Indonesian Journal of Global Health Research
Volume 7 Number 3, June 2025
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

ANTIBIOTIC RESISTANCE IN THE PEDIATRIC INTENSIVE CARE UNIT: LITERATURE REVIEW

Nina Melina Br Ginting[1], Hendri Wijaya[1,2], Arlinda Sari Wahyuni[3], Yunnie Trisnawati[1,2], Rita Evalina[1,2], Ayodhia Pitaloka Pasaribu[1,2]*
[1]Department of Pediatrics, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia
[2]Adam Malik Hospital, Jl. Bunga Lau No.17, Kemenangan Tani, Medan Tuntungan, Medan, Sumatera Utara 20136, Indonesia
[3]Department of Public Health and Community Medicine, Faculty of Medicine, Universitas Sumatera Utara, Jl. Dr. Mansyur No.5, Padang Bulan, Medan Baru, Medan, Sumatera Utara 20155, Indonesia
*ayodhia@usu.ac.id

ABSTRACT
Antibiotics have been overused, the unwise use of antibiotics has become a special concern and has led to resistance. Almost 50% of antibiotic therapy is initiated inappropriately and without correct identification of the etiological agent. The high number of inappropriate antibiotic prescriptions contributes to the occurrence of antibiotic resistance and increased risk of death. MDR pathogens result in a 40% increase in mortality in hospital-acquired infections. The purpose of this study was to discuss the pattern of the resistance of antibiotic therapy in pediatric patients admitted to the PICU. Method: The search strategy was conducted through three databases (Google Scholar, Pubmed, Science Direct) which published during 2015-2025, using MeSH words “Antibiotic Resistance” AND “Pediatric intensive care unit”. There were thousand studies found, then by using the PRISMA flowchart, which total ten studies were included. PICU has a higher ratio of pathogen composition and bacterial resistance. Many factors can lead to antibiotic resistance, it might be caused by unnecessary or suboptimal prescribed antibiotic therapy from community before, previous health care and the hospital itself. The high number of inappropriate antibiotic prescriptions contributes to the occurrence of antibiotic resistance. Antibiotic resistance can lead to longer hospital stays and increased risk of mortality.

Keywords: antibiotic resistance; multidrug-resistant; pediatric intensive care unit

How to cite (in APA style)
Ginting, N., Wijaya, H., Wahyuni, A., Trisnawati, Y., Evalina, R., & Pasaribu, A. P. (2025). Antibiotic Resistance in the Pediatric Intensive Care Unit: Literature Review. Indonesian Journal of Global Health Research, 7(3), 375-384. https://doi.org/10.37287/ijghr.v7i3.6087.

INTRODUCTION

The use of antibiotics has been documented long before the modern antibiotic era, from 350-550 AD in Egypt until now.(Aminov, 2010; Iskandar et al., 2022). Over time, antibiotics have been overused, so that the unwise use of antibiotics has become a special concern and has led to resistance.(Durand et al., 2019; M, 2018). Some antibiotics are given to children for a much longer period of time than needed or at the wrong total daily dose. This misuse of antibiotics has many negative consequences. The high number of inappropriate antibiotic prescriptions contributes to the occurrence of antibiotic resistance (Nasso et al., 2022).

Pediatric intensive care unit (PICU) is a unit of a hospital, with specialized staff and equipment, devoted to the observation, care and therapy of pediatric patients who are critically ill, injured, or with life-threatening or potentially life-threatening diseases with a dubious prognosis.(Pudjiadi et al., 2011). Broad-spectrum antibiotics are frequently used in the PICU because infections affect a significant percentage of patients in this population (Willems et al., 2021). There are significant differences in the empirical antibiotic use prevalence in PICUs between developed and developing countries. A study in 10 tertiary hospitals in the United States in 2019 it was found that 58% of PICU patients received at least

1 type of antibiotic during treatment, this shows a significant decrease because the use of empirical antibiotics in PICU patients in 2010-2014 was 69.5% (Chiotos et al., 2023). In developing countries, almost all PICU patients use antibiotics, even a study in the PICU of tertiary hospitals in Egypt and Pakistan showed 100% patients received antibiotic therapy (Abbas et al., 2016; Sakhr et al., 2018). The use of antibiotics in several hospital PICUs in Indonesia varies, ranging from low (around 20%) to high (around 80%) (Sundariningrum et al., 2020; Yuniar et al., 2013). The median recommended duration of antibiotic therapy for the original scenarios ranged from 7- 10 days. The length of antibiotic treatment was prolonged in all cases due to another factors, such as positive bacterial cultures, the severity of the illness, the presence of an immunodeficiency, and whether the infection was acquired in a hospital (Chiotos et al., 2017).

