

Characteristics and Outcomes of Blood Culture- Positive Versus Blood Culture- Negative Patients Admitted in Pediatric Intensive Care Unit in Chittagong Medical College Hospital

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ABSTRACT

Background: Only a few studies investigated the association of a positive blood culture with mortality in the pediatric population, the predictive significance of a positive blood culture in children admitted to the Pediatric Intensive Care Unit (PICU) remains uncertain. This study aimed at evaluating the characteristics and outcomes of negative blood culture compared to those of positive blood culture in children admitted to the PICU of Chittagong Medical College Hospital (CMCH).

Materials and methods: A retrospective cohort study was conducted at the PICU of CMCH. All pediatric patients, from 1 month to 12 years of age, admitted between October 2021 and March 2022 were included in the study. All blood culture samples sent from patients hospitalized in the PICU of CMCH between October 2021 and March 2022, were evaluated retrospectively. Information collected includes the demographic data, Primary diagnosis, and outcome of the patients.

Results: Of the 214 patients, 29 (13.6%) had a positive blood culture whereas 185 (86.4%) had a negative bacterial blood culture. Pneumonia was extremely common, present in 65.5% and 34% of the patients, respectively in culture positive and negative patients, and tended to result in a positive culture ($p < 0.001$). Mortality was more in negative blood culture (11.9%) versus 6.9% in positive blood culture ($p = 0.428$). Culture-negative patients have a shorter median PICU stay (10 days) than culture-positive patients (15 days) ($p < 0.001$).

Conclusion: The negative bacterial blood culture constitutes a substantial proportion of pediatric patients admitted to PICU. However, culture results were not associated with PICU mortality.

Key words: Blood culture; PICU; Outcome.

Introduction

PICU is predominantly concerned with the management of children with acutely life-threatening conditions in a specialized unit and caring for such critically ill children remains one of the most demanding and challenging aspects of the field of Pediatrics. Infections remain one of the major problems in PICU and are the leading cause not only of admission, but also mortality in developing countries.^{1,2} In South America, a 2021

study showed a high prevalence of sepsis and sepsis-related mortality in a sample of children admitted to PICU, with a quarter of deaths occurring within the first 24 hours of PICU admission.³

Blood culture is fundamental to the definition of sepsis and further management in children with suspected sepsis admitted to a PICU.⁴ However, blood cultures in patients with suspected sepsis are often negative, and isolation of specific organisms by culture remains challenging.⁵ Although 28%- 49% of cases of severe sepsis in adults have been described to be culture-negative, data are limited on the epidemiology and outcomes in the pediatric population of those with culture-negative severe sepsis.⁶ Studies suggest that mortality is not impacted by identification of an infective pathogen and that many clinical characteristics are similar between patients with or without microbiologically documented infection.^{7,8} However, these studies were limited by only including adult patients. The medical literature is surprisingly devoid of information about patients with culture-negative sepsis and very few studies are available from PICU setting.⁹ Hence, it was aimed to compare the characteristics between culture positive and negative PICU admitted patients, and to determine whether culture status is associated with mortality.

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Materials and methods

This descriptive study was conducted in the PICU of the Department of Pediatrics, CMCH, Chattogram, Bangladesh. Approval was obtained from the Ethical Review Committee of Chittagong Medical College (Date: 27.04.2022, number: 2016/324). Informed consent was not obtained from the patients because the study was conducted retrospectively.

All blood culture samples sent from patients in the PICU between October 2021 and March 2022, were evaluated retrospectively. Information collected includes the demographic data, Primary diagnosis and outcome in terms length of PICU stay and PICU mortality.

A total of 10 beds were present in the PICU. Blood culture samples were obtained half an hour or just before initiation of antibiotic treatment and just before the next dose in patients who were receiving antibiotic treatment. Blood culture was done by BactAlert 3D automated method and VersaTREK automated blood culture system in two private laboratories (Chevron Private Limited and VersaTREK automated blood culture of Chattogram. Patients' antibiotics were rescheduled based on the culture and sensitivity report.

Once data collection were completed, data were compiled and tabulated according to key variables. Non-parametric data were expressed as median values [25th percentile (Q1)-75th percentile (Q2)] and compared between groups by the Mann-Whitney U test. Frequency data were expressed as percentages (%) and compared between groups by using Chi-square test or Fisher's exact test as appropriate. The SPSS Statistics for Windows (Version 23.0.) statistical program was used for data processing and analysis. p value <0.05 was considered as significant statistically.

Results

It was found that 214 blood culture samples were sent from the PICU during the study period. Growth was found in 29 (13.6%) blood cultures. The patients' median (Q1, Q3) ages were 9.0 (1.8-34.5) and 11.0 (2.3-48.0) months in the positive and negative bacterial blood culture groups, respectively. Females were predominant in the positive culture group and opposite trend was observed in the negative blood culture group. However, there were no statistically significant differences in the age and sex between the two groups. Most of the patients (75.9%) were from rural areas in both groups (Table I).

Table I Demographic characteristics of the PICU patients (n=214)*

Attributes	Positive blood culture (n=29)		Negative blood culture (n=185)		p value
	n	%	n	%	
Age, months					
≤12 months	18	62.1	81	43.8	0.066*
>12 months	11	37.9	104	56.2	
Median (IQR)	9.0 (1.8-34.5)		11.0 (2.3-48.0)		
Sex					
Male	12	41.4	100	54.1	0.204*
Female	17	58.6	85	45.9	
Residence					
Urban	7	24.1	50	27.1	0.744*
Rural	22	75.9	135	72.9	

*Data were expressed as frequency and percentage if not mentioned otherwise. IQR: Interquartile Range.

*Chi-square test.

