FULL PAPER

Main clinical and laboratory features of children with sepsis: A single-center prospective study in central vietnam

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Sepsis, a life-threatening inflammatory response to infection, is a major cause of death in children worldwide, with a higher mortality rate in developing countries due to delayed diagnosis and treatment. This study investigates the clinical, laboratory features and prognostic factors of sepsis in children to improve outcomes. This prospective observational study was done in April 2022 to July 2023 at Pediatric Centre of Hue Central Hospital examined 69 pediatric sepsis cases. Sepsis clinical features and prognostic variables in 69 children were examined in this study. Males outnumbered females (1.2:1) at 32 months, the median age. Most infections were respiratory (30.4%), followed by skin/soft tissue (27.5%) and gastrointestinal tract (26.1%). About 30% of patients had early severe symptoms such hypotension, weak pulse, and protracted capillary refill. At 37.7%, respiratory and cardiovascular organs were most damaged, followed by hematologic (30.4%). Total mortality was 20%, with 35% within 24 hours. Multiple organ dysfunction and reduced consciousness predicted bad outcomes the most (OR 65.6 and 18.7). Among laboratory markers, thrombocytopenia was the biggest death risk factor (OR 17.8). To improve paediatric sepsis outcomes, early detection of severe symptoms and risk factors is crucial. Despite diverse presentations and a high mortality rate (29%), early identification of multiple organ dysfunction, impaired consciousness, and low platelets in pediatric sepsis is crucial for improved survival through aggressive management.

*Corresponding Author: Van-Tuy Nguyen	KEYWORDS
Email: nguyenvantuy@hueuni.edu.vn Tel.: +84392591326	Child; sepsis; treatment outcome.

Introduction

Sepsis is a medical condition marked by an uncontrolled inflammatory reaction to infection, resulting in severe organ dysfunction that can be fatal. It is a significant contributor to illness and death on a global scale, especially among children [1,2].

Worldwide, the occurrence of sepsis in children is approximately 1.2 million cases, with death rates ranging from 1 to 5% for sepsis and 9 to 20% for severe sepsis [2]. Page | 1709



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Various studies undertaken in both developed and developing countries have consistently shown a significantly greater fatality rate from sepsis in developing nations (35%) compared to developed nations (5%). This disparity is attributed to the delayed diagnosis and treatment of sepsis in poor countries [3].

Sepsis progression is characterized by complexity and rapidity. Clinical features are often diverse and atypical, necessitating a combination of diagnostic laboratory tests, as blood cultures often yield delayed results. Sepsis progresses from a mild state to severe sepsis, septic shock, multiple organ dysfunction syndrome, and potentially death [4]. Curbing childhood sepsis mortality poses a significant challenge for the global community, particularly for developing nations, which bear the brunt of both incidence and fatality rates [5]. A study on sepsis in Vietnamese pediatric patients treated in PICU from 2008 to 2018. The study found gastrointestinal tract infections to be the most common source of sepsis, followed by respiratory tract infections. The outcome was severe, with most patients experiencing organ dysfunction and a high mortality rate of 37% [6].

Motivated by the aforementioned challenges, this study aimed to describe the clinical and laboratory features and investigate prognostic factors associated with sepsis in children.

Experimental

Study subjects

The study included 69 children under the age of 16 who were diagnosed and treated for sepsis at Pediatric Center of Hue Central Hospital.

Patient selection criteria

The study included all paediatric patients ages 1 month to under 16 years who were hospitalised for treatment at the Paediatric Centre of Hue Central Hospital between April 2022 and July 2023 and had a confirmed diagnosis of sepsis.

The sepsis diagnosis was made using the diagnostic criteria outlined by the International Paediatric Sepsis Consensus Conference (IPSCC) in 2005 [7]:

 Sepsis: Sepsis is defined as the presence of the Systemic Inflammatory Response
Syndrome (SIRS) criteria in the presence of an infection.

- *Severe Sepsis*: Severe sepsis is defined as sepsis plus one of the following:

Cardiovascular organ dysfunction: Lactate ≥
4 mmol/L (> 35 mg/dL) or hypotension requiring vasopressors

o Acute respiratory distress syndrome (ARDS):
PaO2/FiO2 ≤ 300 mmHg (40 kPa) or SpO2 ≤ 90% on supplemental oxygen

• *Two or more new organ dysfunctions* (e.g., renal, hepatic, and coagulation)

- *Septic Shock*: Septic shock is defined as sepsis plus persistent hypotension requiring vasopressors to maintain mean arterial pressure (MAP) \geq 65 mmHg in adults or \geq 70 mmHg in children despite adequate fluid resuscitation.

