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CLINICAL PROFILE AND OUTCOME OF CHILDREN WITH SEPSIS ADMITTED IN PEDIATRIC INTENSIVE CARE UNIT IN A TERTIARY CARE CENTRE : A PROSPECTIVE OBSERVATIONAL STUDY

Paediatrics

Dr Poonam Thakur* Assistant Professor, Dept.Of Paediatrics, VMGMC, Solapur. Maharashtra, India *Corresponding Author

Dr Praveen Raghoji Manwar Junior Resident, Department Of Pediatrics, Dr.V.M.G.M.C, Civil Hospital, Solapur

Dr Sachin Bandichode Associate Professor, Dept.Of Paediatrics, VMGMC, Solapur. Maharashtra, India

Dr Sudhir Sarawade Professor And HOD, VMGMC, Solapur. Maharashtra, India

ABSTRACT

Sepsis is a clinical syndrome caused by a dysregulated host response to severe infection. Pediatric sepsis remains a major public health problem and an important cause of morbidity and mortality. The present study aimed to determine the etiology and clinical outcome of sepsis associated with its prognosis among patients admitted to a pediatric ICU. It was a prospective observational study carried among children aged 1 – 14 years at department of paediatrics, tertiary care hospital from Jun 2022 to June 2024. Total 1150 children admitted in PICU, 280 (24.30%) had sepsis.(Fig1) Among children with sepsis, 32(11.4%) had PICU mortality. The majority of the patients were in the age group of 1 to 3 months (60%) & 53% were male. There was no significant association between demographic parameter & risk of mortality Use of inotropes, two or more fluid boluses & need of Mechanical ventilation was significantly associated with mortality. From the results of our study, it is concluded that, incidence of sepsis was 24.3% among PICU admissions and PICU Mortality rate was 11.4%. Among those with mortality, 94% had positive culture.

KEYWORDS

PICU, sepsis, children

INTRODUCTION:

Sepsis is a clinical syndrome caused by a dysregulated host response to severe infection. Pediatric sepsis remains a major public health problem and an important cause of morbidity and mortality, despite the development of standardized treatment guidelines, universal immunization programs and advanced intensive care organ support techniques. Severe sepsis is responsible for > 8% of all pediatric intensive care unit (PICU) admissions and causes > 4.5 million childhood deaths worldwide per year.[1] Although inflammation is an essential host response to any infection, the progression to dysregulation of the normal host response causes the activation of a chain of events that leads to widespread tissue injury, immune and microcirculatory dysregulation and characteristics of systemic inflammatory response syndrome (SIRS). This uncontrolled, dysregulated and self-sustaining intravascular inflammation can lead to end-organ dysfunction in tissues remote from the original insult, progressing rapidly to septic shock with associated multiple organ failure.[2] If not treated in a timely manner, death will occur either as refractory shock, responsible for one-third of deaths within the first 72 h, or as multiple organ dysfunction syndrome (MODS) with respiratory failure and neurological failure that predominate as the main causes of death.[3]

The recognition of sepsis in children is challenging and is related to the high prevalence of common febrile infections, poor specificity of discriminating features, and some capacity of children's physiology to compensate until shock is in an advanced stage.[4] Sepsis outcomes in children are strongly dependent on the timeliness of recognition and treatment. Several worldwide campaigns and recommendations emphasize early recognition and timely diagnosis of sepsis, collectively with appropriate and timely management consisting of prompt use of empiric antimicrobials and early escalation of care.[5] Although this has been shown to reduce mortality, mortality rates remain practically unchanged in high-income settings. Pediatric sepsis is associated with high mortality and morbidity and requires a high level of awareness and suspicion for early diagnosis and timely treatment. Rapid and careful fluid resuscitation, antibiotic administration, and early vasoactive support are critical to reversing shock. The Surviving Sepsis Campaign published very comprehensive guidelines in 2020 for the management of pediatric septic shock and sepsis-associated organ dysfunction that include recommendations for the screening and diagnosis of sepsis. In intensive care units (ICU), the mortality rate from sepsis differs according to the clinical condition on admission and the development of septic shock and multiple organ dysfunction.[6] Furthermore, the etiological agent of the disease and the presence of comorbidities affect the prognosis.[7]

