

## Clinical Profile, Immediate Outcome and Predictors of Poor Outcome of Children in Pediatric Intensive Care Unit with Sepsis

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## ABSTRACT

### Introduction

Sepsis remains a major cause of death in children with death rate ranging from 5% in developed countries to 35% in developing countries. However, data on the predictive factors for poor outcome particularly in developing countries, remain limited. So this study aims to evaluate the clinical profile, immediate outcome and factors associated with poor outcome of the children with sepsis.

### Methods

This retrospective study was conducted in the Pediatric Intensive Care Unit (PICU) at Kanti Children Hospital, Kathmandu. Medical records of patients aged 30 days to 14 years, diagnosed with sepsis based on clinical and laboratory parameters and admitted to the PICU between April 2024 to September 2024 were analyzed. The clinical features, outcome in the form of discharge or death during the hospital stay and factors effecting the poor outcome were tabulated and the data analysis was done by SPSS version 21.

### Results

The total number of patient enrolled in the study were 53. The mean age of the patient was (3.49±0.183) yrs. Among them 31/53(58 %) were male and 22/53(42%) were female. Among them 42/53(79.25%) were Hindus 5/53(9.43%) were Muslims 4/53(7.54%) Buddhist and 2/53 (3.77%) Christian. The most common presenting symptom was fever observed in 50/53(94.4%) of cases. The mortality rate for sepsis was (14/53)26.41% which is statistically significant. Predictors of poor outcome included were the need for dialysis (p=0.016), the presence of Central Nervous System disease (p=0.001), the use of mechanical ventilation (p=0.00), the use of inotropic support (p=0.010) and elevated D-dimer levels (p=0.036).

### Conclusion

Fever was the most common symptom of sepsis with a mortality rate of 26.41%. Key predictors of poor outcome included the need of dialysis, presence of CNS disease, mechanical ventilation, the use of inotropic support and elevated D-dimer level.

### Keywords

*Intensive care; outcome; pediatrics; predictors; sepsis*

## INTRODUCTION

Sepsis is an important cause of morbidity and mortality in children.<sup>1</sup> The clinical features of sepsis includes fever, headache, shortness of breath, cough, abdominal pain, altered sensorium, burning micturition, diarrhoea, oliguria etc.<sup>1,2</sup> The prevalence of severe sepsis and septic shock among hospitalized children ranges from 1 to 26%.<sup>2,3</sup>

World Health Organization data have shown that 80% of death in children less than 4 years is due to sepsis-related deaths.<sup>4</sup> The mortality in developed countries is 5% whereas it is up to 35% in developing countries.<sup>3</sup> To reduce mortality due to sepsis early diagnosis and management is important.<sup>5</sup> Even if sepsis is a major cause of mortality in hospitalized patients, predictive factors for mortality and morbidity are limited, in developing countries.<sup>6-10</sup>

However, we don't have data on the predictive factors for poor outcome particularly in our country. Since sepsis is the important cause of PICU admission, we try to see the problem retrospectively. So, the aim of the study is to find out the clinical profile, immediate outcome and factors associated with poor outcome of the children with sepsis admitted in Kanti Children Hospital.

## METHODS

It is a retrospective study conducted at the Pediatric Intensive Care Unit (PICU) of Kanti children hospital Kathmandu. Ethical approval from the institutional ethical committee was taken. Sepsis involves a systemic inflammatory response syndrome (SIRS) in presence of infection, leading to septic shock and multiorgan system dysfunction based on the 2005 International Pediatric Sepsis Consensus Conference. The records of patients diagnosed with sepsis with clinical and laboratory parameters aged more than 1 months to 14 years admitted to PICU of Kanti children hospital Kathmandu from April 2024 to September 2024 were analyzed.

The demographic profile, clinical features, comorbidities, laboratory parameters of the individual patient, the outcome of the patients in the form of discharge or death within the hospital stay, the factors effecting poor outcome were tabulated. The clinical variables include fever, diarrhea, vomiting, headache, cough, shortness of breath, altered sensorium, seizure, hematuria, oliguria. The predictors of poor outcome in this study are malnutrition, patients on hemodialysis, presence of autoimmune disease, respiratory diseases, congenital heart disease, CNS disease, use of mechanical ventilation, use of inotrope and septic shock. The lab parameters include Hb level, platelet counts, blood sugar, d-dimer, ESR and CRP level. All sepsis patients above 14 years of age, with

known history of diabetes, malignancy, long term cardiac illness, immunodeficiency or patients with long term steroid and immune suppressive therapy were excluded from the study.

