



## ASSOCIATION BETWEEN MICROBIOLOGICAL PATTERNS AND CLINICAL OUTCOME OF PEDIATRIC SEPSIS IN TWO REFERRAL HOSPITALS

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### ABSTRACT

Sepsis is a major cause of morbidity and mortality in the Pediatric Intensive Care Unit (PICU). Diverse microbiological patterns and high antibiotic resistance are thought to contribute to patient clinical outcomes. To analyze the relationship between microbiological patterns and mortality outcomes in pediatric patients with sepsis. This cross-sectional study used medical records of pediatric sepsis patients aged >28 days to <18 years hospitalized in the PICU from January 2022 to December 2024. Data collected included demographic characteristics, microbiological profiles, and mortality outcomes. Analysis was performed using SPSS Statistics v.30 using the Chi-Square or Fisher's Exact Test, followed by linear regression and multivariate logistic regression with a significance level of  $p < 0.05$ . This study involved 114 patients. Ninety-nine children were in Adam Malik Hospital and 15 patients at Prof. Dr. Chairuddin Panusunan Lubis Hospital, University of North Sumatra. Higher mortality proportions were observed in the Gram-positive (53.3%), Gram-negative (44.0%), and fungal (66.7%) groups compared with the culture-negative group (30.5%). No significant association was found between microbiological patterns and mortality. Mortality in pediatric sepsis is multifactorial and may be influenced by factors beyond microbiological patterns and baseline patient characteristics alone.

Keywords: clinical outcomes; microbiological patterns; pediatric sepsis; PICU

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## INTRODUCTION

Sepsis is a complex and life threatening clinical syndrome caused by the body's dysregulated and uncontrolled immune response to a serious infection, rather than a localized reaction, the host's immune system develops a hyperactive systemic inflammatory response, leading to widespread tissue damage, hypoperfusion, and eventually, multiple organ dysfunction syndrome (MODS) (Cruz et al., 2020). Severe sepsis accounts for 8% of cases admitted to pediatric intensive care units (PICU) and is also responsible for causing more than 4.5 million child deaths worldwide each year (Rudd et al., 2020). The burden of this condition disproportionately affects developing and underdeveloped country, where limited resources, delayed clinical presentation, and insufficient supportive care is prevalent, which could aggravate clinical deterioration. Local epidemiological data further highlights the complexity of this issue.

A retrospective study conducted at the PICUs of Adam Malik Hospital Medan and Prof. Dr. Chairuddin Panusunan Lubis Hospital, University of North Sumatra, evaluated diagnosis of sepsis obtained from data in the medical records section in 2018 obtained a total of 87 samples with a mortality rate of 58 sepsis patients (66.7%) (Pratiwi, 2019). This alarmingly high mortality rate underscores a pressing need for localized clinical intervention and continuous quality improvement in critical settings. Furthermore, surviving pediatric sepsis is seldom the end of the clinical journey.

Sepsis carries a risk of new or worsening functional impairment. Survivors frequently experience decreased quality of life and may require prolonged dependence on respiratory support, specialized nutrition, or new medical technologies, on top of that, sepsis survivors are also highly susceptible to recurrent severe infection due to post-sepsis immune suppression, which prolongs length of hospital stay and escalate the socio-economic burden on families and healthcare systems (Weiss & Fitzgerald, 2023).

The early recognition and evaluation of sepsis present significant clinical challenges, particularly in pediatric populations where early physiological signs, such as tachycardia or tachypnea, can often be highly variable and not specific. Thus, Sepsis needs to be evaluated with combination of clinical criteria and various laboratory studies, including inflammatory biomarkers such as C-reactive protein (CRP) procalcitonin, and serum lactate. Nevertheless, the cornerstone of identifying specific etiology remains to be microbiological confirmation, which generally includes blood cultures; however, depending on the suspected source of infection, it may also be required to obtain cultures sample of urine, peritoneum, synovial fluid, sputum, and possibly cerebrospinal fluid (CSF) (Huang et al., 2022; Miranda & Nadel, 2023). In spite of their clinical importance, microbial cultures also have some notable limitations, including a turnaround time of 48 to 72 hours and sometimes a high rate of false negative results, particularly in the settings where empirical antibiotics have been administered prior to microbial culture sample collection.

