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Research

A prospective study on outcomes for the septic shock in children admitted to a tertiary care hospital

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	<h3>Abstract</h3>
<p>Published on: 15 Dec 2023</p>	<p>Background: Pediatric sepsis, sepsis syndromes and septic shock are significant causes of morbidity and mortality among children all over the globe and cause an alarming burden to patient care in Pediatric Intensive Care Units (PICU). With mortality as high as 80% and relative paucity of epidemiological data regarding sepsis in children, there is need for large scale studies to evaluate various aetiologies, risk factors and factors associated with poor outcome in children with various sepsis syndromes.</p> <p>Objectives: To study the prevalence, assess the clinical profile, analyse the laboratory parameters and outcome in patients with septic shock admitted to PICU.</p> <p>Methods: This prospective observational study was carried out between December 2019 and November 2021 in the PICU of a tertiary care hospital. All relevant clinical, laboratory and other data was collected from patients with septic shock aged between 1 month to 14-year.</p> <p>Results: Among all the patients in PICU with shock, septic shock was diagnosed in 8.06% (n=85) cases, 44.5% (n=33) of them being infants. Mean age was 3 year 10 months with male preponderance. Most of them belonged to lower socioeconomic class (86.4%, n=64). Most common presenting symptom was abnormality of body temperature (87.8%, n=65). Incomplete immunization was observed in 43% (n=35). Pallor and anemia were present in almost 2/3rd of cases. <i>Staphylococcus aureus</i> was the most common organism isolated from culture of various body samples (47.6%, n=11). Most of the patients were fluid refractory (93.2%, n=65) and required vasopressor support, with 47% among these requiring ≥ 3 vasopressors. Need for corticosteroid use was associated with adverse outcomes. Various factors having significant association with mortality were inadequate immunisation, anemia, positive growth on blood culture, deranged renal and liver function tests, respiratory failure requiring mechanical ventilation, multi organ dysfunction, need for multiple vasopressors and administration of corticosteroids.</p> <p>Conclusions: Successful management of pediatric septic shock requires good infrastructure, trained staff and protocol based management which may be modified from time to time basing upon constantly changing evidence-based medicine.</p>
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<p>2023 All rights reserved.</p>  <p>Creative Commons Attribution 4.0 International License.</p>	<p>Keywords: sepsis syndrome, pediatric critical care, pediatric septic shock, mortality, septic shock, sepsis, pediatric intensive care unit etc.</p>

INTRODUCTION

Various sepsis syndromes, septic shock and resulting multiorgan dysfunction syndromes (MODS) are commonly encountered in PICU settings, especially in developing countries [1]. Among the continuum of host response to infection, which ranges from sepsis to MODS, septic shock is a subset characterised by cellular, metabolic and circulatory abnormalities which, when progresses unchecked, can result in significant morbidity and mortality [2]. Mortality due to pediatric septic shock ranges from 5% in developed countries to as high as 35% in developing countries [3]. Despite pediatric septic shock being a condition of global concern, adequate epidemiological data regarding sepsis in children is still scarce. Few previous studies have reported incidence of pediatric septic shock in PICUs to be around 2-3% in developed countries and 18-46% in developing countries with mortality as high as 80% [4,5].

With the advent of advanced diagnostic and monitoring equipment, novel therapies and increased awareness about importance of good sanitation and hygienic practices especially after COVID-19 pandemic in developing countries, the prevalence and mortality rate of paediatric septic shock is expected to be decreasing and newer epidemiological studies are the need of the hour to find out the current trend basing upon which modulation of existing protocols can be done for better management patients with septic shock in the PICU [6,7].

Keeping this in mind, the study was conducted in a tertiary care hospital of eastern Odisha which caters to a significantly large group of patients from all over the state and country to find out the recent trends of pediatric septic shock in the patients admitted to the PICU.

OBJECTIVES

- To study the prevalence of septic shock in patients admitted to the PICU.
- To assess the clinical profile, laboratory parameters and outcome in patients with septic shock.
- To find out the association of various clinical and laboratory parameters with various complications and mortality in patients with septic shock.