Exclusion Criteria

 Lack of informed consent: Children or their caregivers were unable or unwilling to provide informed consent to participate in the study.

– *Chronic organ dysfunction*: Children had pre-existing chronic organ dysfunction that could potentially confound the study results or pose additional risks to the participants.

Study design

This study was cross-sectional descriptive study with prospective follow-up. Likewise, this employed a prospective design, enrolling all children admitted to the PICU with sepsis. Comprehensive clinical and laboratory data were collected for each patient. Diagnoses were established and treatment regimens implemented following the Vietnamese Sepsis



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Guideline. Patients were followed longitudinally from admission to discharge or death.

Statistical analysis

The collected data were analyzed using statistical methods appropriate for the study design and type of data. Statistical software Microsoft Excel 2010 and SPSS 26.0 were utilized to perform the analyses.

Comparison of proportions

To compare proportions between groups, the chi-square test was employed. In cases where one or more expected frequencies were less than 5, Fisher's exact test was used.

Clinical features of sepsis in children

Comparison of means

For normally distributed quantitative variables, comparisons of means were conducted using the Student's t-test and ANOVA. In instances where quantitative variables did not follow a normal distribution, medians were compared using nonparametric tests.

Results and discussion

During the study period, a total of 69 children were diagnosed with sepsis. The participants had a median age of 32 months, and the most common age group was 12 to 60 months, representing 46.4% of the participants. The ratio of males to females was 1.2 to 1.

TABLE 1 Clinical	l presentation of sepsis in children by subclass	

		Sepsis subclasses				
Clinical symptoms		All cases (N = 69)	Sepsis (N = 39)	Severe sepsis (N = 4)	Septic shock (N= 26)	<i>P</i> -value
Hypot	ension	21 (30.4%)	2 (5.1%)	0 (0.0%)	18 (73.1%)	< 0.01
Weak	x pulse	21 (30.4%)	1 (2.6%)	1 (25.0%)	19 (73.1%)	< 0.01
Refill ≥ 3	3 seconds	21 (30.4%)	1 (2.6%)	1 (25.0%)	19 (73.1%)	< 0.01
Glasgow s	≤ 11 points	14 (20.3%)	0 (0.0%)	1 (25.0%)	13 (50.0%)	< 0.01
Oliguria	a/anuria	9 (13.0%)	0 (0.0%)	1 (25.0%)	8 (30.8%)	< 0.01
Time in	Median	11.0	11.0	11.0	10.5	>0.05
hospital	25^{th} - 75^{th}	6.0 - 26.0	7.0 - 26.0	6.3 - 23.3	1.8 – 27	>0.05
Outcome	Alive	49 (71.0%)	38 (97.4%)	3 (75.0%)	8 (30.8%)	< 0.01
	Death	20 (29.0%)	1 (2.6%)	1 (25.0%)	18 (69.2%)	< 0.01

30.4% of patients experienced a notable reduction in systolic blood pressure, with the septic shock group having the highest occurrence at 73.1% compared to the sepsis and severe sepsis groups. This disparity was statistically significant (p < 0.01), as seen in Table 1. A weak pulse was observed in 30.4% of patients, with the highest occurrence in the septic shock group (73.1%). This disparity was statistically significant (p < 0.01). A capillary refill time of > 3 seconds was found in 30.4% of patients, with the highest occurrence in the septic shock group (73.1%). This disparity was statistically significant (p < 0.01). Among the patients, 20.3% had a Glasgow Coma Scale (GCS) score of 11 points or below. The septic shock group had the highest prevalence of this condition, with 50.0% of patients affected. This difference was shown to be statistically significant (p < 0.01). Thirteen percent of patients exhibited oliguria, with the septic shock group having the greatest prevalence at



30.8%. This disparity was found to be statistically significant (p < 0.01). Wang *et al.* delineated that individuals diagnosed with sepsis, severe sepsis, and septic shock constituted 50.5% (293 out of 580), 17.4% (101 out of 581), and 32.0% (186 out of 580) of the overall cohort, respectively [8]. A study examining the utilization of the AVPU score by Teresa Bleakly Kortz found that 82% of the sample (n = 331) were classified as "alert". The most prevalent criterion observed was respiratory insufficiency, present in 86.4% (n = 350) of the patient cohort. Subsequently, deviations in temperature, heart rate, and general appearance were documented, with frequencies of 70.9% (n = 287), 60% (n = 243), and 53.3% (n = 216) respectively, within the scrutinized patient population [9].