Primary diseases admitted to patients in PICU with culture-positive results were dominated by respiratory tract infection and followed by nervous system diseases in culture positive and culture negative group (Table II). However, significantly higher proportion of patients with positive blood culture had pneumonia compared to culture negative patients. Regarding the Meningoencephalitis, significantly higher proportion of patients with negative blood culture had pneumonia compared to culture positive patients. Regarding other sites of infection, there was no statistically significant difference between the positive and negative bacterial blood culture groups (Table II).

Table II Primary disease distribution of PICU patients (n=214)

Primary disease	Positive blood culture (n=29)		Negative blood culture (n=185)		p value
	n	%	n	%	
Pneumonia	19	65.5	63	34.0	<0.001*
Meningoencephalitis	3	10.3	53	28.7	0.037*
Acute lymphoblastic leukaemia	2	6.9	7	3.8	0.437*
Congenital heart disease	1	3.4	13	7.0	0.469**
Acute watery diarrhoea	1	3.4	5	2.7	0.897**
Aplastic anaemia	1	3.4	15	8.1	0.375**
Very late-onset septicemia	1	3.4	16	8.6	0.335**
Nephrotic syndrome	1	3.4	13	7.0	0.469**

*Chi-square test, **Fisher's exact test.

Mortality was more in culture negative PICU admitted cases (11.9%) versus 6.9% in the culture positive without any statistical significance in our study, which indicated a similar proportion of deaths in both groups. The two groups differ significantly in terms of their median stay in PICU, which was comparatively higher the culture positive cases than the culture negative cases (Table III).

Table III Outcomes of the PICU admitted patients: positive versus negative blood culture

Variables	Positive blood culture (n=29)		Negative blood culture (n=185)		p value
	n	%	n	%	
No. of antibiotics used					
Single	5	17.2	25	13.5	0.567*
Multiple	24	82.8	163	86.5	
Length of PICU stay, days					
Median (IQR)	15.0 (10.0-17.0)		10.0 (7.0-11.0)		<0.001†
Expired in PICU					
No	27	93.1	163	88.1	0.428*
Yes	2	6.9	22	11.9	

*Data were expressed as frequency and percentage if not mentioned otherwise, *Chi-square test; †Mann-Whitney U test.

Discussion

The study showed that only 13.6% of the PICU admitted children had a positive bacterial blood culture, which is like Hazwani et al.'s study where the culture positivity rate was 14.3%.⁹ However, the positivity rate was lower than that Morin et al.'s study (30%).¹⁰ The reasons for these findings may be attributed to the aggressive empiric outpatient therapy of infections and early administration of antibiotic therapy before cultures are drawn in patients when infections is suspected in the primary hospitals or in pediatric wards. Other potential explanations include increasing infections with viruses and anaerobic bacteria, particularly in immuno compromised patients, which may cause severe sepsis, as we investigated only the blood culture for aerobic bacterial and fungal organisms in the study.

Study conducted in adult patients with sepsis indicated that patients with positive blood culture were significantly older than the patients with negative blood culture, which was not reflected in pediatric patients.⁸ In the present study, age distribution was similar in both culture positive and culture negative group. Similar findings were reported by Hazwani et al.⁹ Regarding the gender distribution patients with positive blood culture in the current study demonstrated female was higher than male, but males were dominating in the negative blood culture group without any statistical significance. Study findings confirm the findings of Hazwani et al.'s study and indicated that age and sex had no influence on the blood culture positivity in PICU admitted patients.⁹ In the present study, significantly higher proportion of patients with positive blood culture had pneumonia compared to culture negative patients. Regarding the Meningoencephalitis, significantly higher proportion of patients with negative blood culture had pneumonia compared to culture positive patients.

The results demonstrated that the mortality rate in the positive blood culture group was lower than that in the negative bacterial blood culture group, like the study by Gupta et al, but contrary to the study of Hazwani et al.^{11,9} However, the difference in the mortality between two groups was not significant statistically in the present study and a recent research by Sigakis et al. demonstrated that people with culture-negative and those with culture-positive sepsis demonstrated similar characteristics and, after adjusting for illness severity, similar mortality rates.⁸

In the present study, the culture positive and culture negative groups differ significantly in terms of their median stay in PICU, which was comparatively higher the culture positive cases than the culture negative cases. This was probably attributed to the antibiotic rescheduling and monitoring the disease courses in culture positive patients. It is to be noted that significant differences between culture-negative and culture-positive sepsis are identified in a study conducted in adult ICU patients, with the former group having fewer comorbidities, milder severity of illness, shorter hospitalizations, and lower mortality.⁷

Limitations

This study had some limitations. First, the data collection was retrospective. Therefore, there is a risk of missing data, and information bias. Second, there was restriction the analysis to aerobic bacterial cultures and few fungal cultures only. Expansion of the analysis to include other types of organisms, i.e., viruses, could be useful for understanding the association between the culture status and outcome. Third, this was a single-center study with small sample size. Finally, using PICU mortality as an outcome does not capture the impact of culture results on patients surviving with major long-term morbidity.

Conclusion

Findings of the research indicate that a negative bacterial blood culture constitutes a substantial proportion of pediatric patients managed in PICU. However, these pediatric patients have similar mortality rate compared to positive bacterial blood cultures. Despite this, obtaining cultures are important as, when positive, the sensitivities will affect the class of antibiotic and treatment duration.

Recommendations

Negative cultures should not give the clinician a false sense of reassurance – patients are still at risk of death. Considering the findings and limitations of the present study, further large-scale multicenter study is desirable to determine the predictor of mortality in PICU patients in Bangladesh.

Disclosure

All the authors declared no competing interest.

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