Most children treated in emergency rooms and admitted to ICU with sepsis/septic shock show no bacterial isolation, which varies according to age, immune status and geographic location.[8] The distribution of etiological agents changed considerably in the pediatric population according to their age and setting. The most frequent sites of infection in children with severe sepsis, are the lungs (50- 60%), abdomen (20-25%), urinary tract (7- 10%), the central nervous system (<5%) and blood stream (<5%). Bacteremia occurs in 40-60% of patients with septic shock.9 The ICU stay, with appropriate monitoring and treatment targeting the stabilization of clinical and laboratory parameters, is essential in the management of children with sepsis. The proper handling and initiation of vasoactive drugs in a timely manner combined with the monitoring and treatment of possible organ dysfunctions determine the disease progression and the presence or absence of complications and sequelae. In addition to treatment, other factors are associated with unfavorable progression of sepsis among intensive care patients, including the diagnosis time and host reaction responses to the infection.[10] Epidemiological variables and clinical findings on admission also may be predictors of progression to multiple organ failure, complications or death. Identifying these factors may contribute to improved and updated protocols for the diagnosis and treatment of sepsis. Furthermore, understanding the current etiological profile of sepsis, including the possible impact of vaccination programs, is essential to guide antibiotic therapy and reduce the risk of death.

The present study aimed to determine the etiology and clinical outcome of sepsis associated with its prognosis among patients admitted to a pediatric ICU.

Methodology:

It was a prospective observational study carried among children aged 1 – 14 years at department of paediatrics, tertiary care hospital from Jun 2022 to June 2024. Children admitted in PICU, with suspected sepsis & fulfilling age adjusted pSOFA criteria were enrolled in this study. Children aged less than 28 days & more than 14 years & have received antibiotics for more than 72 hours before presenting to our hospital were excluded. Sample size was calculated using formula $N=(Z\alpha/2)^2 * (PQ) / E2$. The calculated sample size was 280.

Data were collected using pre-designed semi-structured study

proforma. After taking written informed consent from parents demographic data, clinical information like diagnosis, general & systematic examination, reports of laboratory investigation were recorded. Blood cultures were collected prior to initiation of antibiotics. Severity of illness was calculated based on pSOFA on day 1, 2 and 3. Final outcome of the patient was PICU mortality.

Data was fed in master chart by using MS excel. Data was expressed as frequency and percentages, means, median, standard deviations and range in tabular and graphical format. Statistical comparison between two groups was made using the Chi-square test (categorical variables). p-values with two tailed. Statistical significance was set at $p \leq 0.05$.

Operational Definition:

Diagnosis Of Sepsis Was Done According To International Consensus Guidelines 2005:

- **SIRS:** The presence of at least two of the of the following 4 criteria, one of which must be abnormal temperature or leucocyte count:

1. Core temperature of > 38.5
2. Tachycardia, defined as heart rate > 2 SD above normal for age in absence of external stimulus, chronic drugs or painful stimuli; Or Otherwise explained persistent elevation over a 0.5 to 4 hr. time period OR In children < 1-yr-old, persistent bradycardia over 0.5 hr (mean heart rate < 10th percentile for age in absence of vagal stimuli, Beta blockers drugs, or congenital heart disease)
3. Respiratory rate > 2 SD above normal for age or acute need for mechanical ventilation not related to neuromuscular disease or general anesthesia
4. Leukocyte count elevated or depressed for age (not secondary to chemotherapy) or > 10% immature neutrophil

- **Sepsis:** SIRS in the presence of, or as a result of suspected or proven infection.

The therapeutic interventions were started from the time of diagnosis was suspected and included early aggressive fluid resuscitation, early administration of empiric antibiotics, oxygen supplementation, and early infusion of inotropic agent. A central venous line was inserted among all children admitted with septic shock in pediatric intensive care. All patients were managed as per standard clinical guidelines for management of sepsis in children. The management includes placement of central venous catheter, appropriate fluid resuscitation, use of inotropes, empirical antibiotics, and blood component transfusion.

