The appropriate empirical therapy is given based on the bacterial pattern and sensitivity at the site. The appropriate use of empirical antibiotics can help reduce the neonatal mortality rate. This study aimed to evaluate bacterial patterns and antibiotic sensitivity in neonatal sepsis patients at RSUP Dr. M. Djamil Padang period 2018-2021. This study is a descriptive study that used a total sampling method with 63 samples that met the inclusion criteria. The results showed that neonatal sepsis was most commonly found in neonates aged 4-28 days, which were mostly male, had a birth weight < 2500 grams, had a mortality rate of 25.4%, and neonatal pneumonia was the most comorbid disease. The most common causative bacteria were <i>Klebsiella pneumoniae</i> and <i>Staphylococcus haemolyticus</i>. <i>Klebsiella pneumoniae</i> is sensitive to amikacin, tigecycline, meropenem, and ertapenem. <i>Staphylococcus haemolyticus</i> was sensitive to tigecycline, nitrofurantoin, vancomycin, linezolid, and quinupristin / dalfopristin. This study concluded that the most common bacteria causing neonatal sepsis were <i>Klebsiella pneumoniae</i> and <i>Staphylococcus haemolyticus</i>. <i>Klebsiella pneumoniae</i> was sensitive to amikacin, tigecycline, meropenem, and ertapenem. <i>Staphylococcus haemolyticus</i> was sensitive to tigecycline, nitrofurantoin, vancomycin, linezolid, and quinupristin / dalfopristin. Clinicians are expected to review the clinical practice guidelines for neonatal sepsis to suit bacterial patterns and their sensitivity to antibiotics.</p>
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INTRODUCTION

Sepsis is a clinical syndrome caused by dysregulation systemic inflammatory response to infection. Sepsis is one of the leading causes of neonatal morbidity and mortality worldwide. (Plunkett & Tong, 2015). Neonatal sepsis is a clinical syndrome with symptoms of systemic

infection followed by bacteremia and occurs in the first month of life. (Nizet & Klein, 2011). According to United Nations data Inter-agency Group for Child Mortality Estimates (UN IGME), there were 5 million children worldwide who died before reaching the age of 5 years in 2020. Half of these deaths occurred during the neonatal period. (UN IGME, 2021). Severe neonatal infections, including sepsis, are a significant cause of neonatal mortality and long-term morbidity. According to World Health Organization data Organization (WHO), there are around 1.3 to 3.9 million cases of neonatal sepsis annually and in 2018, around 15% of all neonatal deaths worldwide were caused by sepsis. (WHO, 2020). The incidence of neonatal sepsis is higher in developing countries. compared to developed countries (Aminullah, 2014). In Indonesia, according to data from the Indonesian Ministry of Health in 2019, neonatal sepsis became reason fourth most death neonates (703 cases) (Indonesian Ministry of Health, 2020).

In the Perinatology Unit of Haji Adam Malik General Hospital, Medan in 2015-2016, there were 154 neonates confirmed with neonatal sepsis with positive blood cultures, consisting of 94 males and 60 females. (Hasibuan, 2018). According to the time of appearance of signs and symptoms, neonatal sepsis is divided into sepsis neonatorum early onset that occurs less than 72 hours after birth which is generally caused by vertical transmission from mother to baby and sepsis neonatorum Late onset occurs after 72 hours of life and is generally caused by environmental or hospital transmission. (Voller & Myers, 2016). Sepsis can be caused by various microorganisms and bacteria is the most common cause of neonatal sepsis (Efendi, 2013). Based on research at Haji Adam Malik General Hospital Medan, the bacteria that most often cause infections were found to be *Staphylococcus*. sp, *Pseudomonas* sp and *Enterobacter* sp. These bacteria are sensitive to vancomycin, amikacin, and meropenem. (Sianturi et al., 2012).

Pathogenic bacteria that cause sepsis differ in each country and also in each hospital, so this affects the choice of antibiotic therapy. The choice of antibiotics must be based on the bacteria that cause the infection obtained from blood cultures and the results of antibiotic sensitivity tests against the bacteria. However, culture and sensitivity tests take a long time (48–72 hours). In neonatal sepsis, antibiotics must be given as soon as possible, so as a guideline for giving empirical antibiotics without waiting for the results of culture and sensitivity tests that are quite long, the pattern of bacteria that cause sepsis and sensitivity to antibiotics must be known. (Mayetti & Imilda, 2016).