MATERIALS AND METHODS

This hospital based prospective observational study was carried out between December 2019 and November 2021 (2-year period) in the Pediatric Intensive Care Unit (PICU) of SCB Medical College and Hospital, Cuttack and SVPPG Institute of Paediatrics, Cuttack. All relevant data was collected from patients aged between 1 month to 14-year who were diagnosed to be in shock at the time of admission to hospital or during the hospital stay, fulfilling the criteria of septic shock. The population that was excluded from the study were those not fulfilling the criteria for septic shock, discharged/left hospital against medical advice (LAMA) or consent for this study denied from the parents or the caregivers or data records or laboratory investigations were incomplete. Sample size was calculated using Fischer's formula i.e.,

$$n = Z^2 (1-p) p / d^2$$

where,

n = desired sample size

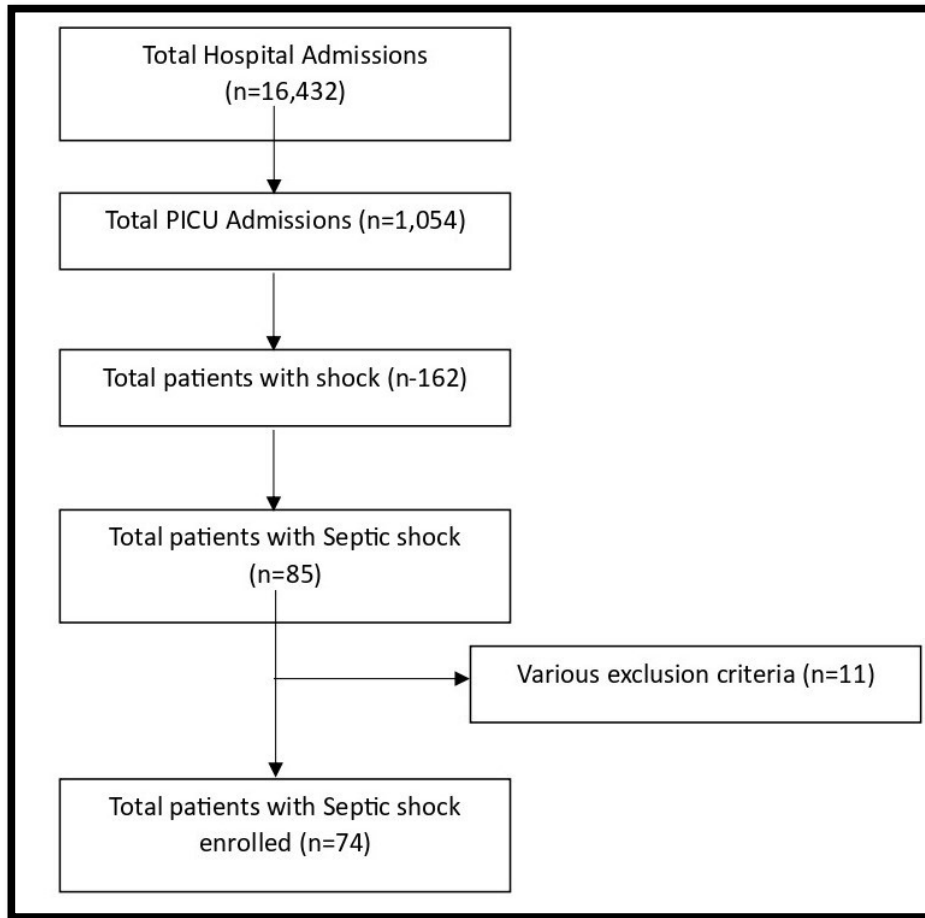
z = value representing 95% confidence interval (1.96)

d = absolute amount of error tolerated (5% chance of error)

p = prevalence (5% as observed from previous study) [7].

The desired sample size was calculated to be 73.

After obtaining approval from Institutional Review Board (Institutional Ethics Committee, S.C.B. Medical College and Hospital, Cuttack IEC application number 578, dated 11.02.2021) and informed consent from parents or guardians; demographic profile, detailed history, clinical presentation, laboratory parameters, details regarding end-organ dysfunction, need for inotropes and mechanical ventilation were obtained and recorded. Appropriate investigations like Complete Hemogram, serum electrolytes, C-reactive protein (CRP), blood glucose, renal function test, blood culture by BACTEC method, Cerebrospinal Fluid (CSF) study, urinalysis, blood gas estimation, chest x-ray, ultrasonography were done to identify the aetiology. Outcome was assessed basing upon improvement or deterioration during the course of illness including the duration of PICU admission and final clinical diagnosis. Data was collected and analysed using statistical software SPSS (software version 26). Categorical variables were expressed in numbers and percentages while continuous variables were expressed as minimum, maximum, mean, median, standard deviation as appropriate. Chi square test was used to determine the association between different variables. A level of 5% was taken i.e., $p < 0.05$ was considered significant.



Flow Chart 1: Study period

Out of 16,432 hospital admissions in the study period, a total of 74 patients were included in the study as per the flow chart given.