Bacteria adapt to their environment and evolve in ways that ensure their survival. If something stops their ability to grow, such as antibiotics, genetic modification can occur, making the bacteria immune to the drug and allowing them to survive. This is the natural process of bacteria to develop drug resistance (Uddin et al., 2021). Bacteria can acquire resistance through new genetic mutations that help the bacteria survive or by obtaining DNA from already resistant bacteria. There are also genetic changes, where bacterial DNA can change and alter protein production, leading to different bacterial components and receptors that make the bacteria unrecognizable to antibiotics. Bacteria that share an environment may have intrinsic genetic determinants of resistance that will alter the bacterial genome. And when bacteria can share genetic components with other bacteria and transfer resistant DNA through horizontal gene transfer. Usually, bacteria acquire external genetic material through three main stages: transformation or DNA incorporation, transduction and conjugation. (Habboush & Guzman, 2024). Bacteria that showed resistance to at least one compound from three or more antimicrobial groups were classified as MDR. Multidrug-resistant organisms (MDROs) such as Methicillin-resistant Staphylococcus aureus (MRSA) and some Gram-negative bacteria are widespread in the PICU. These pathogens are associated with high mortality rates among neonates, infants and children in intensive care. (Bazaid et al., 2023). In the Middle East, almost 90% of newborns admitted to the Pediatric Intensive Care Unit suffer from resistant bacterial infections, while in some areas of Southeast Asia as many as 83% of children suffer from antibiotic-resistant E. coli infections (Romandini et al., 2021).

Antibiotic resistance has also occurred in many parts of Indonesia, with the percentage of resistance to penicillin and sulfamethoxazole being 62% in 2012, while Acinetobacter baumanii was declared 100% MDR (Kartasasmita et al., 2020). The World Health Organization (WHO) estimates that each year worldwide, infections caused by multidrug resistant bacteria cause 700,000 deaths of all ages, of which approximately 200,000 are newborns. MDR pathogens result in a 40% increase in mortality in hospital-acquired infections (Romandini et al., 2021).A study in Saudi Arabia revealed that Methicillin-resistant Staphylococcus aureus (MRSA) was the primary multidrug-resistant bacteria found in the PICU (Bazaid et al., 2023). A study of 191 patients showed the most often prescribed antimicrobial drugs for empirical treatment were aminoglycosides, cephalosporins, and penicillins. The sufficient treatment group was more likely to utilize the first-generation drug, which was the most widely used cephalosporin. Methicillin-sensitive Staphylococcus aureus (MSSA) accounted for 81% of the staphylococcal infections in the group receiving sufficient empirical treatment (Dar et al., 2024). Antibiotic resistance can lead to longer hospital stays, increased risk of death and treatment failure (Nasso et al., 2022). Empirical therapy is the cause of misuse and overuse of antibiotics. Almost 50% of antibiotic therapy is initiated inappropriately and without correct identification of the etiological agent.(Ventola, 2015). In order to ensure proper treatment, prevent toxicity, and prevent the development of antibiotic resistance, it is essential to optimize the use of antibiotics (Willems et al., 2021).

In most cases, empirical antibiotic treatment is initiated early while awaiting the results of diagnostic work-up and cultures (Willems et al., 2021). The cause of inappropriate antibiotic use is the lack of knowledge about the pathogens associated with different infections, and the pharmacokinetic and pharmacodynamic characteristics of certain classes of antibiotics. Antibiotics are still frequently prescribed for incorrect diagnoses, such as viral infections. Other factors too such as the lack of dedicated pediatric clinical trials on antibiotics such as adult pharmacokinetic and pharmacodynamic data to the pediatric population (with body weight or body surface area as the only differentiating indicators) contribute to the dearth of high-level of evidence knowledge and strict pediatric guidelines for children to get pharmacological doses appropriate to their needs. Other issues such as the lack of antibiotic options in pediatrics due to specific contraindications in children affect the range of antibiotic options to treat infections (Romandini et al., 2021). Until now antibiotic resistance is a burden in the management of infectious pediatric patients, especially patients admitted to the PICU where mortality rates are still high in patients with multidrug resistant Pediatric intensive care specialists and infectious disease physicians are faced with the challenge of rapidly delivering appropriate broad-spectrum antibiotics to critically ill patients with infections, while limiting unnecessary antibiotic exposure in an era of growing antibiotic resistance (Chiotos et al., 2023). The purpose of this study was to discuss the pattern of the resistance of antibiotic therapy in pediatric patients admitted to the Pediatric Intensive Care Unit (PICU).

