Original Research Article

Predictors of outcome in pediatric septic shock: Experience from a tertiary care teaching hospital

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Abstract

Introduction: Septic shock is a common admission diagnosis in PICU. It is associated with high mortality. **Aim:** The current study aimed at determining the predictors of outcome in pediatric septic shock in patients admitted to the PICU of a tertiary care teaching hospital. **Patients and Methods:** It was a prospective, observational study done in a time period of 6 months (November 2018 to April 2019) during which patients of septic shock were evaluated. All cases were examined clinically and investigated with Complete Blood Count, Blood Culture and Sensitivity, urine routine examination, urine Culture and Sensitivity, tracheo-bronchial aspirate (in case of ventilated patients) and arterial blood gas analysis were done as a part of study protocol. The data so procured was analysed statistically and documented and the result was evaluated. **Results:** A total of 54 patients of septic shock were admitted to the PICU during the study period of whom 47 patients were finally included as per the study protocol. Of these 9 patients expired and the remaining were discharged. On evaluating the role of different demographic, clinical and laboratory parameters between survivors and non- survivors for their association with mortality, only delayed capillary refill time on admission (p=0.008) and low mean pH (p=0.008) showed a statistically significant association with mortality. **Conclusion:** A delayed capillary refill time on admission and a low mean pH were statistically significant predictors of mortality in this study.

Keywords: Septic shock, Mortality, Capillary refill time, Low

Introduction

Sepsis is the most common cause of morbidity and mortality in pediatric population, in the developing countries [1,2]. The global data on sepsis estimates that infection accounts for more than 80% mortality in under-five children. Septic shock is a dreaded and potentially fatal complication of sepsis.

Septic shock has been found to be the most common type of shock occurring in Pediatric Intensive Care Unit with an incidence of around 35% [3]. In India, overall mortality rate in patients with pediatric septic shock is around 47% which is comparable to global figure of around 50% [3]. However, even when considering such high mortality figures, very few studies have been done till date to assess predictors of outcome in septic shock, especially in Indian scenario, to the best of our knowledge.

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Aim and Objectives

The present study was undertaken to analyze predictors of poor outcome in septic shock.

Patients and Methods

The study was carried out in the Pediatric Intensive Care Unit of the Department of Pediatrics at a tertiary care teaching hospital. It was a prospective, observational study done in a time period of six months (November 2018 to April 2019).

All children aged 1 month – 18 years, admitted with or having developed septic shock during the course of hospital stay were included.

Patients of malignancy, on immuno suppressive or chemotherapy drugs, who left the treatment in between or whose parents did not consent, were excluded.

Diagnostic criteria

Septic Shock: Sepsis plus cardiovascular organ dysfunction as described below [4].

Despite >40ml/kg of isotonic intravenous fluid in one hour:

- Hypotension of blood pressure less than fifth percentile for age or systolic blood pressure less than two SD below normal for age, or
- Need for vasoactive drug to maintain blood pressure, or
- Any two of the following:
- Unexplained metabolic acidosis: base deficit > 5mEq/L.
- Increased arterial lactate > two times upper limit of normal.
- Oliguria: urine output < 0.5mL/kg/hour.
- Prolonged capillary refill time: > five seconds.
- Core to peripheral temperature gap > 3°C (5.4°F).

Systemic Inflammatory Response Syndrome (SIRS): Two of four criteria, one of which must be abnormal temperature or abnormal leukocyte count [4]

1. Core temperature > 38.5°C (101.3°F) or < 36°C (96.8°F) (rectal, bladder, oral or central catheter)
2. Tachycardia:

- Mean Heart Rate > two SD above the normal for age in absence of external stimuli, chronic drugs or painful stimuli, or
- Unexplained persistent elevation of heart rate over 0.5 - 4hr, or
- In children less than one-year old, persistent bradycardia over 0.5hr (mean heart rate less than tenth percentile for age in absence of vagal stimuli, beta blockers, congenital heart diseases).

3. Respiratory Rate more than two 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 more than 10% immature neutrophils.

Sepsis: SIRS in the presence of or as a result of suspected or proven infection [4].

Refractory Septic Shock: Septic shock which lasts for more than one hour and does not respond to fluid or pressor administration [4].

Multi Organ Dysfunction Syndrome (MODS): MODS is defined as a clinical syndrome characterized by the development of progressive and potentially reversible physiologic dysfunction in two or more organs or organ systems that is induced by a variety of acute insults, including sepsis and homeostasis cannot be maintained without intervention [4].

Outcome was defined on the basis of survival. The patients who completely recovered from septic shock and got discharged uneventfully, were categorised as survivors while those who expired during the treatment were categorised as non-survivors.

A written informed consent was obtained in a language well understood by the parents/guardians.

A detailed history, general physical examination and systemic examination findings at the time of diagnosis of septic shock, were recorded on a standardized proforma.