In our study, 89.9% of children had an identified focus of infection. Among these, the respiratory tract was the most common focus, accounting for 30.4%, followed by skin/soft tissue and the gastrointestinal tract with prevalences of 27.5% and 26.1%, respectively. The least common foci were the musculoskeletal system (4.3%) and the renal-urinary tract (1.4%). The respiratory and gastrointestinal tracts are the most prevalent

foci of infection in sepsis because they represent two pathways of easy exposure and transmission of pathogens from the surrounding environment through ingestion, sneezing, coughing, etc. Wang et al. reported that the respiratory tract was the most frequent site of infection (52.9%), followed by the abdominal cavity (13.8%) [8].

In our study, the most frequently affected organ systems were the respiratory (37.7%) and cardiovascular (37.7%) systems, followed the hematologic system (30.4%). by Neurological, renal, and hepatic dysfunction each occurred in 20.3% of patients. Weiss et al. similar findings, reported with а predominance of respiratory (82.7%), cardiovascular (70.2%), hematologic (30.9%), and hepatic (25.2%) organ dysfunction [4].

The treatment outcomes for our study subjects were as follows: 71.0% survived and 29.0% died. Among the fatalities, 35% of children died within the first 24 hours of admission to resuscitation. Our findings indicate a higher mortality rate compared to global studies. Mishra *et al.* reported a mortality rate of 7.3% for sepsis in PICU settings [10]. Boeddha *et al.* reported a mortality rate of 6% (51/795) [11].

Characteristic	Alive (N = 49)	Death (N = 20)	OR (95%CI)	<i>P</i> -value
Have an underlying	8 (38.1%)	13 (61.9%)	9.5 (2.9 – 31.3)	< 0.01
medical condition				
Refill ≥ 3 seconds	9 (42.9%)	12 (57.1%)	6.7 (2.1 - 21.1)	< 0.01
Hypotension	8 (38.1%)	13 (61.9%)	9.5 (2.9 - 31.3)	< 0.01
Weak pulse	7 (33.3%)	14 (66.7%)	14.0 (4.0 - 48.7)	< 0.01
Glasgow ≤ 11	3 (21.4 %)	11 (78.6%)	18.7 (4.3 - 80.9)	< 0.01
Oliguria	2 (22.2 %)	7 (77.8%)	12.7 (2.3 - 68.4)	< 0.01
Multi-organ failure	11 (36.7%)	19 (63.3%)	65.6 (7.9 - 546.8)	< 0.01

TABLE 2 Association of clinical Features with treatment outcomes

This study demonstrated a significantly higher mortality rate in patients with underlying comorbidities (61.9%) compared to those without comorbidities (14.6%). The presence of underlying comorbidities was associated with a 9.5-fold increased risk of mortality in sepsis (OR = 9.5; p < 0.01) (Table 2). Consistent with our findings, Rusmawatiningtyas *et al.* also reported a higher prevalence of underlying comorbidities in the non-survivor group (47.8%) and a significantly elevated risk of mortality in patients with comorbidities (p < 0.001) [12].

Patients who had a capillary refill time of 3 seconds or more had a death rate of 57.1%, which was significantly greater than the

mortality rate of 16.7% observed in patients with a capillary refill time of less than 3 seconds. There was a strong association between a longer capillary refill time and a 6.7 times higher risk of mortality (OR = 6.7; p <0.01). A low Glasgow Coma Scale (GCS) score of 11 points or less was shown to be much more common among those who did not survive compared to those who did survive with a GCS score higher than 11 points. This low GCS score was related with a significantly higher chance of mortality, with an 18.7-fold increase in risk. The statistical analysis showed a strong correlation (OR = 18.7; p < 0.01). The oliguria presence was shown to be strongly correlated with a higher mortality rate of 77.8%, in contrast to patients with normal urine output



who had a mortality rate of 21.7%. Oliguria was identified as a significant risk factor for mortality, with a 12.7-fold increased risk (OR = 12.7; p < 0.01) (Table 2).