Appropriate empirical therapy should be based on the bacterial pattern and sensitivity at the site. Bacterial patterns and their sensitivity to antibiotics can change due to the large number of bacteria that are resistant to certain antibiotics, so identification of bacterial patterns needs to be done periodically to choose the appropriate antibiotic. Therefore, it is necessary to conduct research to determine the bacterial pattern and sensitivity to antibiotics in patients with neonatal sepsis at Dr. M. Djamil Padang General Hospital for the period 2018-2021 with the aim of reducing morbidity and mortality in neonates.

RESEARCH METHODS

This type of research is descriptive research. This research was conducted at the Medical

Records Installation and Microbiology Laboratory of Dr. M. Djamil Padang General Hospital from December 2022 – February 2023. The sample in this study was taken using the total sampling technique. The population in this study were patients diagnosed with neonatal sepsis by pediatricians who were treated at the Perinatology of Dr. M. Djamil Padang General Hospital in the period 2018-2021. The sample in this study included all populations listed in the medical records that met the inclusion and exclusion criteria. The inclusion criteria were all neonates diagnosed with neonatal sepsis by pediatricians at the Perinatology of Dr. M. Djamil Padang General Hospital in the period 2018-2021 and patients with positive blood culture results. The exclusion criteria were microorganisms that cause neonatal sepsis that are not bacteria.

RESULTS AND DISCUSSION

Total sample in this study were 272 patients diagnosed with neonatal sepsis in 2018-2021. The excluded samples were 209 samples (76.8%), so that those that met the inclusion and exclusion criteria in this study were 63 samples (23.2%) diagnosed with neonatal sepsis with positive culture results.

Neonatal Sepsis Patients

Table 1. Characteristics Neonatal Sepsis Patients

Characteristics	n (n=63)	%
Age		
0-3 days	19	30.2
4-28 days	44	69.8
Gender		
Man	32	50.8
Woman	31	49.2
Birth Weight		
< 2500 grams	40	63.5
2500-4000 grams	21	33.3
> 4000 grams	2	3.2
Mortality		
Life	47	74.6
Die	16	25.4
Disease companion (n=60)		
Neonatal pneumonia	23	38.3
<i>Hyaline membrane disease</i>	12	20.0
<i>Transient tachypnea of the newborn</i>	6	10.0
<i>Neonatal jaundice</i>		
<i>Omphalocele</i>	7	11.7
<i>Necrotizing enterocolitis</i>	3	5.0
Jejunioileal atresia	2	3.3
Esophageal atresia	2	3.3

Characteristics	n (n=63)	%
Malformation anorectal	1	1.7
<i>Multiple congenital anomalies</i>	1	1.7
<i>Hirschsprung's disease</i>	1	1.7
<i>Neonatal seizure</i>	1	1.7
	1	1.7

Based on Table 1, it was found that that neonatal sepsis patients with positive culture results that meet criteria the most inclusion and exclusion aged 4-28 days (69.8%). Research This in line with study Apriliana at Abdul Muluk Hospital, Bandar Lampung, who discovered that the most frequent incidence of neonatal sepsis found in neonates age over 4 days (79%) (Apriliana et al., 2013). The incidence of sepsis onset slow usually due to Because horizontal transmission of bacteria after baby born from environment around or House sick (infection) nosocomial). Factors that increase risk onset of sepsis slow related with environment maintenance baby like a baby's age treated, room care, prolonged parenteral nutrition, infections originating from from tool maintenance babies, and procedures invasive, such as taking sample too much blood frequent, intubation, ventilation mechanics, and installation catheter (Odabasi & Bulbul, 2020).

Based on type sex neonatal sepsis patients were mostly male (50.8%). The results of the study This similar with research conducted Cool in 2019 at Prof. Dr. RD Kandou Manado General Hospital which received that neonatal sepsis is more many in men namely 22 people (55%) while Woman namely 18 people (45%) (Kereh et al., 2019). By theoretical mentioned that baby man own risk of sepsis is twice as high big than baby women. This is associated with role sex-linked factors in susceptibility host to infection. Genes located on the X chromosome affect function gland thymus and synthesis immunoglobulin, the presence of two chromosomes produce diversity more genetic big for defense immunology Woman (Aminullah, 2014).