Results

During the study period of 6 months, total 117 cases were admitted in PICU. There were 94 cases of shock of different etiologies and of these 54 cases of septic shock were enrolled in the study. Among the enrolled patients 3 did not give consent to participate in the study, 4 patients left against medical advice and 9 patients expired during the course of the illness. Thirty eight of 47 (38/47 = 80.8 %) cases enrolled in the study were discharged after recovery while 9 (9/47 = 19.1%) expired.

On analysis of clinical symptoms as predictors of outcome, fever was the most common symptom present in all the patients. Details of other parameters and their association with the outcome are mentioned in Table 1. On analysis of the vital parameters, a delayed capillary refill time (>3 seconds) was a statistically significant (p=0.008) predictor of poor outcome with all the 9 patients having failed to survive, having a prolonged CRT on admission. Statistical association of the other vital parameters with outcome is shown in Table 2. Amongst the laboratory predictors, a low mean pH (Table 3) on admission had a statistically significant (p=0.008) association with a poor outcome. None of the other laboratory markers of sepsis (Table 4) or any positive microbiologic culture (Table 5) was found to have significant statistical association with outcome.

Table-1: Clinical symptoms as a predictor of outcome (n=47).

S.N.	Characteristic	Expiry (n=9)	Discharge (n=38)	Statistical significance
1.	Fever	9 (100%)	38 (100%)	-
2.	Altered mental status	3 (33.3%)	16 (42.1%)	χ^2=0.387; p=0.720#
3.	Breathlessness	8 (88.9%)	23 (60.5%)	χ^2=2.607; p=0.138#
4.	Abdominal pain	3 (33.3%)	17 (44.7%)	χ^2=0.387; p=0.713#
5.	Decreased urine output	1 (11.1%)	8 (21.1%)	χ^2=0.465; py=0.667#
6.	Bleeding	1 (11.1%)	3 (7.9%)	χ^2=0.097; p=1.000#

#Fisher exact test

Table-2: Vital parameters as a predictor of outcome (n=47).

S.N.	Characteristic	Expiry (n=9)	Discharge (n=38)	Statistical significance
1.	Heart rate (according to age)			χ^2=1.629; p=0.579#
	Below normal	0	0	
	Normal	0	6 (15.8%)	
	Above normal	9 (100%)	32 (84.2%)	
2.	Blood pressure			χ^2=0.242; p=1.000#
	Below normal	9 (100%)	37 (97.4%)	
	Normal	0	1 (2.6%)	
	Above normal	0	0	
3.	Respiratory rate			χ^2=0.242; p=1.000#
	Below normal	0	0	
	Normal	0	1 (2.6%)	
	Above normal	9 (100%)	37 (97.4%)	
4.	Temperature			χ^2=0.064; p=1.000#
	Below normal	0	0	
	Normal	2 (22.2%)	10 (26.3%)	
	Above normal	7 (77.7%)	28 (73.7%)	
5.	**Capillary refill time**			**χ^2=6.909; p=0.008#**
	Normal	**0 (0%)**	**18 (47.4%)**	
	Delayed CRT	**9 (100%)**	**20 (52.6%)**	

#Fisher exact test

Table-3: Arterial Blood gas parameters as a predictor of outcome (n=47)

S.N.	Characteristic	Expiry (n=9)	Discharge (n=38)	Statistical significance
1.	**Mean pH+SD**	**7.20+0.09**	**7.29+0.08**	**'t'=2.776; p=0.008**
2.	Mean pO_2+SD	88.62+22.83	124.78+67.37	't'=1.577; p=0.122
3.	Mean pCO_2+SD	42.06+9.26	35.26+11.23	't'=1.682; p=0.100
4.	Mean HCO_3^-+SD	16.88+3.50	19.06+4.61	't'=1.326; p=0.191

#Fisher exact test

Table-4: Laboratory markers of sepsis as a predictor of outcome (n=47)

S.N.	Characteristic	Expiry (n=9)	Discharge (n=38)	Statistical significance
1.	Mean TLC+SD ('000)	15.28+7.31	14.67+8.11	't'=0.206; p=0.838
2.	Mean Polymorphs+SD	71.0+21.22	72.79+17.77	't'=0.262; p=0.795
3.	Mean RBS+SD	122+48.16	114.95+43.51	't'=0.429; p=0.670
5.	Mean CRP+SD	3.76+2.58	5.56+6.93	't'=0.763; p=0.449
6.	Mean ESR+SD	23.44+12.60	25.74+13.53	't'=0.462; p=0.646

#Fisher exact test

Table-5: Microbiological positivity as a predictor of outcome (n=47)

SN	Characteristic	Expiry (n=9)	Discharge (n=38)	Statistical significance
1.	Positive blood culture	0	1 (2.6%)	-
2.	Positive urine culture	2 (22.2%)	4 (10.5%)	χ^2=0.894; p=0.344
3.	Other body fluid positivity	1 (11.1%)	11 (28.9%)	χ^2=1.22; p=0.270

Discussion

In present study, 38 patients got discharged after completion of treatment and 9 expired during hospital stay while 4 patients went LAMA and hence were lost to follow up. Out of these 47 cases, 38 (38/47 = 80.9%) were discharged after recovery and 9 (9/47 = 19.1%) expired. The mortality rate in different series has shown a considerable variability. Khan et al [5] reported a series of severe sepsis and septic shock cases with mortality rate of 24%, although the septic shock patients were studied for a time frame of 2 years. Ghimire et al [6] in their series reported mortality rate as 25.53%.

