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COMPARISON OF OUTCOME OF CHILDREN WITH SEPSIS WITH AND WITHOUT POSITIVEBLOOD CULTURES IN THE PICU OF A TERTIARY CARE HOSPITAL

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Abstract

Objective:
To determine the outcome of children admitted with sepsis and to compare the in-hospital mortality in culture-negative sepsis (CNS) with culture-positive sepsis (CPS) patients.

Methods:
A total of 189 children with clinical diagnosis of sepsis with age 4-months to 16-years were recruited from 1-November-2024 to 31-January-2025. Venous blood samples were collected from all patients and sent to the hospital's microbiology department for analysis to determine whether they had CPS or CNS. Each patient was monitored through to their discharge from the hospital, with a maximum follow-up period of 30 days to assess in-hospital mortality rates.

Results:
The study involved 189 subjects with a mean age of 3.2±2.6 years. In terms of gender distribution, 103 (54.4%) of the participants were male. Regarding type of sepsis, CPS was diagnosed in 107 (56.6%) patients and CNS in 82 (43.3%) patients. Among the CPS group, 25 individuals (23.4%) experienced in-hospital mortality. In contrast, the CNS group, saw a lower mortality rate, with only 10 (12.2%) deaths (p-value 0.05).

Conclusion:
There is a significant number of pediatric patients having CNS admitted with sepsis suspicion. The mortality rate in CPS is higher in comparison to CNS patients.

INTRODUCTION

Sepsis represents a major public health challenge, ranking as one of the leading causes of illness and death globally, while also placing a substantial burden on healthcare resources (Rudd et al., 2020). Each year, approximately 1.2 million children are affected by sepsis, making this population particularly vulnerable (Fleischmann-Struzek et al., 2018). In pediatric intensive care units (PICUs), sepsis is identified in about 4-8% of patients, with mortality rates for affected children varying significantly—from 4% to as high as 50%. These rates depend on numerous factors, including the severity

of the disease, individual risk factors, geographical location, and the resources available in healthcare settings (Weiss et al., 2020). A guideline specifically addressing sepsis in children highlights a troubling disparity between low and middle-income countries compared to high-income countries. In lower-income regions, the mortality rate from sepsis is considerably higher, with reports showing 31.7% in these areas versus 19.3% in wealthier nations (Fernández-Sarmiento et al., 2022). The risk of death is notably elevated in specific geographical regions, with African nations reporting a mortality risk of 7.89, followed by Asia at 3.81, and South America at 2.91 (Hilarius et al., 2020).

The understanding and management of sepsis have evolved significantly in recent years, yet accurately predicting mortality in pediatric patients remains a complex and daunting task (Bracht et al., 2019; Menon et al., 2022). Blood cultures play a crucial role in defining sepsis and guiding the treatment of children suspected of having this condition. Nevertheless, it is common for these blood cultures to yield negative results, making the identification of specific pathogens through culture particularly challenging (Thorndike and Kollef, 2020). In adults, studies indicate that approximately 28% to 49% of severe sepsis cases are culture-negative. However, there is a notable lack of data regarding the epidemiology and outcomes associated with culture-negative severe sepsis (CNSS) in the pediatric demographic (Sigakis et al., 2019).

The aim of proposed study is to determine the outcome of children admitted with sepsis and to compare the in-hospital mortality in CNS with CPS patients.

METHODS:

A total of 189 children with clinical diagnosis of sepsis with age 4-months to 16-years were recruited from 1-November-2024 to 31-January-2025. The following clinical criteria was used for sepsis determination; hypotension, fever >38.5 °C, O_2 saturation <92%, hypothermia (core body temperature <98.6 °F), heart rate >100 beats/min and reduced urine output (<0.5 ml/kg/hr for at least 2 hours despite fluid resuscitation). While patients with microbiogically proven fungal, or viral infections, hematologic malignancies, having immunodeficiency or tumors were excluded.

Venous blood samples were collected from all patients and sent to the hospital's microbiology department for analysis to determine whether they had culture-positive or culture-negative sepsis. Each sample, approximately 3 ml, was inoculated into brain heart infusion broth and incubated at a temperature of 37°C. Subcultures were performed on sheep blood agar and MacConkey agar upon visual detection of turbidity or, if no turbidity was observed, on the first, fourth, and seventh days. Bacterial isolates were identified based on their distinctive morphological characteristics on the respective media, followed by Gram staining. Confirmation was achieved through a series of biochemical tests according to standard procedures. For Gram-positive organisms, tests included coagulase, catalase, bacitracin susceptibility, and optochin susceptibility, among others. In contrast, for Gram-negative organisms, tests such as triple sugar iron test, sulfur indole motility, Simmons citrate test, and urea hydrolysis were utilized. Patients whose cultures were positive for bacterial growth on the seventh day were classified as having culture-proven sepsis, while those with negative blood culture findings were identified as having culture-negative sepsis.

All patients received standard sepsis treatment according to the hospital's established protocols, under the guidance of an ICU consultant. Each patient was monitored through to their discharge from the hospital, with a maximum follow-up period of 30 days to assess in-hospital mortality rates.

Data was analyzed in SPSS v25 software. Chi-square test was applied to compare in-hospital mortality in CNS and CPS patients.