Birth weight the most neonatal sepsis patients is heavy born low namely < 2500 grams (63.5%). Research results This in line with Fauzi 's 2020 research at Dr. Sardjito General Hospital, Yogyakarta, found that that neonatal sepsis is common experienced neonate with birth weight < 2500 grams, namely 46 patients (73.02%).² Babies with birth weight low at risk tall experiencing neonatal sepsis because of Not yet perfect level maturity of body organs like liver, lungs, digestion and brain so that baby with birth weight low often experience complications and can end with death.²²

In the research this is also obtained that neonatal sepsis mortality rate of 25.4% and patients who survived by 74.6%. The results of the study This in line with Nainggolan's research at H Adam Malik General Hospital, Medan, which found that patient with neonatal sepsis that is not die as many as 57 people (70.4%) and patients who died as many as 22 people (29.6%) (Nainggolan, 2016). Fast and appropriate handling of sepsis through diagnosis and identification reason with fast, eliminate source infection, administration antibiotics empirically correct, preventing things pathogenic which can cause septic shock and prevent organ damage can lower number morbidity and mortality neonate (Faridah et al.,

2016).

Disease many companions found in neonatal sepsis patients in the study This is neonatal pneumonia of 23 people (36.5%). The results of the study This in line with Fauzi 's 2020 research at Dr. Sardjito General Hospital, Yogyakarta, found that that disease accompanying most was pneumonia amounting to 27 cases (84.38%) followed by with omphalitis amounted to 3 cases (9.38%) (Fauzi et al., 2020). Symptoms that make neonate treated with sepsis suspect is congested breath, lethargy, hypothermia, and symptoms in the respiratory tract digestion. Shortness of breath breath become common symptoms appeared in neonatal sepsis patients (Roeslani et al., 2013). Symptoms it can also be occurs in neonatal pneumonia patients. In a journal mentioned that manifestation clinical sepsis and pneumonia are interrelated overlap overlap and have organ involvement and regimen treatment similar empirical (Nissen, 2007).

Bacterial Pattern Causes of Neonatal Sepsis

Table 2. Bacteria Causes of Neonatal Sepsis

Microorganism	Species	n (n=63)	%
Gram Negative Bacteria	<i>Klebsiella pneumoniae</i>	18	28,6
	<i>Acinetobacter baumannii</i>	4	6,3
	<i>Enterobacter cloacae complex</i>	3	4,8
	<i>Moraxella group</i>	1	1,6
	<i>Acinetobacter sp.</i>	1	1,6
	<i>Enterobacter aerogenes</i>	1	1,6
	<i>Pantoea sp.</i>	1	1,6
	<i>Pseudomonas stutzeri</i>	1	1,6
	<i>Burkholderia cepacia</i>	1	1,6
	<i>Serratia marcescens</i>	1	1,6
	<i>Pseudomonas fluorescens</i>	1	1,6
Gram Positive Bacteria	<i>Staphylococcus haemolyticus</i>	17	27,0
	<i>Staphylococcus epidermidis</i>	9	14,3
	<i>Staphylococcus capitis</i>	2	3,2
	<i>Staphylococcus cohnii</i>	1	1,6
	<i>Staphylococcus saprophyticus</i>	1	1,6

Based on Table 2 it is known that that the most abundant bacteria found is *Klebsiella pneumoniae* as many as 18 samples (28.6%) and *Staphylococcus haemolyticus* as many as 17 samples (27.0%), followed by *Staphylococcus epidermidis* as many as 9 samples (14.3%) and *Acinetobacter baumannii* as many as 4 samples (6.3%). The results of the study This in line with study The Matondang in 2021 at H Adam Malik General Hospital Medan which found that the most abundant bacteria found is *Klebsiella pneumoniae* (34.1%), followed *Acinetobacter baumannii* (29.3%) and *Escherichia coli* (12.2%) (Matondang, 2021). Research results this is also in line with study Giofani who discovered bacteria most causes of neonatal sepsis at Arifin Achmad Regional Hospital, Riau Province sequentially that is *Coagulase-negative Staphylococci* (CoNS) as many as 24 samples (35.3%), *Serratia marcessens* as

many as 9 samples (13.2%), and *Acinetobacter baumannii* as many as 5 samples (7.3%) (Giofani, R; Oyong, 2016). *Klebsiella pneumoniae* is Gram- negative bacteria that are shaped rod-shaped, non- motile, and classified as bacteria optional anaerobic, and many found in the mouth, skin and intestines as normal flora *Klebsiella pneumoniae* is pathogen opportunistic gram- negative bacteria that are capable of colonize, invade, and cause infections in various place anatomy body man. Bacteria This can causes sepsis and meningitis in neonates and infants premature and infection serious about children with disturbance system immune, and can cause infection channel Urinary tract infection nosocomial (Piperaki et al., 2017).