RESULTS

Out of the total number of patients hospitalised, 6.41% (n=1,054) required admission to PICU, amongst which 15.37% (n=162) developed shock at any point during their illness. Sepsis was attributed as the cause in 8.06% (n=85) of cases developing shock. Majority of these patients were infants (44.5%, n=33) and around 2/3rd (n=46) were under-5 children. The mean age was 3-year 10 month with slight male preponderance (56.8%, n=42). Significant proportion (86.4%, n=64) belonged to lower socioeconomic class based upon the modified Kuppuswamy scale 2021.

The most common symptom at presentation was change in body temperature (hypothermia or fever) which was present in 87.8% (n=65) cases. Central nervous system manifestations like convulsions, altered sensorium were observed in 43.2% (n=32) and 39.1% (n=29) cases respectively. A minority of population had complaints related to the gastrointestinal symptoms like vomiting (62.1%, n=46), abdominal pain (35.1%, n=26) or distension (40.5%, n=30).

Out of 65 patients presenting with change in body temperature, 4 had hypothermia (5.4%) while 61 had fever (82.4%). Mean duration of fever was 5.4 days (± 3.6) ranging from 2 days to 20 days. Out of the total, 52.7% (n=39) of the children had up to date immunisation according to national immunisation schedule, patients with incomplete vaccination status were observed to be more predisposed to poor outcomes. Pallor was the most common general examination finding (70.2%, n=52). Icterus, cyanosis and clubbing were present in 19% (n=14), 13.5% (n=10) and 4% (n=3) cases respectively. Patients having pallor demonstrated significant association with mortality (57.6%, n=30). Among the patients with septic shock, anemia was present in 67.5% (n=50) cases and leucocytosis was present in 55.4% (n=41) cases. Neutrophil predominance was seen in 22.9% (n=21) cases while lymphocytic in 22.9% (n=17) cases. Thrombocytopenia was seen in around 1/3rd patients (n=23). The most common electrolyte abnormality observed was hypocalcemia (56.7%, n=42) followed by hyponatremia (28.3%, n=21) and hypernatremia (27%, n=20). Hypokalemia (21.6%, n=16) and hyperkalemia (14.9%, n=11) were

occasionally seen. Derangement of sodium levels (both hypo and hypernatremia) was associated with significant mortality. Elevated CRP levels were seen in majority of cases (85.1%, n=63) and abnormal renal function parameters were found in 56.8% cases (n=42). Blood gas analysis was done in 53 patients which revealed metabolic acidosis to be most common (45.3%, n=24) finding.

Table 1: Epidemiological Profile and presenting complaints

Parameters	Numbers	Percentages	Number of deaths	χ^2	p value	
Demographic profile						
Age	1 month – 1 year	33	44.5%	18	1.589	0.6618
	1 year – 5 years	13	17.5%	7		
	5 years – 10 years	13	17.5%	5		
	>10 years	15	20.2%	6		
Males	42	58.3%	20	0.004	0.9493	
Lower SES	32	43.2%	33	3.456	0.063	
Completely immunized as per age	39	52.7%	10	15.514	<0.001	
Death	36	48.65%				
General Examination findings						
Pallor	52	70.2%	30	7.582	0.0058	
Edema	40	54%	17	0.8038	0.3699	
Lymphadenopathy	29	39.2%	11	1.6783	0.1951	
Hematological Findings						
Anemia	50	67.5%	29	7.0845	0.0077	
Leucocytosis	41	55.4%	25	2.4244	0.1194	
Thrombocytopenia	23	31.08%	14	2.4662	0.11632	
Presenting Symptoms						
Fever	61	82.43%				
Fever during presentation	Up to 5 days	29	39.18%			
	5-10 days	24	32.42%			
	>10 days	8	10.8%			
Vomiting	46	62.1%				
Breathlessness	40	54%				
Cough	38	51.3%				
Convulsion	32	43.2%				
Abdominal distension	30	40.5%				

BACTEC blood culture of 42 patients were sent, out of which 20 samples (47.6%) showed growth after 72 hours. Appropriate biological specimens were sent on case-to-case basis out of which total Culture Positivity was found in 32 patients. 6 patients had growth in 2 specimens while 1 patient was found to have growth in all 3 samples tested. Staphylococcus aureus was the most common organism isolated (i.e., 33.3%, n=11) followed by Enterococcus spp, E. coli and Acinetobacter spp.