Microbiologically, Sepsis in children is generally caused by an array of Gram-negative or Gram-positive bacteria, although the relative prevalence, virulence, and resistance patterns of these pathogens may vary significantly across different geographic regions and healthcare facilities. Common gram-positive pathogens often include *Staphylococcus aureus* and *Streptococcus pneumoniae*, while the most commonly found gram-negative pathogens frequently involves *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, although, in the last decade the prevalence of *Acinetobacter baumannii* is increasing especially in intensive care settings in Asia (Shao et al., 2024). Studies investigating the etiology of pathogens causing sepsis or sepsis in children are still very limited, so that recommendations for first-line empirical therapy depending on the pattern of germs and local epidemiology are difficult (A.a.w et al., 2019; Weiss et al., 2020). Inappropriate initial antibiotic therapy has been shown to be an independent predictor of mortality, emphasizing the critical need for institution specific antibiograms.

Furthermore, analysis and primary research related to the complex interplay of factors dictating the outcomes of severe infections in children still remains sparse. In addition to chronological age, host factors, such as the presence of underlying congenital diseases, immunodeficiencies, malnutrition, and other comorbidities, are major determining factors of both susceptibility to infection and the final clinical outcome (Agyeman et al., 2017). The relationship between specific causative pathogen and the risk of mortality is also a subject of ongoing debate within the scientific community. For instance, Ani et al., showed that specific highly virulent strains, such as Methicillin-resistant *Staphylococcus aureus* (MRSA) and Methicillin-sensitive *Staphylococcus aureus* (MSSA) carry a much higher risk of death compared to *Enterococcus* and most Gram-negative organisms (Ani et al., 2015). Conversely, conflicting findings from a comprehensive study by Zahar et al. Suggested that mortality from sepsis might actually be independent of the causative pathogenic organism. Based on a large multicenter analysis of data from 12 ICUs in France from 1996 to 2009, which included 4,006 first episodes of sepsis, it was found that mortality rates in community-, hospital-, and PICU-acquired sepsis were not statistically related to identity of the causative pathogenic organism, the primary anatomical location of infection, or the presence of confirmed bacteremia (Zahar et al., 2011).

This discrepancy suggests that the ultimate clinical outcome is rarely determined by the pathogenic organism alone. Instead, a highly complex combination of the host physiological response to

infection, baseline vulnerabilities, and specific, localized cellular responses to particular organisms likely contribute to the varied clinical symptoms and distinct survival rate observed in critical care settings. The hyper inflammatory “cytokine storm” phase of sepsis, followed by profound immune suppression, may dictate the patient’s clinical trajectory far more than the exact species of bacteria circulating in their bloodstream (Ani et al., 2015; Hazwani et al., 2020).

Because clinical studies investigating the specific etiology, microbial shifts and pathogens specific outcome pediatric sepsis are still very few, implementing global guidelines into effective local clinical pathways faces various difficult challenges. The lack of local data causes the creation of tailored recommendations for first line empirical therapy practically impossible without relying on guesswork (A.a.w et al., 2019; Weiss et al., 2020). Delaying optimal therapy or utilizing broad spectrum antibiotics unnecessarily not only worsens individual patient outcomes but also drives broader crisis of antimicrobial resistance.

Therefore, comprehensive, locally grounded research is urgently needed to bridge these critical knowledge gaps. This study aims to analyze the current patterns of germs that cause sepsis in children in our specific clinical setting and thoroughly evaluate their impact, be it direct or indirect, on patient mortality outcomes. By characterizing the local microbiological landscape and correlating it with patient survival, this research seeks to empower clinicians with data driven insights, ultimately refining empirical antibiotic protocols, optimizing resource allocation in the PICU, and improving the overall survival and post discharge clinical trajectories for critically ill children.