Staphylococcus haemolyticus is part from the normal flora of the skin and one of the species main CoNS. Species This contributes 10-20% of infection clinical CoNS. CoNS moment This is one of pathogen nosocomial main, with *Staphylococcus epidermidis*, *Staphylococcus cohnii*, and *Staphylococcus haemolyticus* become the most prominent species (Assa et al., 2020). There are several infection clinically caused *Staphylococcus haemolyticus* infection among them bacteremia, meningitis, infection eye, infection skin, peritonitis, infection channel urinary tract infection and nosocomial (Eltwisy et al., 2022).

Sensitivity Pattern Bacteria Causes of Neonatal Sepsis Antibiotics

Table 3. Sensitivity Patterns Gram Negative Bacteria to Antibiotics in Neonatal Sepsis Patients at Dr. M. Djamil Padang General Hospital 2018-2021 Period

Antibiotics	Bacteria	
	K. pneumoniae (n=18)	A. baumannii (n=4)
	% sensitive	
Ampicillin	0	
Amikacin	100	100
Aztreonam	0	
Ceftazidime	0	25
Ciprofloxacin	66.7	75
Ceftriaxone	0	25
Cefazolin	0	0
Ertapenem	94.4	
Cefepime	27.8	50
Nitrofurantoin	44.4	
Gentamicin	0	75
Meropenem	94.4	50
Ampicillin/Sulbactam	0	50
Trimethoprim/ Sulfamethoxazole	72.2	50
Tigecycline	94.4	100
Piperacillin/Tazobactam	66.7	75

Table 4. Sensitivity Patterns Gram Positive Bacteria to Antibiotics in Neonatal Sepsis Patients at Dr. M. Djamil Padang General Hospital 2018-2021 Period

Antibiotics	Bacteria	
	S. haemolyticus (n=17)	S. epidermidis (n=9)
	% sensitive	
Ciprofloxacin	11.8	22.2
Clindamycin	11.8	22.2
Erythromycin	0	0
Nitrofurantoin	94.1	100
Gentamicin	11.8	33.3
Levofloxacin	11.8	22.2
Linezolid	88.2	100
Moxifloxacin	11.8	22.2
Oxacillin	5.9	11.1
Benzylpenicillin	0	0
Quinupristin / Dalfopristin	82.4	100
Rifampicin	35.3	66.7
Trimethoprim/ Sulfamethoxazole	70.6	66.7
Tetracycline	64.7	77.8
Tigecycline	100	100
Vancomycin	88.2	100

Tables 3 and 4 show pattern sensitivity Gram negative and Gram positive bacteria to antibiotics. Based on Table 3, it was obtained that sensitivity gram negative bacteria to antibiotics highest is *Klebsiella pneumoniae* is sensitive to *amikacin* (100%), *tigecycline* (94.4%), meropenem (94.4%), and ertapenem (94.4%). While That Based on Table 4, it was found that that sensitivity gram positive bacteria to antibiotics highest is *Staphylococcus haemolyticus* sensitive to *tigecycline* (100%), nitrofurantoin (94.1%), *vancomycin* (88.2%), linezolid (88.2%), and quinupristin / dalfopristin (82.4%).

In the research The Matondang in 2021 at H Adam Malik General Hospital was found that *Klebsiella pneumoniae* sensitive against tigecycline (100%) and fosfomycin (100%) (Matondang, 2021). In Nazir's research at *the Department of Microbiology, Government Medical College, India*, it was found that *Coagulase-negative Staphylococci* (CoNS) of which 44.64% are *Staphylococcus haemolyticus* sensitive to linezolid, *vancomycin*, and *tigecycline* (Nazir, 2019). Research results This show number excellent tigecycline sensitivity to bacteria reason most neonatal sepsis, namely *Klebsiella pneumoniae* and *Staphylococcus hemolytic* with number sensitivity > 94%. Tigecycline is active glycylycline oppose Lots Gram positive and negative microorganisms aerobic and anaerobic, and microorganisms atypical (Cercenado, 2007). In the research This *Klebsiella pneumonia* also have high sensitivity to *amikacin*, meropenem, and ertapenem. *Amikacin* is one of antibiotics group aminoglycosides