Patients diagnosed with multiple organ dysfunction syndrome (MODS) had a mortality rate of 63.3%, which was much greater than the mortality rate of 2.6% observed in patients without MODS. The MODS presence was linked to a 65.6 times higher chance of death in sepsis (odds ratio = 65.6; p < 0.01). Our findings align with those of Bansude *et al.*, who observed a substantial correlation between the development of MODS and mortality, with a p-value of 0.001 [13].

Laboratory features of sepsis in children

TABLE 3 Laboratory features of sepsis in children by subclass
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	Sepsis subclasses				
Laboratory features	All cases (N = 69)	Sepsis (N = 39)	Severe sepsis (N = 4)	Septic shock (N = 26)	<i>P</i> -value
White blood cells	12.4	14.9	10.7	3.7	< 0.01
(10 ⁹ /L)	(4.8 - 19.7)	(11.3 - 21.5)	(2.6 - 14.6)	(0.9 - 14.2)	< 0.01
Platelet	247.0	265.0	274.0	87.5	< 0.01
(10 ⁹ /L)	(99.5 - 330.0)	(235 - 376.0)	(59.8 - 470.3)	(21.0-196.5)	< 0.01
CRP (mg/L)	110.1 (42.0 - 308.2)	109.5 (60.1 - 188.3)	94.5 (20.6-305.5)	125.2 (24.6-257.6)	> 0.05
Creatinine (µmol/L)	46.9 (35.5 - 81.6)	38.8 (30.3 - 53.3)	108.1 (34.1 - 232.2)	79.3 (48.0 - 161.8)	< 0.01
SGPT (U/L)	29.5 (18.0 - 81.0)	21.4 (12.1 - 38.9)	382.1 (87.6 - 2264.9)	49.2 (30.5 - 194.2)	< 0.01
SGOT (U/L)	51.5 (29.6 - 139.6)	40.0 (25.3 - 53.7)	720.8 (202.5 - 2882.4)	115.1 (49.7 - 520.1)	< 0.01
Lactate (mmol/L)	2.8 (1.8 - 4.5)	2.0 (1.3 - 3.0)	2,3 (2.0 - 3.4)	3.8 (2.7 - 6.9)	< 0.01

This work revealed a significantly lower median white blood cell count in septic shock patients (3.7×10^9 /L; 0.9-14.2) compared to sepsis (14.9×10^9 /L; 11.3-21.5) and severe sepsis (10.7×10^9 /L; 2.6-14.6) groups (p < 0.05) (Table 3). Septic shock patients also exhibited a significantly lower median platelet count (87.5×10^9 /L; 21.0-196.5) compared to sepsis (265.0×10^9 /L) and severe sepsis (274.0×10^9 /L) groups (p < 0.01). The median serum C-reactive protein (CRP) level was 110.1 mg/L (62.7-191.5), with the highest value observed

in the septic shock group (125.2 mg/L; 24.6-257.6). However, this difference was not statistically significant (p = 0.98). The highest median serum creatinine level was found in the severe sepsis group (108.1 µmol/L; 34.1-232.2) compared to the sepsis (38.8 μ mol/L) and septic shock (79.3 µmol/L) groups (p < median 0.01). The serum alanine aminotransferase (SGPT) and aspartate aminotransferase (SGOT) levels.

In Shannon Byler's investigation concerning pediatric patients, elevations in



CRP, ESR, lactic acid, and procalcitonin levels exhibited specificity, albeit lacked sensitivity, in discerning children manifesting SIRS who subsequently progressed to severe sepsis. Noteworthy, surpassing defined thresholds of these biomarkers may exert influence on clinical decision-making regarding the initiation of fluid therapy, antibiotic administration, hospitalization, and the imperative for intensive care [14].

