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Original Research Article

A Prospective Assessment of Predictors of Outcome in Pediatric Septic Shock

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Abstract

Aim: To determines the predictors of outcome in pediatric septic shock in patients admitted to the PICU of a tertiary care hospital in Bihar Region.

Material & Methods: The study was carried out in the Pediatric Intensive Care Unit of the Department of Pediatrics in Nalanda medical College and Hospital, Patna, Bihar. It was a prospective, observational study done in a time period of seven months.

Results: During the study period of 6 months, total 120 cases were admitted in PICU. There were 86 cases of shock of different etiologies and of these 50 cases of septic shock were enrolled in the study. On analysis of the vital parameters, a delayed capillary refill time (>3 seconds) was a statistically significant (p=0.005) predictor of poor outcome with all the 8 patients having failed to survive, having a prolonged CRT on admission. Statistical association of the other vital parameters with outcome.

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 in children is a significant cause of morbidity and mortality worldwide. [1] The mortality rate of sepsis in children from pediatric intensive care unit (PICU) of developing countries is higher than 50%. [2] World Health Organization statistics have shown that 80% of death in children <4 years can be classified as sepsis-related deaths. [3] Assessment of severity of illness at admission is important for effective patient management, prognostication, and optimum utilization of resources. [4] Patient's outcome in PICU of developing country is affected by not only by clinical diagnosis at admission but also by demographic characteristics of the population, available infrastructure, and admission policies of PICU.

In the absence of specialized pediatric sepsis scores, some hospitals have implemented home-grown computerized sepsis prediction systems, which may benefit from site specificity [5].

Computerized prediction systems offer a compelling alternative to manual application of generalized scoring systems. Such systems may access electronic health record (EHR) data for clinical decision support. These systems have the potential to identify septic patients who might otherwise have a delay in diagnosis or be missed entirely and could provide early warning of sepsis for hospitalized pediatric patients on hospital wards or in intensive care. Studies in adults show that the setting of hospital-acquired sepsis among inpatients is both distinct and substantially more deadly [6-8], and children with hospital acquired sepsis have higher risk of delayed sepsis care than those presenting to an emergency department [9].

In India, overall mortality rate in patients with pediatric septic shock is around 47% which is comparable to global figure of around 50% [10]. 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.

Material & Methods:

The study was carried out in the Pediatric Intensive Care Unit of the Department of Pediatrics in Nalanda medical College and Hospital, Patna, Bihar. It was a prospective, observational study done in a time period of seven months.

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.

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

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

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

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.

Outcome was defined on the basis of survival. The patients who completely recovered from septic shock and got discharged uneventfully, were categorized as survivors while those who expired during the treatment were categorized 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 120 cases were admitted in PICU. There were 86 cases of shock of different etiologies and of these 50 cases of septic shock were enrolled in the study. 42 of 50 (84%) cases enrolled in the study were discharged after recovery while 8 (16%) 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.

Table 1: Clinical symptoms as a predictor of outcome (n=50).

Characteristic	Expiry (n=8)	%	Discharge (n=42)	%	P-value
Fever	9 (100%)	100	38 (100%)	100	-
Altered mental status	3 (33.3%)	50	16 (42.1%)	42.85	χ^2=0.462; p=0.874#
Breathlessness	8 (88.9%)	87.5	23 (60.5%)	76.19	χ^2=2.778; p=0.177#
Abdominal pain	3 (33.3%)	37.5	17 (44.7%)	50	χ^2=0.291; p=0.701#
Decreased urine output	1 (11.1%)	12.5	8 (21.1%)	26.19	χ^2=0.382; p=0.573#
Bleeding	1 (11.1%)	1	3 (7.9%)	11.90	χ^2=0.095; p=1.000#

On analysis of the vital parameters, a delayed capillary refill time (>3 seconds) was a statistically significant (p=0.005) predictor of poor outcome with all the 8 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.

Table 2: Vital parameters as a predictor of outcome (n=50).

Characteristic	Expiry (n=8)	Discharge (n=42)	Statistical significance
Heart rate (according to age)			χ^2=1.652; p=0.472#
Below normal	0	0	
Normal	0	8 (19.04%)	
Above normal	8 (100%)	34 (80.96%)	
Blood pressure			

Below normal	8 (100%)	41 (97.6%)	χ^2=0.218; p=1.000[#]
Normal	0	1 (2.3%)	
Above normal	0	0	
Respiratory rate			
Below normal	0	0	
Normal	0	2 (4.7%)	χ^2=0.279; p=1.000[#]
Above normal	8 (100%)	40 (95.2%)	
Temperature			
Below normal	0	0	
Normal	2 (25%)	12 (28.5%)	χ^2=0.089; p=1.000[#]
Above normal	6 (75%)	30 (71.4%)	
Capillary refill time			
Normal	0 (0%)	15 (35.7%)	χ^2=6.572; p=0.005[#]
Delayed CRT	8 (100%)	27 (64.2%)	

Amongst the laboratory predictors, a low mean pH (Table 3) on admission had a statistically significant (p=0.005) association with a poor outcome.