All the data were entered into Microsoft Excel sheets. The data were analyzed using SPSS Version 21.0. Categorical variables were expressed as proportions and continuous variables as mean (standard deviation [SD]) or median (interquartile range [IQR]). All quantitative variables (between the groups of death and survivors) were compared by unpaired t-test; categorical variables were compared by Chi-square test or Fisher's exact test. Nonparametric tests were adopted for the skewed distribution.  $P < 0.05$  was considered as significant.

## RESULTS

Among the 120 patients with sepsis admitted in PICU, 67 were excluded because they did not fulfill the inclusion criteria. So, the total number of children (aged 1 months to 14 years) enrolled in this study was 53. The median age of the patient is  $2.5 \pm 4.46$  years. Among them 31 (58 %) were male and 22 (42%) were female. Among them 42 (79.25%) were Hindus 5 (9.43%) were Muslims 4 (7.54%) Buddhist and 2 (3.77%) Christian. The baseline characteristics of the patient is given in Tables 1 and 2. The most common symptom of presentation was fever 50 (94.4%). The median length of hospital stay was  $7 \pm 5$  days. The frequency of symptoms at presentation is given in Table 3.

### Predictors of outcome

The predictors of outcome associated with sepsis enrolled in this study are malnutrition 10/53 (10.9%), six had moderate malnutrition and 4 had severe malnutrition. Congenital heart disease 4/53 (7.5%), AKI requiring dialysis 3/53 (5.6%), presence of autoimmune disease 3/53 (5.6%), presence of respiratory disease 32/53 (60.3%), CNS disease 7/53 (13.2%), use of mechanical ventilation 11/42 (20.76%), use of inotropic support 12/53 (22.65%) and septic shock 13/53 (24.5%). The lab parameters associated with outcome are hypoglycemia 19/53 (35.85%), thrombocytopenia 13/53 (24.5%), raised D-dimer 6/53 (11.3%), raised ESR 41/53 (77.3%) and raised CRP 44/53 (83.01%). The detail is given in Table 1 and 2.

The most common clinical condition was presence of respiratory disease 32/53 (60.3%). Pneumonia 9, bronchial asthma-3, bronchiolitis 5, empyema thoracic 3, pleural effusion 2. Four patients had severe pneumonia. The congenital heart disease include one Atrial septal defect, one Ventricular septal defect and one Severe pulmonary stenosis. CNS disease include Meningoencephalitis in one patient, one pediatric stroke, one status epilepticus, one focal seizure and one hypoxic ischemic

**Table 1.** Clinical profile of patients (n=53)

Clinical characterteristics		Total	Mortality				p-value
			No		Yes		
			n	%	n	%	
Sex	Male	31 (58.5)	24	61.5	7	50	0.53
	Female	22 (41.5)	15	38.5	7	50	
Age (Median ± IQR (Years))		2.5±4.46	1.67±3.42	-	4.5±7	-	0.23
Length of stay (Median ± IQR (days))		7±5	7±4	-	5±7	-	0.46
Nutritional status	Normal	43 (81.1)	31	79.5	12	87.7	0.70
	Moderate Malnutrition	6 (11.3)	4	10.3	2	14.3	
	Severe Malnutrition	4 (7.6)	4	10.3	0	0	
Referral Cases	No	6(11.3)	3	7.7	3	21.4	0.32
	Yes	47 (88.7)	36	92.3	11	78.6	
Septic Shock	No	40 (75.5)	31	79.5	9	64.3	0.26
	Yes	13(24.5)	8	20.5	5	35.7	
Kidney dialysis	No	50 (94.3)	39	100	11	78.6	0.02
	Yes	3 (5.7)	0	0	3	21.4	
Respiratory disease	No	21 (39.6)	14	35.9	7	50	0.36
	Yes	32 (60.4)	25	64.1	7	50	
CNS diseases	No	46 (86.8)	37	94.9	9	64.3	0.01
	Yes	7 (13.2)	2	5.1	5	35.7	
Mechanical ventilation	No	42 (79.2)	36	92.3	6	42.9	<0.001
	Yes	11 (20.8)	3	7.7	8	57.1	
Use of Ionotropic support	No	41 (77.4)	35	89.7	6	42.9	0.001
	Yes	12 (22.6)	4	10.3	8	57.1	
Autoimmune disease	No	50 (94.3)	37	94.9	13	92.9	1
	Yes	3 (5.7)	2	5.1	1	7.1	