METHOD

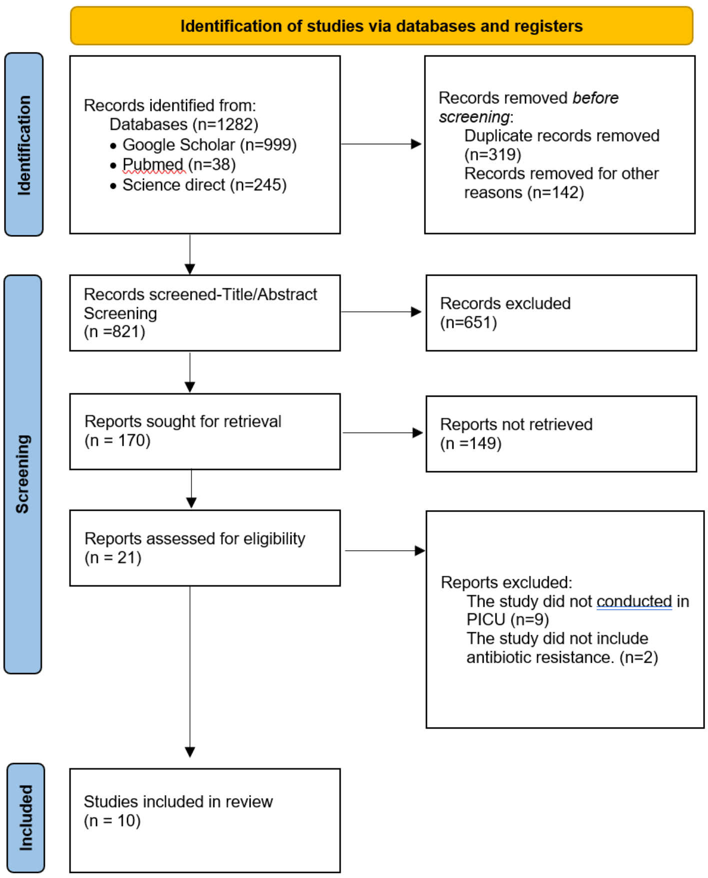

Diagram 1. Flowchart Prisma

The search strategy was conducted through three databases (Google Scholar, Pubmed, Science Direct). Additional inclusion criteria of the reviewed references were those published during the last ten years, from 2015 to 2025, medical subject headings (MeSH) "Antibiotic

Resistance" AND "Pediatric intensive care unit". The retrieved articles focused on the pattern of resistance of antibiotic in the PICU, especially patients who classified as multidrug resistance (MDR). This article also discussed in terms of the appropriateness of antibiotic therapy, duration, dose and interval of antibiotic use, and types of antibiotics used.

RESULT

Table 1.
Literature Review Results

Authors	Year	Location	Study design	Sample	Main Findings
Kyo et al.	2019	Kyoto, Japan	Retrospective observational study	247 patients	- The detection rate of methicillin-resistant Staphylococcus epidermidis (MRSE) was higher in the inappropriate empiric therapy group than that in the appropriate empiric therapy group (18% vs 6%, p 1⁄4 0.02). - The detection rate of extended spectrum b-lactamase producing Enterobacteriaceae were as low as 4% of total events, and no events of carbapenem-resistant Enterobacteriaceae or multidrug-resistant Pseudomonas aeruginosa were detected in this study - 213 patients (86%) were treated with appropriate empiric antibiotic therapy and 34 patients (14%) were treated with inappropriate empiric antibiotic. - Inappropriate empiric antibiotic therapy is associated with poor 28-day mortality in pediatric patients with bloodstream infections.
von Beck et al.	2025	Budapest, Hungary	Retrospective study	1136 patients	- Pathogen-specific resistance analysis showed that the most frequently resistant species was *Escherichia coli* (*E. coli*) (16.9%), with a high prevalence of ESBL strains. Patients with *E. coli* infection who received ceftriaxone, ciprofloxacin, or piperacillin/ tazobactam were resistant in 19.6%, 36.4%, and 25.6% of cases, respectively - Antibiotic resistance was not statistically significant to mortality rates however patients who have resistance to at least one antibiotic, but still receive adequate antibiotic therapy (combination), tend to have a lower mortality rate compared to those who do not receive adequate therapy. - The resistance rate to empirical antibiotics was 14.5%, with mortality rates of 38.6% and 61.8% within 30 days and one year.
El-Nawawy et al.	2018	Egypt	Prospective observational study	264 patients	- 24 patients had PICU-acquired infection (13.63%) and most of them are MDR (61.1%), 30.56% XDR, and 5.56% PDR. - PICU-acquired infections related to different devices. - The most common gram- negative bacteria acquired from PICU that were resistant to antibiotics are K. pneumoniae (30.5%) and Acinetobacter baumanii (22.22%) - Mortality rates increase fourfold when infections are caused by MDR pathogens and can lead to initial treatment failure.
Rezk et al.	2021	Cairo, Egypt	Prospective study	282 patients	- 26 out of 282 patients is MDR gram-negative bacteria with a mortality percentage of MDR patients is higher than non-MDR. - Most common MDR microorganisms are Acinetobacter (50%) and Klebsiella (42.8%). - The risk factors for MDR pathogen colonization in 26 patients are age < 1 year and underlying chest disease. - MDR patients did have significantly greater PICU stay than those non- infected (median 16.5 days and have longer ventilation - MDR patients treated in PICU have a lower survival rate compared to the non-MDR patient group. - The high percentage of MDR in several PICUs may be caused by misuse of antibiotics in outpatient care, treatment of viral infections with antibiotics, inappropriate dosage,