## **METHOD**

This cross-sectional study was conducted to assess the relationship between microbiological patterns and clinical outcomes in pediatric patients with sepsis treated at the Pediatric Intensive Care Units (PICU) of Adam Malik Hospital (HAM) and Prof. Dr. Chairuddin Panusunan Lubis Hospital, University of North Sumatra (CPL USU). Data were obtained retrospectively from medical records over a three-year period, spanning from January 2022 to December 2024, with data collection continuing until all required research data were fully gathered. Prior to initiation, this study was formally approved by the Health Ethics Committee of the Faculty of Medicine, University of North Sumatra (reference number 490/KEPK/USU/2025).

The target population comprised pediatric patients aged greater than 28 days to less than 18 years who experienced sepsis, while the accessible population specifically included those within this demographic who were admitted to the PICU during the study window. Sampling was conducted using a total sampling technique, meaning every subject who met the criteria during the research period was included in the study. The initial screening process involved tracing patient medical records in the PICU database based on the primary sepsis diagnosis assigned by the attending physician using the ICD-10 code of A41.9. This study included these pediatric patients whether their sepsis was established clinically or definitively confirmed based on blood culture results. To maintain data integrity, patients were strictly excluded if they had incomplete medical records which causes missing crucial analytical data, or if they were neonatal patients (aged 0–28 days) who initially received care in the neonatal unit and whom care were subsequently continued in the PICU. For all selected subjects, researchers systematically recorded comprehensive baseline data. This included demographic characteristics such as age and gender, alongside anthropometric measurements encompassing body weight, length or height, and calculated the patients nutritional status. The data collection also detailed admission parameters, including patient arrival status (whether patient was self-admitted or referred from another facility), the origin of the infection (categorized as community-acquired (Infection proven by the presence of pathogenic organism in blood culture taken <48 hours of hospitalization) or hospital-associated (Infection proven by the presence of pathogenic organism in blood culture taken  $\geq$  48 hours of hospitalization), any

additional secondary infectious diagnoses, and the frequency of the patient's infection episodes. To thoroughly establish the microbiological profile, culture results were meticulously grouped into broad categories: Gram-positive, Gram-negative, anaerobic, fungal, negative (no growth), or polymicrobial (more than one species of pathogenic organisms (bacteria or fungi) found in the same culture specimen). Alongside the microbiological data, detailed clinical outcomes were collected from the medical records to evaluate disease severity and patient trajectory. These outcomes included the primary measure of patient mortality.

The collected data were then processed using the Statistical Package for the Social Sciences (SPSS) computer software. To determine the relationship between microbiological patterns and outcomes in pediatric patients with sepsis, a bivariate analysis using the Chi-Square test was performed. If the assumptions of the Chi-Square test are not met, then the bivariate analysis uses the alternative Fisher's Exact Test, then continued with multivariate analysis of the outcomes using logistic regression.

## RESULT

This study involved 114 pediatric sepsis patients treated in the Pediatric Intensive Care Unit (PICU) of H. Adam Malik Hospital (99 patients) and Prof. Dr. Chairuddin Panusunan Lubis Hospital, University of North Sumatra (15 patients) who met the inclusion criteria. The demographic characteristics of the study participants can be seen in Table 1.