Table 2: Investigations, complications, organisms isolated

Biochemical abnormalities	Numbers	Percentage	Number of deaths	χ^2	p Value
Hypocalcemia	42	56.75%	22	1.007	0.315
Hyponatremia	21	28.37%	12	4.65	0.0308
Hypokalemia	16	21.62%	6	0.138	0.709
CRP-Q positivity	63	85.13%	32	2.0785	0.149
Deranged renal function test	42	56.75%	29	20.871	<0.001
Metabolic acidosis	24	32.43%	11	4.02	0.0447
Complications associated with shock					
MODS	40	54.05%	29	22.018	<0.001
Mechanical ventilation	52	70.27%	34	22.955	<0.001
Compensated shock	38	51.35%	13	5.3667	0.02
Encephalopathy	38	51.35%	24	7.882	0.0049
AKI	35	47.29%	29	33.6	<0.0001
Vasopressors and steroids required					
3 vasopressors	32	43.25%	27	33.68	<0.001

2 vasopressors	25	33.78%	5		
Steroids used	30	40.54%	21	10.4324	0.0012
Duration of PICU stay					
Up to 5 days	21	28.37%	19		
5-10 days	30	40.54%	5	0.518	0.9149
Pathogenic organisms isolated (n=40)					
Urine	13	32.5%			
Blood	20	50%			
Staphylococcus aureus	11	27.5%			
Enterococcus	7	17.5%			
E coli	6	15%			
Acinetobacter	6	15%			

CSF analysis was done in 28 out of 74 patients (i.e., 37.9%) revealing leucocytosis in 22 (78.6%) with polymorphonuclear cell predominance in 11 patients (39.3%) and lymphocytic predominance in 8 patients (28.6%). A single patient showed albumin-cytological dissociation. Of all the laboratory parameters, growth in blood culture, deranged liver function tests and renal function tests were significantly associated with mortality. Renal impairment, being an indicator of end-organ damage, was found to be highly significant. Nearly half of all cases of septic shock presented with hypotension (48.65%, n=36). Among the various complications observed in these patients, most common was respiratory failure requiring mechanical ventilation (70.3%, n=52) followed by MODS (54%, n=40) and encephalopathy (51.35%, n=38). All these features were significantly associated with mortality, respiratory failure and MODS being the highest. Five patients improved with fluid resuscitation while 69 (93.24%) were fluid refractory requiring inotropes/vasopressors. Most common vasopressor used was Noradrenaline. A total of 35 patients (47.3%) required 3 or more vasopressors for management of shock. There was a significant association between number of vasopressors used and mortality. Corticosteroids were used in 30 cases (40.54%) either due to primary causes or to manage catecholamine refractory shock. There was a significant association between the need of corticosteroids and mortality. Mean duration of PICU stay was 9 days (1day-48days). Majority (40.5%, n=30) patients had a stay lasting from 5-10 days. Duration of PICU stay was not significantly associated with mortality. The most common cause of septic shock diagnosed among patients in our study was pneumonia (24.32%, n=18).

Table 3: Aetiology and predisposing factors

Parameters	Numbers	Percentages
Aetiology of Septic Shock		
Pneumonia	18	24.32%
Meningitis	16	21.62%
Septicemia	13	17.56%
Scrub Septicemia	6	8.10%
Urosepsis	5	6.75%
Empyema	4	5.4%
MIS-C	4	5.4%
Malaria	4	5.4%
Diabetic Ketoacidosis	2	2.7%
Intraventricular hemorrhage	2	2.7%
Major predisposing Factors		
Severe acute malnutrition	9	12.16%
Congenital heart disease	7	9.45%
Moderate acute malnutrition	3	4.05%
Chronic kidney disease	3	4.05%
Chronic liver disease	3	4.05%
Tuberculosis	2	2.7%
Prematurity	2	2.7%

Mortality rate being 47.29% (n=35) in our study. Various factors having significant association with mortality were inadequate immunisation, anemia, serum Sodium abnormality (hyponatremia or hypernatremia), positive growth on blood culture, deranged renal and liver function tests, complications like respiratory failure requiring mechanical ventilation, multi organ dysfunction, need for multiple vasopressors and administration of corticosteroids.

DISCUSSION

Out of total PICU admission, shock was associated in 15.37% (n=162) and prevalence of septic shock was 8.06% (n=85). Despite adequate western data indicating around 2% prevalence of pediatric septic shock, there is a paucity of data regarding incidence of shock in developing countries. Similar studies done in Maharashtra and Punjab have demonstrated prevalence of septic shock to be 9% and 4.3%, respectively [8,9]. The higher prevalence found in our study may be attributed to the fact that our hospital is a tertiary care hospital acting as one of the highest referral centres for the state of Odisha, delay in recognising critical illnesses and delayed transfer to higher centres for better management. Slight male preponderance found in our study (i.e., 1.3:1) was in contrast to that found in some other studies [9].