Authors	Year	Location	Study design	Sample	Main Findings
					and incomplete administration of antibiotics beforehand.
Fan et al.	2016	Beijing, China	Retrospective observational study	287 patients	- The most isolate were from Gram-negative bacteria. - The highest resistance of antibiotic rate from S. pneumoniae were clindamycin (100.0%), erythromycin (100.0%), and tetracycline (95.5%). - For S. aureus isolates, the highest resistance rate were erythromycin (81.8%), clindamycin (77.3%), and penicillin (64.8%). - For Klebsiella pneumoniae, the highest resistance rate were cefepime (76.2%), SXT (70.0%), and imipenem (69.0). The rate of MDR was 13,1% with the mortality rate reached 2.6%.
Wang et al.	2020	Wuhan, China	Case-control study	79 patients	- Incidence of multi-drug resistant infections was 8.72% (79/906) , with the most cases were were 28 cases of Carbapenem-based antibacterial drug Acinetobacter baumannii, 24 cases of MRSA, 22 cases of PDR-P aeruginosa - The logistic multiple regression analyses indicated that coma, parenteral nutrition, 2 or more antibiotics use and the duration of mechanical ventilation > 5 days were independent risk factors associated with MDRI (all $p < 0.05$). Odds ratio of the duration of mechanical ventilation > 5 days was 5.67.
Ergul et.al	2017	Turkey	Retrospective observational study	4239 patients	- Growth was found in 324 (7.6%) blood cultures - Methicillin resistance was found with a rate of 89.2% in coagulase-negative staphylococci. High rates of gentamicin (67.9%) and streptomycin (67.9%) resistance were found in Enterococcus spp. - In Enterobacteriaceae, resistance to imipenem and meropenem was found at rates of 33,3 and 10,3% respectively. Carbapenem and amikacin resistance was found with a rate of 100%. A high rate of carbapenem resistance was found in Pseudomonas spp. (62.5% for imipenem and 43.8% for meropenem).
Cetin et. al	2022	Kayseri, Turkey	Retrospective study	99 patients	- The highest resistance rate was seen against ceftazidime (76.5%) and cefepime (71.9%) in Klebsiella spp. Piperacillin-tazobactam and meropenem resistances in P. aeruginosa were 54.2% and 76.1%, respectively. A. baumannii, amikacin resistance was 50%, and gentamicin resistance was 81.6%. Meropenem resistance was 12.5% in S. marcescens strains. - High dose gentamicin and ampicillin-sulbactam resistances were 50% and 25%, respectively. Methicillin resistance was 100% and 50% in coagulase-negative staphylococci and S. aureus. - The use of carbapenem before an infection episode increased significantly, and the rate of carbapenem resistance reached 100% over the years in Pseudomonas aeruginosa and Klebsiella spp - 40.4% of the patients diagnosed with bacterial HAI died due to infection. The mortality rate was similar in Gram-

Authors	Year	Location	Study design	Sample	Main Findings
					negative and Gram-positive infections
Murni et.al	2016	Yogyakarta	Prospective cohort study	170 171 patients	- Of the 168 nosocomial pathogenic bloodstream isolates, 148 (88%) were gram-negative bacteria and 20 (12%) were gram-positive bacteria - The majority of pathogens were resistant to third generation cephalosporins, cefotaxime and ceftriaxone, but were sensitive to ceftazidime. - Eleven patients (6%) developed infections caused by MDR organisms, of whom 7 died. DR organisms causing nosocomial bloodstream infections were associated with increased risk of death with RR of 17.9 (95% CI: 5.2 - 61.8)
Putra et al.	2019	Surabaya, Indonesia	Descriptive study	4144 patients	- Antibiotic sensitivity pattern of gram negative bacteria were showed that almost all of the isolate are resistant to; penicillin cephalosporin, tetracycline, chloramphenicol, sulfa and quinolones groups - Among gram negative bacteria isolate, Cefo-sulbactam has the highest susceptibility rate (87.71%) for B. cephacea in blood, nitrofurantoin (97.53%) for E. coli in urine, cefo-sulbactam (88.09%) for P. aeruginosa in sputum. Amikacin, Cefo-sulbactam and imipenem (93.75%) had highest sensitivity for K. pneumonia in ETT isolate and at the last cefo-sulbactam (100%) also had highest sensitive for S. malthopnilia in pleural isolates - Gram positive bacteria antibiotic sensitivity pattern, are showed that almost all of isolate resistant for aminoglycoside, penicillin, macrolide, tetracycline, and carbapenem antibiotic groups. In gram positive bacteria isolate, Linezolid (100%) has highest susceptibility rate for S. cohnii in CSF fluid and vancomycin (100%) high sensitive for P. aeruginosa in pus/wound swab isolated.