Table 1.  
Characteristics of the study participants

| Characteristics                    | Total (n=114) | HAM (n=99)  | CPL USU (n=15) |
|------------------------------------|---------------|-------------|----------------|
| Age, f (%)                         |               |             |                |
| < 1 year                           | 31 (27.2)     | 24 (24.2)   | 7 (46.7)       |
| 1 to < 2 years                     | 18 (15.8)     | 13 (13.1)   | 5 (33.3)       |
| 2 to < 5 years                     | 11 (9.6)      | 9 (9.1)     | 2 (13.0)       |
| 5 to < 12 years                    | 27 (23.7)     | 27 (27.3)   | 0 (0.0)        |
| 12 to < 18 years                   | 27 (23.7)     | 26 (26.3)   | 1 (7.0)        |
| Sex, n (%)                         |               |             |                |
| Male                               | 62 (54.4)     | 54 (54.5)   | 8 (53.3)       |
| Female                             | 52 (45.6)     | 45 (45.5)   | 7 (46.7)       |
| Body Weight, median (IQR), kg      | 11.1 (22.0)   | 20.6 (24.3) | 6 (6.7)        |
| Body Height, median (IQR), cm      | 96.5 (66.2)   | 107 (70.0)  | 70 (35.0)      |
| Nutritional Status, f (%)          |               |             |                |
| Underweight                        | 39 (34.2)     | 33 (33.3)   | 6 (40.0)       |
| Severely underweight               | 24 (21.1)     | 22 (22.2)   | 2 (13.3)       |
| Normal nutritional status          | 45 (39.5)     | 38 (38.4)   | 7 (46.7)       |
| Overweight                         | 3 (2.6)       | 3 (3.0)     | 0 (0.0)        |
| Obesity                            | 3 (2.6)       | 3 (3.0)     | 0 (0.0)        |
| Patient Admission Status, n (%)    |               |             |                |
| Self-admission                     | 31 (27.2)     | 31 (31.3)   | 0 (0.0)        |
| Referral                           | 83 (72.8)     | 68 (68.7)   | 15 (100.0)     |
| Source of Infection, f (%)         |               |             |                |
| Community-acquired infection       | 80 (70.2)     | 71 (71.7)   | 9 (60.0)       |
| Hospital-acquired infection        | 34 (29.8)     | 28 (28.3)   | 6 (40.0)       |
| Primary Diagnosis, f (%)           |               |             |                |
| Bronchopneumonia                   | 81 (71.1)     | 72 (72.7)   | 9 (60.0)       |
| Central nervous system infection   | 10 (8.8)      | 9 (9.1)     | 1 (6.7)        |
| Gastrointestinal infection         | 12 (10.5)     | 7 (7.1)     | 5 (33.3)       |
| Other respiratory tract infections | 8 (7.0)       | 8 (8.1)     | 0 (0.0)        |
| Urinary tract infection            | 3 (2.6)       | 3 (3.0)     | 0 (0.0)        |
| Episodes of Infection, f (%)       |               |             |                |
| 1 episode                          | 61 (53.5)     | 46 (46.5)   | 15 (100.0)     |
| > 1 episode                        | 53 (46.4)     | 53 (53.5)   | 0 (0.0)        |

Based on Table 2, mortality outcomes were analyzed by comparing each culture-positive group with the culture-negative group as the reference. Mortality was 69.5% (41/59) in the culture-

negative group, 46.7% (7/15) in the Gram-positive group ( $p=0.132$ ), 56.0% (14/25) in the Gram-negative group ( $p=0.316$ ), 83.3% (10/12) in the polymicrobial group ( $p=0.488$ ), and 33.3% (1/3) in the fungal group ( $p=0.241$ ), with no statistically significant differences observed in any comparison.

Table 2.

## Relationship between microbiological patterns and outcomes (mortality)

| Mortality Outcome                   | Non-survivors (n=73) | Survivors (n=41) | p-value            |
|-------------------------------------|----------------------|------------------|--------------------|
| Culture-negative (n=59) (Reference) | 41 (69.5)            | 18 (30.5)        |                    |
| Gram-positive (n=15)                | 7 (46.7)             | 8 (53.3)         | 0.132 <sup>a</sup> |
| Gram-negative (n=25)                | 14 (56.0)            | 11 (44.0)        | 0.316 <sup>a</sup> |
| Polymicrobial (n=12)                | 10 (83.3)            | 2 (16.7)         | 0.488 <sup>a</sup> |
| Fungal (n=3)                        | 1 (33.3)             | 2 (66.7)         | 0.241 <sup>a</sup> |

<sup>a</sup>Mann-Whitney U

Based on the bivariate analysis between demographic characteristics and mortality in Table 3, no statistically significant association was found between all studied variables and mortality ( $p > 0.05$ ).