that work with hinder bacterial protein synthesis with bound with ribosome bacteria and have good activity in oppose gram negative bacteria (Sizar et al., 2022). Carbapenems (meropenem and ertapenem) are part from antibiotics β - lactam which has spectrum wide range of activities to Lots Gram positive and Gram negative bacteria that work with hinder biosynthesis wall cell bacteria (Armstrong et al., 2021). In this study This *Staphylococcus haemolyticus* also have high sensitivity to nitrofurantoin, *vancomycin*, linezolid, and quinupristin / dalfopristin. *Vancomycin* is antibiotics glycopeptides that provide effect bactericide with hinder synthesis wall cell bacteria. *Vancomycin* is antibiotics spectrum area that has activity against MRSA and in general used For infection weight caused gram positive bacteria ("Vancomycin," 2020).

Antibiotics empirical methods used in the Perinatology Unit of Dr. M. Djamil Padang Hospital, namely ampicillin sulbactam plus gentamicin as therapy line First, cefoperazone sulbactam as line second, and meropenem as line third. In a study at Prof. DR. RD Kandou Manado General Hospital, it was found that that therapy empirical therapy given to neonatal sepsis patients is combination of ampicillin and gentamicin as antibiotics line First. Antibiotics line second namely ceftazidime and amikacin, whereas antibiotics line the third given is meropenem (Kereh et al., 2019). In the study This obtained that gram negative bacteria resistant to antibiotics line First, namely ampicillin sulbactam and gentamicin, and Gram positive bacteria were also found resistant to gentamicin. *Klebsiella pneumoniae* can produce enzyme betalactamase so that can hydrolyze ring beta- lactams found in antibiotics betalactam, in addition That bacteria this also has urease enzyme and enzyme citric permiase so that cause resistance to antibiotics penicillin, cephalosporin, and aztreonam (Tarina & Kusuma, 2017). *Staphylococcus haemolyticus* including in group ConS considered nature resistant to various type antibiotics, such as beta- lactam groups, gentamicin, erythromycin, and ciprofloxacin (Eltwisy et al., 2022).

CONCLUSION

Based on the results of this study, it was concluded that neonatal sepsis is most commonly found in neonates aged 4-28 days, the most common gender is male, the most common birth weight is <2500 grams, the mortality rate is 25.4%, and the most common comorbidity is neonatal pneumonia. The bacteria that cause neonatal sepsis that are most commonly found are *Klebsiella pneumoniae* and *Staphylococcus haemolyticus*. *Klebsiella pneumoniae* is sensitive to amikacin, tigecycline, meropenem, and ertapenem. *Staphylococcus haemolyticus* is sensitive to tigecycline, nitrofurantoin, vancomycin, linezolid, and quinupristin / dalfopristin.

REFERENCES

- Aminullah, A. (2014). Sepsis pada bayi baru lahir. In *Buku Ajar Neonatologi* (1st ed., pp. 170–187). IDAI.
- Apriliana, E., Rukmono, P., Erdian, D., & Tania, F. (2013). Bakteri penyebab sepsis neonatorum dan pola kepekaannya terhadap antibiotika. *Seminar Nasional Sains & Teknologi V, November*, 583–590.
- Armstrong, T., Fenn, S., & Hardie, K. (2021). JMM Profile: Carbapenems: a broad-spectrum