Based on Table 1, 10 journals with study characteristics and research results were obtained. All of these literatures are in the range of 2015 - 2025 with inclusion and exclusion criteria met. A study by Kyo et al reported the rate of empirical antibiotic discrepancy reached 14% of cases and was significantly associated with 28-day mortality. The detection rate of methicillin-resistant Staphylococcus epidermidis (MRSE) was higher in the inappropriate empiric theraphy group than that in the appropriate emipiric theraphy group. (Kyo et al., 2019). Research by El-Nawawy et al reported resistance rates in PICU reached 13.63%, which majority of them were MDR pathogens. Mortality rates were reported to reach 4 times in MDR pathogens which can cause treatment failure (El-Nawawy et al., 2017).

A study by Rezk et al reported that 9.2% of patients suffered MDR, which a higher mortality rate in MDR pathogens. The high percentage of MDR in some PICUs was caused by the misuse of antibiotics in outpatient care, treatment of viral infections with antibiotics, inappropriate dosage, and incomplete administration of antibiotics beforehand (Rezk et al., 2021). Research by von Beck et al reported the rate of antibiotic resistance reached 14.5%. The study reported that antibiotic resistance was not significantly associated with mortality rates, but mortality rates were found to be lower in patients with antibiotic resistance who still received adequate antibiotics (von Beck et al., 2025). Research conducted by Wang et al reported the incidence of multi-drug resistant infections was 8.72, with the most cases were cases of Carbapenem-based antibacterial drug Acinetobacter baumannii. The logistic multiple regression analyses indicated that coma, parenteral nutrition, 2 or more antibiotics use and the duration of mechanical ventilation > 5 days were independent risk factors associated with MDRI (all $p < 0.05$)(Wang & Xia, 2020). Research conducted by Fan et al reported the resistance rates of S. pneumoniae to clindamycin, erythromycin, and tetracycline were a high prevalence. For S. aureus isolates, the highest resistance rate were erythromycin, clindamycin, and penicillin. Among gram-negative bacteria such as Klebsiella pneumoniae, the highest resistance rate were cefepime, SXT, and imipenem. The rate of MDR was 13,1% with the mortality rate reached 2.6% (Fan et al., 2024).

Research conducted by Cetin et al reported the highest resistance rate was ceftazidime and cefepime in Klebsiella spp. The use of carbapenem before an infection episode increased significantly, and the rate of carbapenem resistance reached 100% over the years in Pseudomonas aeruginosa and Klebsiella spp. 40.4% of the patients diagnosed with bacterial HAI died due to infection. The mortality rate was similar in Gram-negative and Gram-positive infections (Cetin et al., 2022). Research conducted by Ergul et al. reported the most common Gram-positive bacteria was coagulase-negative staphylococci, meanwhile the most common Gram-negative bacteria was Klebsiella pneumoniae. Methicillin resistance was found with a rate of 89.2% in coagulase-negative staphylococci and in 66.6% of Staphylococcus aureus strains. High rates of gentamicin (67.9%) and streptomycin (67.9%) resistance were found in Enterococcus spp. In Enterobacteriaceae, resistance to imipenem and meropenem was found at rates of 33,3 and 10,3% respectively. Carbapenem and amikacin resistance was found with a rate of 100%. A high rate of carbapenem resistance was found in Pseudomonas spp. (62.5% for imipenem and 43.8% for meropenem) (Ergül et al., 2017).

Research conducted by Putra et al reported the antibiotic sensitivity pattern of gram negative bacteria were showed that almost all of the isolate are resistant to penicillin cephalosporin, tetracycline, chloramphenicol, sulfa and quinolones groups. Gram positive bacteria antibiotic sensitivity pattern, are showed that almost all of isolate resistant for aminoglycoside, penicillin, macrolide, tetracycline, and carbapenem antibiotic groups (Wayan Putra et al., 2019). Research conducted by Murni et al revealed the majority of pathogens were resistant to third generation cephalosporins, cefotaxime and ceftriaxone, but were sensitive to ceftazidime. In general, nosocomial gram-negative pathogens had the highest susceptibility to amikacin, ciprofloxacin and imipenem. Overall, MDR organisms causing nosocomial bloodstream infections were associated with increased risk of death (Murni et al., 2016).