Table 3.

## Bivariate Analysis of Demographic Characteristics and Mortality

| Characteristics                    | Non-survivors (n=73) | Survivors (n=41) | p-value            |
|------------------------------------|----------------------|------------------|--------------------|
| Age, f (%)                         |                      |                  |                    |
| < 1 year                           | 23 (31.5)            | 8 (19.5)         | 0.490 <sup>a</sup> |
| 1 to < 2 years                     | 9 (12.3)             | 9 (22.0)         |                    |
| 2 to < 5 years                     | 6 (8.2)              | 5 (12.2)         |                    |
| 5 to < 12 years                    | 17 (23.3)            | 10 (24.4)        |                    |
| 12 to < 18 years                   | 18 (24.7)            | 9 (22.0)         |                    |
| Sex, f (%)                         |                      |                  |                    |
| Male                               | 40 (54.8)            | 22 (53.7)        | 1.000 <sup>b</sup> |
| Female                             | 33 (45.2)            | 19 (46.3)        |                    |
| Nutritional Status, f (%)          |                      |                  |                    |
| Underweight                        | 25 (34.2)            | 14 (34.1)        | 0.660 <sup>b</sup> |
| Severely underweight               | 17 (23.3)            | 7 (17.1)         |                    |
| Normal nutritional status          | 26 (35.6)            | 19 (46.3)        |                    |
| Overweight                         | 2 (2.7)              | 1 (2.4)          |                    |
| Obesity                            | 3 (4.1)              | 0 (0.0)          |                    |
| Patient Admission Status, f (%)    |                      |                  |                    |
| Self-admission                     | 19 (26.0)            | 12 (29.3)        | 0.827 <sup>a</sup> |
| Referral                           | 54 (74.0)            | 29 (70.7)        |                    |
| Source of Infection, f (%)         |                      |                  |                    |
| Community-acquired infection       | 48 (65.8)            | 32 (78.0)        | 0.204 <sup>a</sup> |
| Hospital-acquired infection        | 25 (34.2)            | 9 (22.0)         |                    |
| Primary Diagnosis, f (%)           |                      |                  |                    |
| Bronchopneumonia                   | 53 (72.6)            | 28 (68.3)        | 0.299 <sup>b</sup> |
| Central nervous system infection   | 4 (5.5)              | 6 (14.6)         |                    |
| Gastrointestinal infection         | 9 (12.3)             | 3 (7.3)          |                    |
| Other respiratory tract infections | 6 (8.2)              | 2 (4.9)          |                    |
| Urinary tract infection            | 1 (1.4)              | 2 (4.9)          |                    |
| Episodes of Infection, f (%)       |                      |                  |                    |
| 1 episode                          | 42 (57.5)            | 19 (46.3)        | 0.328 <sup>a</sup> |
| > 1 episode                        | 31 (42.5)            | 22 (53.7)        |                    |

In the logistic regression analysis, OR values greater than 1 were obtained for the variables of culture results, age, nutritional status, patient arrival status, and origin of infection, while OR values less than 1 were obtained for the variables of gender, additional diagnosis, and infection episode. All 95% confidence intervals included the value 1, with the p value of each variable greater than 0.05 (Table 4)