Majority of children with septic shock in our state were under-5 children with 44.5% being infants. While the median age in our study was 3 year 10 months, other studies that have included neonates have found a median age as low as 4 months [9]. More than 4/5th of the population belonged to a lower socio-economic status family. This may be explained by the relatively under developed immune system in this age, the poor sanitary practices, the lack of awareness to seek health care services and reiterates the importance of our need to reemphasise the sepsis prevention measures in the younger population, especially under-5 children belonging to poor families. Presence of fever, vomiting, tachypnoea in the majority of children corroborates with our finding of pneumonia as the commonest clinical diagnosis in such children. Similar data has been obtained by other studies done in India and abroad [10,11].

The poor prognosis in incompletely immunised children found in our study underlines the association of vaccine preventable diseases with septic shock and emphasizes the need to strengthen the immunisation program in our state and our country [12].

Common clinical findings found in the majority of study population were pallor, edema and lymphadenopathy, 71%, 54% and 39% respectively. Malnutrition revealed in 26.05% of under-5 children was primarily due to improper feeding practices or secondary to underlying disease. This indicates that anemia and malnutrition continue to remain the leading risk factors for disease burden in India and are significantly associated with mortality in patients with septic shock [13].

Although hypocalcemia, hyperkalemia and hypokalemia were found in patients with septic shock, only hyponatremia and hypernatremia were significantly associated with mortality in such patients. Hyponatremia is known to be associated with higher admission rates, higher body temperatures, leucocytosis and higher CRP levels in pediatric septic shock and is an important parameter before considering fluid management in such children [14]. Deranged renal and liver function showed significant mortality association in our study which may be attributed to poor end organ perfusion.

Most common organism isolated from various culture studies was *Staphylococcus aureus* followed by *Enterococcus* spp, which was similar to that found in other studies [13]. This relatively low yield of culture may be increased by increasing the point of care quality, ensuring proper aseptic sampling methods among health care personnel and by ensuring proper handling and transport to the processing laboratory.

Relatively higher prevalence of hypotension requiring higher doses with multiple inotropes/vasopressors was associated with high mortality and has been seen in other studies conducted from time to time [7-9].

Respiratory failure requiring mechanical ventilation, multi organ dysfunction syndrome and encephalopathy were associated with higher mortality and can be attributed to the severity of the end organ dysfunction present in these patients [8]. Higher mortality associated with shorter duration of PICU stay may be attributed to the delay in transfer to PICU and relative scarcity of ICU beds in comparison to the huge number of patients being catered to in our institution.

The mortality rate in our study was 47.29% which was less than that reported in other studies conducted in the country [15-17]. The recent COVID-19 pandemic, increased awareness among critical care physicians on mechanical ventilation and intensive care and advent of newer drugs and advanced instruments used for monitoring and treatment of septic shock among pediatric patients can explain the relatively lower mortality found in our study in comparison to older studies [18].

Limitations of this study

Although it is a single centre study involving patients belonging to as many as 10 districts of Odisha, a Multicentre study with larger number of cases of different geographic locations can improve the external validity of the study.

CONCLUSION

Septic shock remains a major cause of morbidity and mortality among pediatric patients; pneumonia being the commonest underlying aetiology. Under-5 children still remain the most vulnerable group. Successful management of pediatric septic shock requires good infrastructure, trained staff and protocol-based management which may be modified from time to time basing upon constantly changing evidence-based medicine. Raising awareness about current burden of septic shock among health care providers, especially those working in

peripheral health facilities can go a long way in ensuring early recognition, timely referral and appropriate supportive therapy which will prove immensely helpful during the most \ critical period of patient transport. While surviving sepsis campaign guidelines have been derived from developed countries, there is an urgent need for more practical guidelines for developing countries in order to have desirable outcomes in our resource limited settings.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Institutional Ethics Committee, S.C.B. Medical College and Hospital, Cuttack - 753007 issued approval 578. The protocol titled "Study of Septic Shock in Children Admitted to Pediatric Intensive Care Unit" has been approved by the Institutional Ethics Committee, S.C.B. Medical College and Hospital, Cuttack - 753007 by IEC Appln. No:- 578 dated 11.02.2021 for a period of 3 years. Animal subjects: All authors have confirmed that this study did not involve animal subjects or tissue.

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