**Table 2.** Clinical profile of patients (n=53)

Laboratory and Clinical conditions		Total	Mortality				p-value
			No		Yes		
			n	%	n	%	
Hypoglycemia	No	34 (64.2)	27	69.2	7	50	0.12
	Yes	19 (35.8)	12	30.8	7	50	
Thrombocytopenia	No	40 (75.5)	28	71.8	12	85.7	0.47
	Yes	13 (24.5)	11	28.2	2	14.3	
D-dimer raised	No	47 (88.8)	37	94.9	10	71.4	0.04
	Yes	6 (11.3)	2	5.1	4	28.6	
Raised ESR	No	12 (22.6)	10	25.6	2	14.3	0.48
	Yes	41 (77.4)	29	74.4	12	85.7	
Raised CRP	No	9 (17)	7	17.9	2	14.3	1
	Yes	44 (83)	32	82.1	12	85.7	



**Table 3.** Clinical features of the subjects (n=53)

Clinical features	Number (%)
Fever	50 (94.4%)
Vomiting	40 (75.5%)
Diarrhoea	20 (37.7%)
Cough	49 (92.5%)
Headache	20 (37.7%)
Shortness of breath	47 (88.8%)
Seizure	6 (11.3%)
Altered sensorium	10 (18.9%)
Hematuria	5 (9.4%)
Oliguria	2 (3.8%)

encephalopathy and two Cerebral Palsy.

### Mortality

In this study 14 out of 53 patient died with a mortality rate of 26.41%. Among the 53 patients 2 patients went on left against medical advice (LAMA) while 2 patients were discharged on request (DOR) while 35 patients were discharged (66.03%). It is given in Table 4. The most common comorbid condition associated with death was Respiratory disease 32/53(60.3%), pneumonia being the most common (7/53=13.2%). The clinical conditions associated with poor outcome which are statistically significant are Patient requiring dialysis (P=0.016), presence of CNS disease (0.001), patient on mechanical ventilation (p<0.001) and the use of ionotropic support (0.010). The clinical condition not statistically significant are respiratory disease, septic shock, autoimmune disease, malnutrition and congenital heart disease. The detail is given in Table 1. The laboratory parameters associated with poor outcome which is statistically significant is presence of raised D-dimer (p=0.04). The other parameters like raised ESR, raised CRP, thrombocytopenia and hypoglycemia are not statistically significant. The detail is given in Table 2.

### DISCUSSION

The median age of the patient is  $2.5 \pm 4.46$  years, which is similar to study done by Kumar G et al.<sup>11</sup> The lower age may be due to low immunity in younger age. Ghimire JJ in a study found male effected more than female which is consistent with this study.<sup>12</sup> Among the symptoms analyzed the most common symptom was found to be fever which is similar to study done by Bhatta M et al.<sup>13</sup> The most common clinical condition associated with sepsis was presence of respiratory disease and the leading cause was Pneumonia which is consistent with the other studies.<sup>13,14</sup> The median length of hospital stay was  $7 \pm 5$  days. Most of the other studies the length of hospital stay was longer

**Table 4.** Outcome of the subjects (n=53)

Outcome	Number (%)
Death	14(26.41%)
Left against medical advice (LAMA)	2 (3.8%)
Discharge on request (DOR)	2 (3.8%)
Discharged	35(66.03%)

as compared to this study.<sup>14,15</sup> The reason behind is few patients are severely diseased like septic shock (22%), use of ionotropic support (24%) and patient on mechanical Ventilation (20%) as compared to other studies.