- antibiotic. *Journal of Medical Microbiology*, 70(12), 0–4.
<https://doi.org/10.1099/jmm.0.001462>
- Assa, N., Artana, I., Kardana, I., Putra, P., & Sukmawati, M. (2020). The characteristics of neonatal sepsis in Low Birth Weight (LBW) infants at Sanglah General Hospital, Bali, Indonesia. *Intisari Sains Medis*, 11(1), 172–178.
<https://doi.org/10.15562/ism.v11i1.522>
- Cercenado, E. (2007). Tigecycline: A new antimicrobial agent against multiresistant bacteria. *Therapy*, 4(3), 255–270.
- Efendi, S. (2013). Sepsis neonatal; Penatalaksanaan terkini serta berbagai masalah dilematis. *Simposium Ilmiah Dan Workshop Meet The Professor*.
- Eltwisy, H., Twisy, H., Hafez, M., Sayed, I., & El-Mokhtar, M. (2022). Clinical infections, antibiotic resistance, and pathogenesis of *Staphylococcus haemolyticus*. *Microorganisms*, 10(6).
- Faridah, N., Machlaurin, A., & Subagijo, P. (2016). Analisis efektivitas biaya penggunaan antibiotik terhadap pasien sepsis pediatrik di Rawat Inap RSD dr. Soebandi Kabupaten Jember pada tahun 2014. *E-Jurnal Pustaka Kesehatan*, 4(2), 255–262.
- Fauzi, R., Nuryastuti, T., & Puspitasari, I. (2020). Analisis faktor resiko sepsis neonatal terhadap clinical outcome di Neonatal Intensive Care Unit (NICU). *Indonesian Journal of Hospital Administration*, 3(2), 86–93.
- Giofani, R; Oyong, N. I. (2016). Evaluation usage of antibiotic to sepsis neonatus patient in RSUD Arifin Achmad Province Riau. *Jurnal Online Mahasiswa Fakultas Kedokteran*, 3(2), 1–22.
- Hasibuan, B. (2018). Comparison of microbial pattern in early and late onset neonatal sepsis in referral center Haji Adam Malik hospital Medan Indonesia. *IOP Conference Series: Earth and Environmental Science*, 125(1), 3–8.
- Kemendes RI. (2020). *Profil kesehatan Indonesia tahun 2019*. Kementerian Kesehatan Republik Indonesia.
- Kereh, T., Wilar, R., & Tatura, S. (2019). Analisis penggunaan antibiotik pada pasien sepsis neonatorum di Neonatal Intensive Care Unit RSUP Prof. Dr. R. D. Kandou Manado. *E-Clinic*, 8(1), 21–26.
- Matondang, H. (2021). *Gambaran pola kuman pada bayi baru lahir dengan sepsis neonatorum di Unit Neonatologi Rumah Sakit Haji Adam Malik Medan tahun 2020*. Universitas Sumatera Utara.
- Mayetti, M., & Imilda, I. (2016). Pola bakteriologis dan uji sensitivitas pada sepsis neonatorum awitan dini. *Sari Pediatri*, 11(5), 326.
- Nainggolan, T. (2016). *Karakteristik neonatus yang mengalami sepsis di RSUP Haji Adam Malik Medan tahun 2014-2015*. Universitas Sumatera Utara.
- Nazir, A. (2019). Neonatal sepsis due to coagulase negative *Staphylococci*: a study from Kashmir valley, India. *International Journal of Contemporary Pediatrics*, 6(2), 650.
<https://doi.org/10.18203/2349-3291.ijcp20190705>
- Nissen, M. (2007). Congenital and neonatal pneumonia. *Paediatric Respiratory Reviews*, 8(3), 195–203.

- Nizet, V., & Klein, J. (2011). Bacterial sepsis and meningitis. In *Remington and Klein's infectious diseases of the fetus and newborn infant* (7th ed., p. 222). Elsevier Health Sciences.
- Odabasi, I., & Bulbul, A. (2020). Neonatal sepsis. *The Medical Bulletin of Sisli Etfal Hospital*, 54(2), 142–158.
- Piperaki, E., Syrogiannopoulos, G., Tzouveleakis, L., & Daikos, G. (2017). Klebsiella pneumoniae: Virulence, biofilm and antimicrobial resistance. *Pediatric Infectious Disease Journal*, 36(10), 1002–1005.
- Plunkett, A., & Tong, J. (2015). Sepsis in children. *BMJ*, 350(June), 1–13.
- Roeslani, R., Amir, I., Nasrulloh, M., & Suryani. (2013). Faktor risiko pada sepsis neonatorum awitan dini. *Sari Pediatri*, 14(6), 363–368.
- Sianturi, P., Hasibuan, B., Lubis, B., Azlin, E., & Tjipta, G. (2012). Gambaran pola resistensi bakteri di unit perawatan neonatus. *Sari Pediatri*, 13, 431–436.
- Sizar, O., Rahman, S., & Sundareshan, V. (2022). Amikacin. In *StatPearls [Internet]*. StatPearls Publishing.
- Tarina, N., & Kusuma, S. (2017). Deteksi bakteri Klebsiella pneumonia. *Jurnal Farmaka*, 15(2), 119–126.
- UN IGME. (2021). *Levels & trends in child mortality report 2021*. United Nations Children's Fund.
- Vancomycin. (2020). In *LiverTox: Clinical and research information on drug-induced liver injury [Internet]*. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases.
- Voller, S., & Myers, P. (2016). Neonatal sepsis. *Clinical Pediatric Emergency Medicine*, 17(2), 129–133.
- WHO. (2020). *Global report on the epidemiology and burden of sepsis: current evidence, identifying gaps and future directions*. WHO.