Table 4.  
Logistic Regression Analysis of Demographic Characteristics and Microbiological Patterns  
Associated with Mortality

| Variable                 | Odds Ratio (OR) | 95% Confidence Interval (95% CI) | p-value |
|--------------------------|-----------------|----------------------------------|---------|
| Culture result           | 1.121           | 0.795–1.581                      | 0.514   |
| Age                      | 1.012           | 0.764–1.342                      | 0.931   |
| Sex                      | 0.965           | 0.424–2.197                      | 0.933   |
| Nutritional status       | 1.052           | 0.702–1.576                      | 0.805   |
| Patient admission status | 1.195           | 0.439–3.954                      | 0.700   |
| Source of infection      | 2.044           | 0.810–5.161                      | 0.130   |
| Primary diagnosis        | 0.953           | 0.662–1.373                      | 0.797   |
| Episodes of infection    | 0.791           | 0.404–1.547                      | 0.388   |

## DISCUSSION

The mortality rate for all patients in this study reached 64%, this figure is considered very high and far exceeds the average mortality rate in cases of sepsis in children (25%) but is close to the figure reported from PICUs in Indonesia as reported by a meta-analysis by Tan et al (Tan et al., 2019) including 66.7% at Adam Malik Hospital in Medan in 2018 and 21.8% at Zainoel Abidin Regional Hospital. Significant differences between healthcare facilities likely stem from differences in population, patient condition upon admission, and resource limitations (Pratiwi, 2019; Sovira et al., 2020). Although the polymicrobial infection group had the highest proportion of deaths, the difference in mortality between microbiological groups did not reach statistical significance. This finding aligns with a multicenter study in 12 French ICUs that analyzed 4,006 episodes of sepsis and found that mortality was not independently associated with the type of causative microorganism, the location of infection, or the presence of bacteremia (Zahar et al., 2011). In a 2020 study by Hazwani et al., which compared culture-negative and culture-positive sepsis in the PICU and reported no significant difference in mortality between the two groups (Hazwani et al., 2020).

The highest proportion of mortality was found in the polymicrobial group, although statistical significance was not reached. In theory, polymicrobial infections have the potential to cause more severe immune dysregulation through various inflammatory pathways, which can exacerbate the cytokine storm and organ dysfunction (Doualeh et al., 2022; Dyck et al., 2024). The high mortality observed in the culture-negative group can be explained by several mechanisms. The absence of pathogens in a culture does not definitively rule out an underlying infection, as negative results are frequently influenced by the administration of empirical antibiotics prior to sample collection, inadequate sample volume or quality, and the inherent limitations of culture methods in detecting certain pathogens, including viruses and fastidious microorganisms. Furthermore, some patients may experience a severe systemic inflammatory response syndrome (SIRS) driven by non-infectious critical conditions that clinically mimic sepsis. This finding aligns with a 2020 study by Hazwani et al., which compared culture-negative and culture-positive sepsis in the PICU and reported no significant difference in mortality between the two groups. Ultimately, these results support the concept that clinical outcomes in pediatric sepsis are dictated far more by the severity of the host's immune response and the resulting organ dysfunction than by microbiological culture status alone (Hazwani et al., 2020).

Multivariate logistic regression analysis showed no statistically significant variables as independent predictors of mortality. The highest OR was found for the variable of infection origin (HAI vs. CAI), indicating that HAI tends to be associated with a higher mortality rate, although this was not significant, possibly due to the limited sample size. Although the infection origin had the highest OR (OR 2.044), the confidence interval still encompassed 1, making it unable to be considered an independent risk factor. Clinically, however, this trend is highly relevant. Hospital-acquired infections in the PICU setting are frequently driven by the necessity of invasive life-support

devices, such as mechanical ventilators, central venous catheters, and urinary catheters, which disrupt natural anatomical barriers. Furthermore, pathogens responsible for HAIs are often nosocomial strains that exhibit higher rates of multidrug resistance compared to community-acquired infections. Consequently, these infections are inherently more difficult to treat, often requiring broader-spectrum, more toxic antimicrobials, and can precipitate rapid clinical deterioration in already critically ill children, thereby driving the trend toward higher mortality (Murni et al., 2022).