RESULTS:

Total 1150 children admitted in PICU, 280 (24.30%) had sepsis.(Fig1) Among children with sepsis, 32(11.4%) had PICU mortality.(Fig 2)

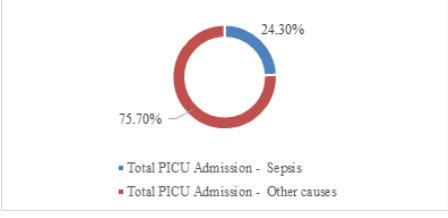

Fig 1: Distribution of total PICU admitted children

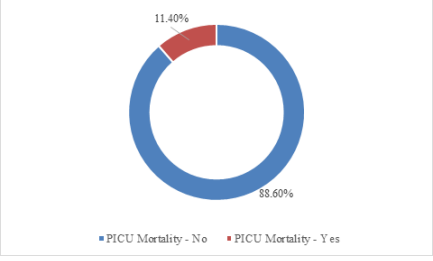

Fig 2: Distribution according to PICU mortality among children with sepsis

Fig 1: Distribution According To Demographic Parameter

Demographic parameter		Mortality				p Value
		No		Yes		
		Frequency	Percentage	Frequency	Percentage	
Age group	1-3 Months	148	60	19	59	0.98
	3-6 Months	22	9	3	9	
	6 months-1 Years	19	8	2	6	
	1-5 years	34	14	5	16	
	5-10 years	8	3	1	3	
	10-14 years	17	7	2	6	
Gender	Female	109	44	15	47	0.75
	Male	139	56	17	53	

The majority of the patients were in the age group of 1 to 3 months (60%) & 53% were male. There was no significant association between demographic parameter & risk of mortality. (Table 1)

Table 2: Distribution According To Clinical Profile

Clinical Profile		Mortality				p Value
		No		Yes		
		Frequency	Percentage	Frequency	Percentage	
Presenting complaints	Fever	248	100	32	100	Reference
	Vomiting	78	31	18	56	<0.01
	Altered mental status	171	69	26	81	0.15
	Breathlessness	18	7	17	53	<0.01
	Abdominal pain	43	17	15	47	<0.01
	Lethargy	60	24	17	53	<0.01
	Rash	25	10	10	31	<0.01
	Headache	7	3	5	32	<0.01
Risk Factor	Congenital anomalies	17	7	5	16	0.08
	Birth asphyxia	12	5	4	13	0.07
	Catheterization	22	9	9	28	<0.01
	Post-operative	24	10	8	25	<0.01
	Malnutrition	22	9	7	22	<0.05
	Unimmunized	9	4	4	13	<0.05
Prior antibiotic use	Yes	12	5	3	9	0.28
	No	236	95	29	91	

All children with sepsis presented with Fever. Other common complaints were altered mental status (70%), vomiting (34%), lethargy (28%), abdominal pain (21%), breathlessness (13%), rash (13%) and headache (4%). The significant risk factor for sepsis was catheterization, post-operative, malnutrition & unimmunized status. (Table 2)

Pneumonia was the most common diagnosis (61%). It was observed that urinary tract infection, meningoencephalitis, pneumonia, osteomyelitis and viral illness was significantly associated with PICU Mortality (p value < 0.01). General physical examination revealed fever in all patients. It was observed that hypotension, respiratory distress, and limb swelling was significantly associated with PICU Mortality. (Table 3)

Table 3 : Distribution According To Clinical Examination Findings

		Mortality				p Value
		No		Yes		
		Frequency	Percentage	Frequency	Percentage	
Diagnosis	Urinary Track Infection	34	14	12	38	<0.01
	Meningoencephalitis	33	13	12	38	<0.01
	Pneumonia	145	58	27	84	<0.01
	Osteomyelitis	3	1	3	9	<0.01
	Gastro-intestinal infection	27	11	7	22	<0.01
	Viral Illness	14	6	7	22	<0.01
Sign	Fever	248	100	32	100	Reference
	Hypotension	35	14	9	28	<0.05
	Tachycardia	192	77	26	81	0.62
	Respiratory distress	81	33	22	69	<0.01
	Drowsiness	49	20	11	34	0.06
	Pallor	32	13	3	9	0.57
	Limb swelling	34	14	10	31	<0.05
	Abdominal Tenderness	38	15	7	22	0.34

	Rash	27	11	6	25	0.19
	Lymphadenopathy	35	14	8	25	0.11
Vitals	Abdominal temp	132	53	19	59	0.51
	Abnormal heart rate	55	22	10	31	0.25
	Abnormal respiratory rate	76	30	11	34	0.66

Bloodstream infections, CNS infections and urinary tract infection were significantly associated with mortality. The most common affected organ system was renal (14%). All the organ failures were significantly associated with PICU Mortality. Significantly higher number of organ failures were found to be significantly associated with PICU Mortality. It was observed that leucopoenia, hypoglycaemia, hyperglycaemia and raised liver enzymes were significantly associated with PICU Mortality. culture positivity was significantly associated with PICU Mortality. (Table 4)