DISCUSSION

Resistance rates of bacterial pathogens detected in intensive care units are gradually increasing. This leads to treatment failure and increases in mortality (Cetin et al., 2022). PICU has a higher ratio of pathogen composition and bacterial resistance. Research conducted by Wang et al. in a tertiary referral center hospital in China stated that the condition of patients in coma, parenteral nutrition, the use of two or more antibiotics, and the duration of mechanical ventilation for more than 5 days were independent risk factors associated with multidrug resistant infection (MDRI) in the PICU. Patients with coma have a higher risk of infection due to more underlying disease and low immunity. Children admitted to the PICU with comatose consciousness are usually due to severe illness and will have a longer treatment period. Extended stay in the PICU increases the use of antibiotics, invasive surgery, and cross-infection between patients. In addition, pathogens in the body can migrate to other tissues and organs, causing endogenous infections. As the hospitalization period increases, human-borne pathogens may invade the body causing exogenous infection, increasing the risk of MDRI (Wang & Xia, 2020).

The high number of inappropriate antibiotic prescribing contributes to the occurrence of antibiotic resistance. Antibiotic resistance can lead to longer hospital stays, increased risk of death and treatment failure (Nasso et al., 2022). The high percentage of MDR in some PICU may be due to antibiotic misuse in outpatients, treatment of viral infections with antibiotics, inappropriate dosing, and incomplete prior antibiotic administration (Rezk et al., 2021). When the antibiotics used by patients reach or will reach the sublethal dose, the selective pressure of antibiotics can force changes in body behaviour, physiology and biochemistry.

The gene and protein expression of resistant bacteria will change, the body's protective and immune defences will gradually weaken, and the risk of MDRI increases. There is a close correlation between the amount of antibiotics used and bacterial resistance (Wang & Xia, 2020). The development of antibiotic resistant in tertiary care centre with large range health service (Java, Indonesia) might be caused by unnecessary, inappropriate, or suboptimal prescribed antibiotic therapy from community before, previous health care and our hospital itself. Most of the patient get different antibiotic from low level heath care centers or due to over the counter sell of antibiotics often in improper dose (Wayan Putra et al., 2019).

Most Gram-negative bacteria were resistant to commonly used broad-spectrum antibiotics such as cefepime, piperacillin-tazobactam, carbapenem, and colistin. Among Gram-positive organisms, antimicrobial resistance has remained consistent. Methicillin resistance has not changed significantly (Cetin et al., 2022). The most common causes of nosocomial bloodstream infections were gram-negative bacteria, in particular P. aeruginosa because it has an extracellular layer containing exopolysaccharides to protect the organism and to serve as an anti-phagocytic defense mechanism, thereby providing advantages over their bacteria competitors/ Moreover, P. aeruginosa can survive in the environment in moist areas. Water supply in hospitals is likely to be an important source for P. aeruginosa colonization and infection, although transmission from contaminated faucets during hand washing process, instead of from within the water supply itself has been described (Murni et al., 2016).

Antibiotic-resistant Gram-negative bacterial infection has a negative impact on survival outcome possibly due to the increased use of inappropriate empirical therapy (Kyo et al., 2019). Infection with resistant organisms was a significant risk factor for mortality in the PICU. Mortality rates quadrupled when infections were caused by MDR pathogens after adjusting for confounding factors such as severity of illness, length of stay in the PICU and device use (El-Nawawy et al., 2017). MDR patients treated in PICU have a lower survival rate compared to the non-MDR patient group with mortality percentage of MDR patients higher than non-MDR (Rezk et al., 2021). However, different results were obtained in von Beck et.al's study in Budapest, Hungary which reported antibiotic resistance was not statistically significant to mortality, but patients who experienced resistance to at least one antibiotic and still received adequate antibiotic therapy (combination) tended to have a lower mortality rate than those who did not receive adequate therapy (von Beck et al., 2025). We need effective program such as infection control and antibiotic stewardship. The latter should provide guidelines for antibiotic prescribing practices, conduct routine surveillance and audit of infection control and antibiotic prescribing practices, apply isolation and universal or standard precautions, and institute cleaning and good hand hygiene practice to prevent cross-transmission (Murni et al., 2016).

CONCLUSION

PICU has a higher ratio of pathogen composition and bacterial resistance. Many factors can lead to antibiotic resistance, it might be caused by unnecessary, inappropriate, or suboptimal prescribed antibiotic therapy from community before, previous health care and our hospital itself. Antibiotic resistance can lead to longer hospital stays and increased risk of death. We should provide guidelines for antibiotic prescribing practices, conduct routine surveillance and audit of infection control and antibiotic prescribing practices, apply isolation and universal or standard precautions, and institute cleaning and good hand hygiene practice to prevent cross-transmission.