RESULTS:

The study involved 189 subjects with a mean age of 3.2 years, exhibiting a standard deviation of 2.6 years. In terms of gender distribution, 54.4% of the participants were male, totaling 103 individuals. The socio-economic status of the participants varied, with 49.7% classified as low income (94 individuals), 29.6% as middle income (56 individuals), and 20.6% as high income (39 individuals). The primary sites of infection were primarily respiratory, affecting 39.1%

of the subjects (74 individuals), followed by genitourinary infections in 34.4% (65 individuals), bloodstream infections in 19.0% (36 individuals), skin/soft tissue infections in 5.2% (10 individuals), and abdominal infections in 2.1% (4 individuals). Regarding comorbidities, immunodeficiency was present in 2.6% of participants (5 individuals), while neutropenia or malignancy was reported in 9.0% (17 individuals) and malnutrition in 11.6% (22 individuals). A history of previous sepsis was documented in 1.6% (3 individuals), congenital heart disease in 4.7% (9 individuals), and congenital or chronic respiratory disease in 6.9% (13 individuals). Lastly, the types of sepsis identified were classified as CPS in 56.6% of the cases (107 individuals) and CNS in 43.3% (82 individuals) (Table 1).

Among the CPS group, which consisted of 107 patients, 25 individuals (23.4%) experienced in-hospital mortality. In contrast, the CNS group, comprising 82 patients, saw a lower mortality rate, with only 10 patients (12.2%) succumbing during their hospital stay. The statistical analysis yielded a P-value of 0.05, indicating that the difference in mortality rates between the two patient groups was deemed significant. Overall, 82 patients (76.6%) in the CPS category survived, while 72 patients (87.8%) in the CNS group were also discharged alive (Table 2).

Table 1. Baseline Characteristics.

Variable	Value (N=189)
Age (Years)	3.2±2.6
Male Gender (%)	103 (54.4%)
Socio-economic Status	
Low Income	94 (49.7%)
Middle Income	56 (29.6%)
High Income	39 (20.6%)
Primary Site of Infection	
Bloodstream	36 (19.0%)
Respiratory	74 (39.1%)
Genitourinary	65 (34.4%)
Skin/Soft Tissue	10 (5.2%)
Abdominal	04 (2.1%)
Comorbidities	
Immunodeficiency	05 (2.6%)
Neutropenia or Malignancy	17 (9.0%)
Malnutrition	22 (11.6%)
History of Previous Sepsis	03 (1.6%)
Congenital Heart Disease	09 (4.7%)
Congenital/ Chronic Respiratory Disease	13 (6.9%)
Type of Sepsis	
CPS	107 (56.6%)
CNS	82 (43.3%)

Table 2. Comparison of In-hospital Mortality in CNS and CPS Patients.

In-hospital Mortality	CPS (N=107)	CNS (N=82)	P-value
Yes (%)	25 (23.4%)	10 (12.2%)	0.05
No (%)	82 (76.6%)	72 (87.8%)	

DISCUSSION:

In the evaluation and management of septic shock in pediatric patients, it is standard practice to conduct microbial cultures to identify any pathogenic organisms. However, the rate of positive culture results is often quite low, and the implications of these results—whether positive or negative—on the course of treatment and the overall prognosis for children experiencing septic shock are still not well defined (Woods-Hill et al., 2023; Miranda and Nadel, 2023). Sepsis presents as a highly variable clinical condition, characterized by a diverse array of signs and symptoms that can evolve over time. Additionally, there are non-infectious causes, such as Kawasaki shock syndrome, hemophagocytic syndrome, and macrophage activation syndrome, that can mimic sepsis, potentially leading to misdiagnosis and, consequently, a decrease in the rate of positive cultures (Paul, 2018).

This research indicated that negative culture outcomes are relatively frequent among children with septic shock, diagnosed in 43.3% patients, aligning with previous studies that have examined similar pediatric cases involving septic shock or severe sepsis. Kim et al. reported CNS in 41.1% patients and Phua et al. reported CNS in 41.5% patients (Kim et al., 2021; Phua et al., 2013). While some studies have reported lower detection rates of CNS, such as study by Hazwani et al. reported CNS in 14.3% patients (Hazwani et al., 2020). While a study by Clemens et al. reported very high rate of CNS (91%) in sepsis suspected pediatric patients (Clemens et al., 2024).

In our study, in-hospital mortality was significantly higher in CPS; 23.4% versus 12.2% in CNS patients. Hazwani et al. conducted a study on frequency and outcomes of culture negative sepsis (CNS) in suspected patients and reported in-hospital mortality in 43% of patients having culture-positive sepsis (CPS) and in 20% of patients with culture-negative sepsis (Hazwani et al., 2020).

While a study by Huang et al. did not find any significant difference in in-hospital mortality rates; 47.6% in CNS and 46.5% in CPS group (Huang et al., 2022).

Our study has a few notable limitations that should be acknowledged. Firstly, it did not take into account cases of sepsis resulting from non-bacterial pathogens or those confirmed through non-culture techniques. Therefore, one should exercise caution when extrapolating our findings to encompass all forms of sepsis beyond bacterial origins. Secondly, in classifying cases as either culture-positive or culture-negative, there is a possibility that some instances were categorized as culture-negative because of inadequate testing. Moreover, various technical challenges might have influenced the results of bacterial cultures. As a result, the classification of culture-negative sepsis might not accurately represent the underlying condition. Nevertheless, given that patients within our study underwent a wide array of culture and serology tests for various pathogenic microorganisms, it appears unlikely that the culture-negative group was significantly affected by the presence of undetected non-bacterial pathogens. Thus, we assert that the definition of culture-negative sepsis used in our research accurately reflects what is observed in clinical practice.

CONCLUSION:

There is a significant number of pediatric patients having CNS admitted with sepsis suspicion. The mortality rate in CPS is higher in comparison to CNS patients.

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