Table 3: Arterial Blood gas parameters as a predictor of outcome (n=50)

Characteristic	Expiry (n=8)	Discharge (n=42)	Statistical significance
Mean pH+SD	7.32 + 0.05	7.38 + 0.05	't'=2.682; p=0.005
Mean pO_2+SD	86.90 + 21.63	122.74 + 66.82	't'=1.461; p=0.152
Mean pCO_2+SD	40.27 + 9.12	35.88 + 11.30	't'=1.770; p=0.102
Mean HCO_3^-+SD	15.62 + 3.49	19.02 + 4.77	't'=1.492; p=0.166

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 4: Laboratory markers of sepsis as a predictor of outcome (n=50)

Characteristic	Expiry (n=8)	Discharge (n=42)	Statistical significance
Mean TLC+SD ('000)	15.63 + 7.52	14.53 + 8.53	't'=0.229; p=0.862
Mean Polymorphs+SD	70.33 + 21.80	72.81 + 16.29	't'=0.289; p=0.766
Mean RBS+SD	120.37 + 48.15	110.38 + 41.55	't'=0.581; p=0.654
Mean CRP+SD	3.64 + 2.61	5.82 + 6.84	't'=0.682; p=0.491
Mean ESR+SD	21.53 + 12.86	25.91 + 12.12	't'=0.530; p=0.793

Table 5: Microbiological positivity as a predictor of outcome (n=50)

Characteristic	Expiry (n=8)	Discharge (n=42)	Statistical significance
Positive blood culture	0	1 (2.3%)	-
Positive urine culture	3 (37.5%)	5 (11.9%)	χ^2=0.863; p=0.351
Other body fluid positivity	2 (25%)	17 (40.4%)	χ^2=1.49; p=0.283

Discussion:

Komorowski et al. [11] developed the AI Clinician, a reinforcement learning model, and retrospective results indicated that patients who received treatments similar to those the model recommended had the

lowest mortality. The AI Clinician was developed with a variety of data inputs, some of which have limited EHR availability or would not have been immediately available to the clinician at the time of treatment. It provides useful treatment recommendations when no gold standard for treatment exists, which is a significant current need in the US healthcare delivery landscape. However, while Komorowski et al. derived some insight into the tool's interpretability by estimating relative importance of model parameters, CDS tools that recommend treatment plans must also provide clinicians with transparency along with treatment recommendations, such that clinicians can easily and efficiently interpret the basis for those recommendations [11-12]. Nemati et al. developed the Artificial Intelligence Sepsis Expert algorithm, a sepsis prediction model derived from a combination of electronic medical record (EMR) and high-frequency physiologic data. Retrospective results indicated that the model could accurately predict the onset of sepsis in an ICU patient 4–12 h prior to clinical recognition [13].

Early recognition, resuscitation, and referral can be lifesaving in sepsis; yet, the majority of children had a fever duration over 48 h and were evaluated by providers at other health facilities prior to presentation at MNH, raising concerns about delays to definitive care. This, too, has been previously described; in South Africa, 40% of critically ill children were evaluated by >1 medical provider prior to referral to a tertiary care center, which resulted in delays in definitive care [14].

We used SIRS criteria to identify patients with sepsis, and though these are the current, accepted criteria to identify pediatric sepsis, there has been much criticism regarding this operational definition [15-17]. One criticism is that the definition of sepsis is highly context-dependent, especially in LMIC settings where diagnostic testing may be entirely unavailable or not available within a time frame relevant to guide acute care [15]. In Uganda, researchers used SIRS criteria to identify sepsis in children with suspected infection; 86% met SIRS criteria, which captured 94% of all inpatient deaths, showing that SIRS criteria is highly sensitive for sepsis, but not specific, nor is it helpful in predicting mortality in this population and setting [16].

In a study by Khilnani et al., it was observed that almost half of children who expired in tertiary care PICU had multiorgan dysfunction. [18-19] Although each one of parameters including the number of organ dysfunction, PRISM score, duration of PICU stay could influence final outcome; however, our study revealed that none of them could independently predict mortality among children with sepsis. Surprisingly, we did not find any significance of malnutrition to the final outcome in contrast to findings of others from India. This could probably generate from the fact that we defined malnutrition on basis of weight for age alone, rather than weight for height and height for age. [20]

Conclusion:

A delayed capillary refill time on admission and a low mean pH were statistically significant predictors of mortality in this study.Sepsis in Indian children is associated with high mortality. The multiorgan dysfunction syndrome, high PRISM score and need for multiple inotropes, deranged hematological and biochemical variables are important risk factors for mortality in combination although we are yet to identify a single independent predictor for overall mortality.