Kurade and Dhanawade [7] reported mortality rate as 60.5% with 15% cases lost during follow up in study duration of 3 years. Compared to this, the present study was conducted for 6 months only. Kaur et al. in their study reported it as 58% [2] On the other hand, Choudhary et al [8] found it as 63.5%. These high mortality rates in different studies indicate sepsis as one of the leading causes of death in developing countries. One of the reasons for relatively lesser mortality rate in present study could be a relatively shorter study time period.

There was no significant association of presenting symptoms between survivors and non-survivors. However, fever was the most common presenting symptom in both the groups followed by breathlessness. In another study, Kurade and Dhanawade in their study reported fever as the most common presenting symptom and predictor of mortality associated with sepsis [7]. Choudhary et al furthermore identified younger age, low GCS at admission, need of mechanical ventilation and a shorter duration of hospital stay, to be significantly associated with mortality among pediatric septic shock patients [8]. In this study, however, it was observed that none of the presenting symptoms were statistically significant predictors of mortality.

This study hence proves that delayed CRT is an important indicator of peripheral perfusion, thus confirming the diagnosis of shock and its early recognition and management is an important predictor of mortality.

Amongst the different vital parameteters studied between the two groups significant statistical association was observed for delayed capillary refill time only. Ghimire et al. on the other hand recognized PRISM III scores as the predictor of mortality among these children [6].

Vasundhara et al assessed clinical parameters and immediate outcome of children with shock in a tertiary care hospital in Andhra Pradesh [9]. Among 75 children with shock, 74.66% children survived, and 25.33% children died.

The factors associated with mortality were low SBP, high 24-hr heart rate, low GCS scores at admission, SpO_2 and urine output at 24 hr and high capillary refilling time at 24 hr. Inotropic need was also significantly higher in non-survivors as compared to that in survivors, in their study.

There was no significant association between the different laboratory and biochemical parameters between the two groups. Kurade and Dhanawade in their series identified leucopenia as a predictor of mortality [7]. In the present study, acidosis (low arterial pH) had a significant statistical association with poor outcome of septic shock.

Kellum in his study discussed that acidosis may be a result of the underlying pathophysiology (e.g. respiratory failure, shock, renal failure) or may also result from the way critically ill patients are managed. Understanding the effects of acid-base on the inflammatory response is relevant as all forms of metabolic acidosis appear to be associated with prolonged hospital and ICU length of stay [10].

Furthermore, Ganesh et al [11] identified change in pH levels and serum lactate levels on day 1 and day 5 of admission as an important predictor of prognosis in patients with septic shock. Hence this study emphasises that low pH may be an important predictor of early recognition and outcome of sepsis.

In present study no statistically, significant difference was found between culture sensitivity of relevant samples between the two groups. Culture sensitivity is important for directing the direction of treatment of specific etiology. Different studies, like that of Ghimire et al and Kurade and Dhanawade have cited infection as the most common source of shock with Staphylococcus aureus as the most common micro – organism [6, 7].

A recent study by Whitney JE et al [12] studied the role of Vascular Endothelial Growth Factor (VEGF) and soluble fms-like tyrosine kinase (sFLT1) in patients with septic shock and found that both are elevated in these patients. sFLT is also associated with worse outcomes. Besides, C-Reactive Protein, the role of no other biomarker was evaluated as a laboratory predictor of poor outcome in patients with septic shock, in the present study.

The reason for our inability to find out association of mortality with a number of clinical and laboratory parameters was relatively much smaller sample size. This is one of the major limitations of the present study.

However, in view of the rural background of our patients, and their beliefs it was difficult to prevent high dropout rate which eventually affected our ability to find out association of different demographic, clinical and laboratory parameters with mortality.

Within these limitations, the present study provided a glimpse of the clinical and laboratory profile of septic shock cases and identified delayed capillary refill time and low mean pH as the statistically significant predictors of mortality.

However, in view of the limitations of study, and a diversified picture of clinical/ laboratory parameters identified as predictors of mortality in different studies, it is also of the view that a single variable cannot be considered to be a reliable predictor of mortality among children with septic shock. Further studies with focus on multivariate relationships or those using some clinically validated scoring systems are recommended on a larger sample size with low dropout rate.

Conclusion

A delayed capillary refill time on admission and a low mean pH were statistically significant predictors of mortality in septic shock, in this study.

What this study adds to the existing knowledge?

A delayed capillary refill time on admission and a low mean pH at admission are significant predictors of mortality in these patients.

Authors' contribution

Dr. Goyal P: Data collection.

Dr. Chandra S: Conceptualized the study and prepared the manuscript.

Dr. Goel S: Data collection.

Dr. Kumar P: Data collection.

Dr. Kumari A: Supervised the research and provided critical feedback.

Dr. Prasad P.L: Supervised the research and provided critical feedback.

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