REFERENCES

Abbas, Q., Ul Haq, A., Kumar, R., Ali, S. A., Hussain, K., & Shakoor, S. (2016). Evaluation of antibiotic use in Pediatric Intensive Care Unit of a developing country. *Indian*

Journal of Critical Care Medicine, *20*(5), 291–294. https://doi.org/10.4103/0972-5229.182197

Aminov, R. I. (2010). A Brief History of the Antibiotic Era: Lessons Learned and Challenges for the Future. *Frontiers in Microbiology*, *1*. https://doi.org/10.3389/fmicb.2010.00134

Bazaid, A. S., Aldarhami, A., Bokhary, N. A., Bazaid, M. B., Qusty, M. F., AlGhamdi, T. H., & Almarashi, A. A. (2023). Prevalence and risk factors associated with drug resistant bacteria in neonatal and pediatric intensive care units: A retrospective study in Saudi Arabia. *Medicine*, *102*(42), e35638. https://doi.org/10.1097/MD.0000000000035638

Cetin, B. S., Şahin, A., Kürkçü, C. A., Küçük, F., Sağıroğlu, P., & Akyıldız, B. N. (2022). Bacteriological Profile and Antimicrobial Resistance Pattern Among Healthcare-Associated Infections in a Pediatric Intensive Care Unit. *The Journal of Pediatric Academy*, *3*(2), 78–84. https://doi.org/10.51271/jpea-2022-189

Chiotos, K., Blumenthal, J., Boguniewicz, J., Palazzi, D. L., Stalets, E. L., Rubens, J. H., Tamma, P. D., Cabler, S. S., Newland, J., Crandall, H., Berkman, E., Kavanagh, R. P., Stinson, H. R., & Gerber, J. S. (2023). Antibiotic Indications and Appropriateness in the Pediatric Intensive Care Unit: A 10-Center Point Prevalence Study. *Clinical Infectious Diseases*, *76*(3), e1021–e1030. https://doi.org/10.1093/cid/ciac698

Chiotos, K., Gerber, J. S., & Himebauch, A. S. (2017). How Can We Optimize Antibiotic Use in the PICU? *Pediatric Critical Care Medicine*, *18*(9), 903–904. https://doi.org/10.1097/PCC.0000000000001261

Dar, A., Abram, T. B., & Megged, O. (2024). Impact of inadequate empirical antibiotic treatment on outcome of non-critically ill children with bacterial infections. *BMC Pediatrics*, *24*(1), 324. https://doi.org/10.1186/s12887-024-04793-0

Durand, G. A., Raoult, D., & Dubourg, G. (2019). Antibiotic discovery: history, methods and perspectives. *International Journal of Antimicrobial Agents*, *53*(4), 371–382. https://doi.org/10.1016/j.ijantimicag.2018.11.010

El-Nawawy, A., Mohsen, A. A., Abdel-Malik, M., & Taman, S. O. (2017). Performance of the pediatric logistic organ dysfunction (PELOD) and (PELOD-2) scores in a pediatric intensive care unit of a developing country. *European Journal of Pediatrics*, *176*(7), 849–855. https://doi.org/10.1007/s00431-017-2916-x

Ergül, A. B., Işık, H., Ay Altıntop, Y., & Altuner Torun, Y. (2017). A retrospective evaluation of blood cultures in a pediatric intensive care unit: A three year evaluation. *Turk Pediatri Arsivi*, *52*(3), 154–161. https://doi.org/10.5152/TurkPediatriArs.2017.5451

Fan, C., Yang, M., Mao, Y., Fang, B., He, Y., Li, R., & Qian, S. (2024). Effect of Antimicrobial Stewardship 2018 on severe pneumonia with bacterial infection in paediatric intensive care units. *Journal of Global Antimicrobial Resistance*, *36*, 444–452. https://doi.org/10.1016/j.jgar.2023.10.017

Habboush, Y., & Guzman, N. (2024). *Antibiotic Resistance*.

Iskandar, K., Murugaiyan, J., Hammoudi Halat, D., Hage, S. El, Chibabhai, V., Adukkadukkam, S., Roques, C., Molinier, L., Salameh, P., & Van Dongen, M. (2022). Antibiotic Discovery and Resistance: The Chase and the Race. *Antibiotics*, *11*(2), 182. https://doi.org/10.3390/antibiotics11020182

Kartasasmita, C. B., Rezeki Hadinegoro, S., Kurniati, N., Triasih, R., Halim, C., & Gamil, A. (2020). Epidemiology, Nasopharyngeal Carriage, Serotype Prevalence, and Antibiotic Resistance of Streptococcus pneumoniae in Indonesia. *Infectious Diseases and Therapy*, *9*(4), 723–736. https://doi.org/10.1007/s40121-020-00330-5

Kyo, M., Ohshimo, S., Kosaka, T., Fujita, N., & Shime, N. (2019). Impact of inappropriate empiric antimicrobial therapy on mortality in pediatric patients with bloodstream infection: a retrospective observational study. *Journal of Chemotherapy*, *31*(7–8), 388–393. https://doi.org/10.1080/1120009X.2019.1623362

M, H. (2018). *Program pengendalian resistensi antimikroba dan pemakaian antibiotik pada anak. Dalam : Hadinegoro S, Moedjito I, Hapsari M, Alam A, penyunting. Buku ajar infeksi & penyakit tropis.* (4th ed.). Ikatan Dokter Anak Indonesia.