Another crucial clinical context is the nutritional baseline of the study population. Based on the demographic data, over half of the patients (55.3%) were classified as either underweight or severely underweight. While nutritional status did not independently predict mortality in the logistic regression model, this high prevalence of malnutrition is a critical factor in pediatric populations in developing nations. Baseline malnutrition is a well-established driver of immunosuppression, which likely contributes to the overall staggering 64% mortality rate across all groups by severely impairing the host's physiological reserve and altering the immune response during severe systemic infections (Agrawal et al., 2023).

These findings suggest that mortality in pediatric sepsis is a multifactorial phenomenon that cannot be explained by a single clinical or microbiological variable. Factors such as delay in diagnosis, appropriateness of antimicrobial therapy, degree of organ dysfunction, patient immune status, and quality of intensive care likely play a greater role in determining patient outcomes (Bracken et al., 2023). Research conducted by Rusmawatiningsya et al. in 2021 in a PICU setting with limited resources found that various factors such as organ dysfunction and the need for vasopressors were stronger predictors of mortality than microbiological characteristics (Harding et al., 2018).

To address the multifactorial nature of pediatric sepsis mortality and the limitations of traditional culture methods, clinical management must adapt. Because standard blood cultures inherently require a 48- to 72-hour turnaround time and are highly susceptible to false-negative results from prior antibiotic administration, relying on them as the sole diagnostic tool can delay definitive care. To bridge this diagnostic gap, clinicians should maximize the utility of rapid inflammatory biomarkers, such as procalcitonin, C-reactive protein, and serum lactate, alongside continuous clinical reassessment to guide early decision making. Furthermore, because inappropriate initial therapy is a known driver of mortality, it is critical for hospitals to develop and utilize standardized, institution-specific antibiograms to eliminate the guesswork in empirical prescribing. Finally, since our findings suggest that patient outcomes are heavily driven by the degree of organ dysfunction and host response rather than the specific pathogen alone, clinicians should prioritize physiology-based early recognition protocols, such as Pediatric Early Warning Scores (PEWS), to ensure timely, life-saving supportive interventions are initiated well before microbiological confirmation is achieved.

The strength of this study lies in its highly relevant focus on current clinical challenges in pediatric intensive care and infectious diseases. By not only evaluating microbiological patterns descriptively but also correlating them with a critical clinical outcome, namely, mortality, this research provides a more comprehensive overview of pediatric sepsis. Furthermore, because the study was conducted in teaching and central referral hospitals, the findings offer a highly representative picture of the microbial patterns and antibiotic resistance currently encountered in actual clinical practice within these settings. However, this study is not without limitations. Primarily, its retrospective design means that the results are highly dependent on the completeness and accuracy of the available medical records. Additionally, the large number of negative blood cultures can limit the microbiological analysis, as not all cases of sepsis can be definitively confirmed by blood culture results. This is due to the possibility that antibiotics were administered before the patient was referred or before the culture was taken, which also significantly influenced the blood culture

results and resulted in the pathogen not being identified. Furthermore, several confounding factors remain that have not been optimally controlled, such as the severity of the disease at PICU admission, the timeliness of antibiotic administration, the presence of comorbidities, and various clinical conditions that developed during treatment. Therefore, the findings of this study must be interpreted as demonstrating associative relationships and cannot directly establish a definitive causal link between the investigated variables.

## CONCLUSION

None of the demographic or clinical variables examined showed a significant association with mortality in the bivariate analysis. Furthermore, multivariable logistic regression also demonstrated that culture results, age, nutritional status, patient arrival status, origin of infection, gender, additional diagnosis, and infection episode were not independent predictors of mortality. These findings collectively reinforce that pediatric sepsis mortality is a highly complex, multifactorial phenomenon. Ultimately, a patient's clinical trajectory and survival are not strictly dictated by the specific causative pathogen or isolated baseline characteristics. Instead, outcomes are likely driven by the dynamic interplay of the host's physiological immune response, the severity and progression of organ dysfunction, and the timeliness and quality of clinical interventions in the intensive care setting.

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