TABLE 4 Association of laborator	<i>i</i> features with treatment outcomes
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Characteristic	Alive (N = 49)	Death (N = 20)	OR (95%CI)	P-value
Hyperleukemia	21 (80.8%)	5 (19.2%	0.4 (0.1 – 1.4)	> 0.05
Thrombocytopenia	9 (36.0 %)	16 (64.0%)	17.8 (4.8 - 66.1)	< 0.01
CRP increased	44 (74.6%)	15 (25.4%)	0.26 (0.1 - 1.3)	> 0.05
SGOP increased	23 (62.2%	14 (37.8%)	2.4 (0.8 – 7.4)	> 0.05
SGPT increased	15 (62.5%)	9 (37.5%)	1.7 (0.6 – 5.1)	> 0.05
Creatinine increases	12 (42.9%)	16 (57.1%)	11.3 (3.1 - 40.7)	< 0.01
Lactate increased	4 (30.8 %)	9 (69.2%)	6.8 (1.6 - 28.0)	< 0.01
Blood cultures positive	11 (52.4%)	10 (47.6%)	3.5 (1.1-10.4)	< 0.05

Patients with thrombocytopenia (64.0%) exhibited a significantly higher mortality rate compared to those without thrombocytopenia (9.1%). Thrombocytopenia was associated with a 17.8-fold increased risk of mortality (OR = 17.8; p < 0.01) (Table 4).

A significantly higher mortality rate was observed in patients with elevated serum creatinine levels (57.1%) compared to those with normal creatinine levels (10.5%). Elevated serum creatinine was associated with an 11.3-fold increased risk of mortality (OR = 11.3; p < 0.01) (Table 4).

Patients who had blood lactate levels more than 4 mmol/L (69.2%) showed a significantly increased death rate in comparison to those with lactate levels below 4 mmol/L (25.0%). An elevated level of lactate in the blood was found to be associated with a 6.8 times higher risk of death (odds ratio = 6.8; p < 0.01) (Table 4). In line with our discoveries, Boeddha *et al.* documented that increased lactate levels upon admission to the paediatric intensive care unit (PICU) were likewise linked to mortality in cases of sepsis [11].

The mortality rate shown a substantial increase in the positive blood culture group (47.6%) when compared to the negative blood culture group (29.8%). Having a positive blood

culture was linked to a 3.5 times higher chance of dying (odds ratio = 3.5; p < 0.01). In line with our results, Rusmawatiningtyas *et al.* observed a correlation between a positive blood culture and death, with a p-value of 0.001 [12].

Nur Farhanah's research suggested that biomarkers should not be used in isolation, but rather in conjunction with other risk factors for septic shock. The prognosis and diagnosis often result from the combined influence of numerous contributing factors. The combination of five biomarkers (white blood cell count, procalcitonin, presepsin, MR-Proadrenomedullin, and lactate), clinical scoring (SOFA score), and additional risk factors (skin and soft tissue infection as well as hypertension) proved to be more accurate in predicting septic shock than any individual factor [15].

Conclusion

Pediatric sepsis carries a high mortality rate (29%) and presents with diverse symptoms and infection sources. This study identified multiple organ dysfunction, impaired consciousness, and low platelet count as the strongest predictors of poor outcomes. Early recognition and aggressive management of

these complications are essential to improve survival rates in children with sepsis.

The limitation of the study

This study is limited by a relatively small sample size and by being conducted at a single centre. In addition, the analysis did not employ a multivariate approach to examine all potential effect factors.

Acknowledgements

We are grateful to Professor Tran Kiem Hao, Head of the Pediatric Center, Hue Central Hospital for his invaluable support throughout this project from its inception.

We extend our sincere thanks to Dr. Nguyen Dac Luong, Dr. Pham Kieu Loc, and the other esteemed doctors in the Pediatric Intensive Care Unit (PICU) and the Pediatric Tropical Department for their dedicated care and follow-up of the patients involved in the study.

We are also indebted to Dr. Pham Thi Ngoc Bich, a Master's student, for her meticulous efforts in data collection and initial organization.

Finally, we acknowledge all individuals who played a role in the implementation of the survey. Their contributions are deeply appreciated.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Authors' Contributions

Chau Duc Nguyen-Huu designed, contributed data analysis and supervised the entire project. Van-Tuy Nguyen designed the study, conducted the experiments, analyzed the data, and participated in writing the manuscript. All authors read, commented on, and approved the manuscript.

Conflict of Interest

Journal of Medicinal

and Pharmaceutical Chemistry Research

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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How to cite this article: Chau Duc Nguyen-Huu, Van-Tuy Nguyen, Main clinical and laboratory features of children with sepsis: A single-center prospective study in central vietnam. Journal of Medicinal and Pharmaceutical Chemistry Research, 2024, 6(11), 1708-1715. Link: https://jmpcr.samipubco.com/article_1964 59.html

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