The mortality rate in this study is 26.41% which is higher than the study done in developed countries (10-20%).<sup>15</sup> The higher mortality rate in our setup could be due to multiple factors like lack of awareness, delay in hospital transport, poor socioeconomic status, lack of proper adequate services and skilled manpower.

In this study factors associated with poor outcome which were statistically significant were patient requiring dialysis, use of mechanical ventilation, use of ionotropic support and presence of CNS disease. The patient with AKI requiring dialysis was 5.6% which is similar to the findings of Kaur G et al (2% -3.5%) and Pedro Tda C et al (2%).<sup>11</sup> Acute Kidney Injury increases the risk of mortality and thus poor outcome in Sepsis patients. It is due to a complex interplay of factors, including inflammation, microcirculatory dysfunction, and metabolic reprogramming, leading to organ dysfunction and death<sup>11</sup>. CNS disease comprises 13.2% with cerebral palsy 3.7% in this study which is similar to the study done by Rusmawatinigtyas D et al.<sup>14</sup> CNS disease is associated with poor outcome is due to widespread brain dysfunction, neuroinflammation, and potential for ischemia, leading to prolonged ICU stays and long-term cognitive and functional impairment<sup>14</sup>.

The use of mechanical ventilation was done in 20% of the patients in this study. Ghimire JJ et al<sup>12</sup> and Vila Perez D et al<sup>16</sup> observed a rate of use of mechanical ventilation (64-68%). The reason behind the less number of patient mechanically ventilated were that the enrolled patient in this study are less sick than other studies. The mechanically ventilated patient are sicker and thus are associated with poor outcome. Also, the number of patients in whom ionotropes were used in this study (22%) were not comparable to the findings made by Bhatta M et al<sup>13</sup> which is 79%. The reason is that the patient are less sicker than other studies ie septic shock patient comprises 24%. The reason behind poor outcome in septic shock patients is delayed diagnosis and treatment, the severity of the underlying

infection, and the presence of pre-existing conditions<sup>13</sup>. Though not statistically significant Malnutrition comprise of 10.9%, Autoimmune disease 5.6% which is similar to the study done by Rusmawatiningtyas D et al.<sup>14</sup> The most common comorbid condition associated with mortality is respiratory disease 60%, Pneumonia comprising of 17% though statistically non-significant. The reason could be that severe respiratory condition i.e. Severe Pneumonia was present in 7.5%. Similarly, heart disease comprises of 7.5% in this study which is comparable to the findings of Kaur G et al (1%-4%)<sup>11</sup> and Pedro Tda C et al.<sup>17</sup>

The laboratory parameters associated with poor outcome which is statistically significant is presence of raised D-dimer ( $p=0.036$ ). This is also consistent to other studies done by Wang et al.<sup>18</sup> The reason behind is likely due to the activation of the coagulation cascade, resulting in microthrombi, endothelial damage, and organ dysfunction. The other parameters not statistically significant in this study are raised ESR, thrombocytopenia, raised CRP and hypoglycemia. These parameters was found to be significant in other studies.<sup>18,19,20</sup> The reason behind is most likely low sample size.

#### Limitations

It is a single centered retrospective study. The sample size is also less in number to establish the recommendations. However, it gives some direction of management of sepsis patients in ICU.

## CONCLUSION

The most common symptom of presentation was fever and the mortality rate was 26.41%. The clinical conditions associated with poor outcome which are statistically significant were patient requiring dialysis, presence of CNS disease, patient on mechanical ventilation and the use of inotropic support. The laboratory parameters associated with poor outcome which is statistically significant was presence of raised D-dimer.

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## CONFLICT OF INTEREST

The author(s) declare that they do not have any conflicts of interest with respect to the research, authorship, and/or publication of this article.

## AUTHOR CONTRIBUTIONS

Study concept and design by Bulu wagley, Ajit Rayamajhi and Pun Narayan Shrestha. Literature review, Methodology, Data collection and manuscript writing by Bulu wagley, Sanjeet Kumar Shrestha and Sadikshya Shah Malla. Data analysis and statistical analysis by Bulu wagley. All authors read and approved the final manuscript.

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