Table 4: Distribution According To Lab Findings

		Mortality				p Value
		No		Yes		
		Frequency	Percentage	Frequency	Percentage	
Infection Type	Bloodstream Infection	22	9	30	94	<0.01
	Respiratory track	20	8	5	16	0.15
	CNS	7	3	5	16	<0.01
	Urinary Track	14	6	9	28	<0.01
	Skin & soft tissue	2	1	1	3	0.23
Organ Failure	Cardiovascular system	8	3	11	34	<0.01
	Acute Respiratory Distress syndrome	14	6	18	56	<0.01
	Renal	24	10	14	44	<0.01
	CNS	17	7	14	44	<0.01
	Haematological	13	5	8	25	<0.01
	Hepatic	18	7	11	34	<0.01
Number of organ dysfunction	0	191	77	11	34	<0.01
	1	43	17	3	9	
	2	4	2	2	6	
	3	2	1	6	19	
	4	4	2	1	3	
	5	3	1	7	22	
	6	1	0	2	6	
Lab investigation	Anaemia	99	40	17	53	0.15
	Leukopenia	29	12	11	34	<0.01
	Leucocytosis	136	55	19	59	0.62
	Coagulopathy	70	28	13	41	0.14
	Hypoglycaemia	40	16	10	31	<0.05
	Hyperglycaemia	25	10	8	25	<0.05
	Raised liver enzyme	78	31	16	50	<0.05
	Base excess(>5)	104	42	16	50	0.38
Culture positive	Yes	22	9	30	94	<0.01
	No	226	91	2	6	

Table 5: Distribution According O Treatment Received In PICU

		Mortality				p Value
		No		Yes		
		Frequency	Percentage	Frequency	Percentage	
Inotropes used	Yes	90	36	23	72	<0.01
	No	158	64	9	28	
≥2 fluid boluses in PICU	Yes	90	36	23	72	<0.01
	No	158	64	9	28	
Need for mechanical ventilation	Yes	59	24	24	75	<0.01
	No	189	76	8	25	

Use of inotropes, two or more fluid boluses & need of Mechanical ventilation was significantly associated with mortality. (Table 5)

Table 6: Independent T Test

Clinical findings	No	Yes	p Value
pSOFA day 1	7.71±1.48	12±0.84	<0.01
pSOFA day 2	7.77±1.43	12±0.86	<0.01
pSOFA day 3	7.63±1.38	11.6±1.07	<0.01
PH	7.44±0.205	7.27±0.295	<0.01
pO2(mmHg)	113.73±6.192	89.5±2.896	<0.01
Pco2(mmHg)	34.56±2.361	40.81±3.105	<0.01
HCO3(mmEq/L)	19.41±15.59	15.59±1.241	<0.01
Length of PICU Stay	121±6.8	69.5±7.9	<0.01

Mean pSOFA score on day 1 (12 vs 7.71 p value < 0.01), day 2 (12 vs 7.77 p value < 0.01) and day 3 (11.6 vs 7.63 p value < 0.01) was significantly higher among those with mortality as compared to those without mortality. ABG analysis revealed that mean pH (7.2 vs 7.4, p value < 0.01), mean pO2 (89.5 vs 113.7 mm Hg, p value < 0.01) and mean HCO3 (15.5 vs 19.4 mEq/L, p value < 0.01) were significantly lower and mean pCO2 (40.8 vs 34.5 mm Hg, p value < 0.01) was significantly higher among those with mortality as compared to those without mortality. Length of stay at PICU was significantly lower among those who died as compared to patients who survived. (Table 6)

DISCUSSION:

In our study, rate of mortality was 11.4%. Mishra et al assessed predictors of poor outcome in pediatric septic shock.[9] Godfrey et al a found that, mortality rate in their hospital was 9.4% In their study, mortality rate was 20%.[10]

In the present study, majority of the patients were in the age group of 1 to 3 months (60%). Bansude et al, y Khan Y et al, Godfrey et al & Pawar et al had similar findings. (10,11,12,13) We observed that fever was reported by all the patients. Other common complaints were altered mental status (70%), vomiting (34%), lethargy (28%), abdominal pain (21%), breathlessness (13%), rash (13%) and headache (4%). It was observed that complaints like vomiting, breathlessness, abdominal pain, lethargy, rash and headache were found to be present significantly more common among those who died as compared to those who survive. Mishra et al reported no significant association of presenting symptoms between survivors and non-survivors.[9] However, fever was the most common presenting symptom in both the groups followed by breathlessness. Also, abnormal vitals were not significantly associated with mortality, a finding which is similar to that of the present study.