References:

1. Carcillo JA. Reducing the global burden of sepsis in infants and children: A clinical practice research

agenda. PediatrCrit Care Med 2005;6: S157-64.
2. Sarthi M, Lodha R, Vivekanandhan S, Arora NK. Adrenal status in children with septic shock using low-dose stimulation test. PediatrCrit Care Med 2007; 8:23-8.
3. Bryce J, Boschi-Pinto C, Shibuya K, Black RE. WHO child health epidemiology reference group. WHO estimates of the causes of death in children. Lancet 2005; 365:1147-52.
4. Pollack MM, Ruttimann UE, Getson PR. Accurate prediction of the outcome of pediatric intensive care. A new quantitative method. N Engl J Med 1987; 316:134-9.
5. Balamuth F, Alpern ER, Grundmeier RW, ChiluttiM,Weiss SL, Fitzgerald JC, et al. Comparison of two sepsis recognition methods in a pediatric emergency department. AcadEmerg Med. 2015:22:1298–306.
6. Rothman M, Levy M, Dellinger RP, Jones SL, Fogerty RL, Voelker KG, et al. Sepsis as 2 problems: Identifying sepsis at admission and predicting onset in the hospital using an electronic medical record–based acuity score. J Crit Care. 2017:38:237–44.
7. Jones SL, Ashton CM, Kiehne LB, Nicolas JC, Rose AL, Shirkey BA, et al. Outcomes and resource use of sepsis-associated stays by presence on admission, severity, and hospital type. Med Care. 2016:54:303–10.
8. Page DB, Donnelly JP, Wang HE. Community-, healthcare-, and hospital-acquired severe sepsis hospitalizations in the University Health System Consortium. Crit Care Med. 2015:43:1945–51.
9. Weiss SL, Fitzgerald JC, Balamuth F, Alpern ER, Lavelle J, Chilutti M, et al. Delayed antimicrobial therapy increases mortality and organ dysfunction duration in pediatric sepsis. Crit Care Med. 2014: 42:2409–17.
10. Singh D, Chopra A, Pooni P A and Bhatia R C. A Clinical Profile of Shock in Children in Punjab, India. Dayanand medical college, Ludhiana, IndPediatr. 2006; 43(7):619-622.
11. Komorowski M, Celi LA, Badawi O, Gordon AC, Faisal AA. The artificial intelligence clinician learns optimal treatment strategies for sepsis in intensive care. Nat Med. 2018:24:1716–20.
12. Shortliffe EH, Sepulveda MJ. Clinical decision support in the era of artificial intelligence. JAMA. 2018:320:2199–200.
13. Nemati S, Holder A, Razmi F, Stanley MD, Clifford GD, Buchman TG. An interpretable machine learning model for accurate prediction of sepsis in the ICU. Crit Care Med. (2018) 46:547–53.
14. Hodkinson P, Argent A, Wallis L, Reid S, Perera R, Harrison S, et al. Pathways to care for critically ill or injured children: a cohort study from first presen-tation to healthcare services through to admission to intensive care or death. PLoS One (2016) 11(1):e0145473.
15. Wiens MO, Kumbakumba E, Kissoon N, Ansermino JM, Ndamira A, Larson CP. Pediatric sepsis in the developing world: challenges in defining sepsis and issues in post-discharge mortality. Clin Epidemiol. 2012:4:319–25.
16. Wiens MO, Larson CP, Kumbakumba E, Kissoon N, Ansermino JM, Singer J, et al. Application of sepsis definitions to pediatric patients admitted with suspected infections in Uganda. PediatrCrit Care Med. 2016:17(5):400–5.
17. HW C., CS, C., GA Y., G, S., & J.A, de S. The Systemic Exclusion of Native Americans from Cancer Clinical Trials. Journal of Medical Research and Health Sciences, 2021:4(8), 1396–1404.
18. Vincent JL, Opal SM, Marshall JC, Tracey KJ. Sepsis definitions: time for

change. Lancet. 2013:381(9868):774–5.
19. Khilnani P, Sarma D, Zimmerman J. Epidemiology and peculiarities of pediatric multiple organ dysfunction syndrome in New Delhi, India. Intensive Care Med 2006; 32:1856-62.
20. Khilnani P, Sarma D, Singh R, Uttam R, Rajdev S, Makkar A, et al. Demographic profile and outcome analysis of a tertiary level pediatric intensive care unit. Indian J Pediatr 2004; 71:587-91.