Murni, I. K., Duke, T., Daley, A. J., Kinney, S., & Soenarto, Y. (2016). Antibiotic Resistance And Mortality In Children With Nosocomial Bloodstream Infection In A Teaching Hospital In Indonesia. *Southeast Asian J Trop Med Public Health*, *47*(5).

Nasso, C., Scarfone, A., Pirrotta, I., Rottura, M., Giorgi, D. A., Pallio, G., Irrera, N., Squadrito, V., Squadrito, F., Irrera, P., Arcoraci, V., & Altavilla, D. (2022). Appropriateness of Antibiotic Prescribing in Hospitalized Children: A Focus on the Real-World Scenario of the Different Paediatric Subspecialties. *Frontiers in Pharmacology*, *13*. https://doi.org/10.3389/fphar.2022.890398

Pudjiadi, A. H., Latief, A., & Budiwardhana, N. (2011). *Buku Ajar Pediatri Gawat Darurat*. Badan Penerbit Ikatan Dokter Anak Indonesia.

Rezk, A. R., Bawady, S. A., & Omar, N. N. (2021). Incidence of emerging multidrug-resistant organisms and its impact on the outcome in the pediatric intensive care. *Egyptian Pediatric Association Gazette*, *69*(1), 25. https://doi.org/10.1186/s43054-021-00071-1

Romandini, A., Pani, A., Schenardi, P. A., Pattarino, G. A. C., De Giacomo, C., & Scaglione, F. (2021). Antibiotic Resistance in Pediatric Infections: Global Emerging Threats, Predicting the Near Future. *Antibiotics*, *10*(4), 393. https://doi.org/10.3390/antibiotics10040393

Sakhr, A. M., Ghazaly, M. M. H., & Mohamad, I. L. (2018). Audit of Antibiotic Uses in Pediatric Intensive Care Unit of Assiut University Hospital. *Med. J. Cairo Univ.*, *86*(7), 3937–3941.

Sundariningrum, R. W., Setyanto, D. B., & Natadidjaja, R. I. (2020). Evaluasi Kualitatif Antibiotik Metode Gyssens dengan Konsep Regulasi Antimikroba Sistem Prospektif RASPRO pada Pneumonia di Ruang Rawat Intensif Anak. *Sari Pediatri*, *22*(2), 109–114.

Uddin, T. M., Chakraborty, A. J., Khusro, A., Zidan, B. R. M., Mitra, S., Emran, T. Bin, Dhama, K., Ripon, Md. K. H., Gajdács, M., Sahibzada, M. U. K., Hossain, Md. J., & Koirala, N. (2021). Antibiotic resistance in microbes: History, mechanisms, therapeutic strategies and future prospects. *Journal of Infection and Public Health*, *14*(12), 1750–1766. https://doi.org/10.1016/j.jiph.2021.10.020

Ventola, C. L. (2015). The Antibiotic Resistance Crisis Part 1: Causes and Threats. *P&T*, *40*(4), 277–283.

von Beck, L. M., Rapszky, G. A., Kiss, V. E., Sandor, S., Gaal-Marschal, S., Berenyi, T., Varga, C., & Fenyves, B. G. (2025). Empiric antibiotic therapy resistance and mortality in emergency department patients with bloodstream infection: a retrospective cohort study. *BMC Emergency Medicine*, *25*(1), 18. https://doi.org/10.1186/s12873-025-01177-0

Wang, Z., & Xia, Z. (2020). What we can do? The risk factors for multi-drug resistant infection in pediatric intensive care unit (PICU): A case-control study. *Italian Journal of Pediatrics*, *46*(1). https://doi.org/10.1186/s13052-019-0769-9

Wayan Putra, I., Setyaningtyas, A., Puspitasari, D., Dwi Wahyu, A., Dharmawati, I., & Latief Azis, A. (2019). Microbial Pattern And Antibiotic Susceptibility In Pediatric Intensive Care Unit Dr. Soetomo Hospital, Surabaya. *Indonesian Journal of Tropical and Infectious Disease*, *7*(5).

Willems, J., Hermans, E., Schelstraete, P., Depuydt, P., & De Cock, P. (2021). Optimizing the Use of Antibiotic Agents in the Pediatric Intensive Care Unit: A Narrative Review. *Pediatric Drugs*, *23*(1), 39–53. https://doi.org/10.1007/s40272-020-00426-y

Yuniar, I., Karyanti, M. R., Tambunan, T., & Rizkyani, N. A. (2013). Evaluasi Penggunaan Antibiotik dengan Kartu Monitoring Antibiotik Gyssens. *Sari Pediatri*, *14*(6).