In the present study, pneumonia was the most common diagnosis (61%). Other diagnosis made were urinary tract infection (16%), meningoencephalitis (16%), gastro-intestinal infection (12%), viral illness (8%), osteomyelitis (2%). It was observed that diagnosis of urinary tract infection, meningoencephalitis, pneumonia, osteomyelitis and viral illness was significantly associated with PICU Mortality. In the study by Pawar et al, common etiologies were pneumonia, meningitis, and urinary tract infection (UTI) associated with congenital anomalies. [13] Catheterization (done by the physicians for medical purposes) and very low birth weight were risk factors in neonates, in paediatrics, common etiologies were pneumonia, meningitis, and urinary tract infection (UTI) associated with catheterization as a risk factor.

In our study, It was observed that bloodstream infections (94% vs 9%), CNS infections (16% vs 3%) and urinary tract infection (28% vs 6%) were significantly more common among those with mortality as compared to those who survived. Similar to our findings, multiple organ dysfunction was found to be significantly associated with mortality (p value < 0.01) in the study by Bansude et al.[11] It was observed that leucopenia, hypoglycemia, hyperglycemia and raised liver enzymes were significantly associated with PICU Mortality. Also, among those with mortality, 94% had positive culture, while among those without mortality, only 9% had mortality. Thus, culture positivity was significantly associated with PICU Mortality. In the study by Shah et al, only 25 out of 200 cases (12.5%) had positive blood cultures.[14] The most common organisms isolated included gram-negative bacilli (pseudomonas) followed by gram positive organisms (staphylococcus aureus). Out of the total 20 urine cultures sent, 7 were positive (3 Candida glabrata, 2 Klebsiella pneumoniae and 2 E. coli). Out of 10 CSF (cerebrospinal fluid) cultures sent, one was positive for Klebsiella pneumoniae.

We observed that mean pSOFA score on day 1 (12 vs 7.71 p value < 0.01), day 2 (12 vs 7.77 p value < 0.01) and day 3 (11.6 vs 7.63 p value < 0.01) was significantly higher among those with mortality as compared to those without mortality. In a similar study, Kaur et al observed that the mean (SD) PRISM score was significantly higher among non-survivors (19.69 [8.19]) as compared with survivors (7.90 [8.32]) (P < 0.001). We observed that, Use of inotropes, two or more fluid boluses & need of Mechanical ventilation was significantly

associated with mortality. Kaur et al observed that 2 or more boluses in PICU was reported significantly higher in non-survivors as compared to survivors (75.8% vs 38.1%, p value < 0.01). In addition, need for mechanical ventilation was significantly associated with mortality. In the present study, length of stay at PICU was significantly lower among those who died as compared to patients who survived. Godfrey et al observed that 59.3% (132/222) of the survivors had prolonged hospital stay of >7 days.[71] Duration of PICU stay was significantly higher in survivors as compared to non-survivors in the study by Kaur et al (125.9 vs 72 hours, p value < 0.01).[15]

CONCLUSION:

From the results of our study, it is concluded that, incidence of sepsis was 24.3% among PICU admissions and PICU Mortality rate was 11.4%. Among those with mortality, 94% had positive culture, while among those without mortality, only 9% had mortality. Of those with culture positivity (n=52), 18 cases (35%) had Klebsiella infection, which was the most common organism isolated. It was observed that for all the infections, age group 1 to 3 months was the most common. Factors associated with mortality were presentation with vomiting, breathlessness, abdominal pain, lethargy, rash and headache, catheterization, post-operative, malnutrition, unimmunized, bloodstream infections, CNS infection, UTI, diagnosis of urinary tract infection, meningoencephalitis, pneumonia, osteomyelitis and viral illness, multiple organ failures, leucopenia, hypoglycemia, hyperglycemia, raised liver enzymes culture positive, increased pSOFA, abnormal ABG parameters, use of inotropes, ≥ 2 fluid boluses, and need for mechanical ventilation.

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