**Original Research Paper**

### Effect of Prehospital Transport Factors on Shock Index, Serum Lactate, and Mortality in Children with Septic Shock: A Prospective Observational Study

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### Abstract

**Context:** Many children with septic shock either present late or are recognized late due to various reasons. Shock index (SI) is a valuable screening tool in identifying high-risk septic patients in emergency department. Whether prehospital transport factors affect SI and clinical outcomes has not been evaluated. **Aim:** Our aim was to evaluate if prehospital transport-related factors such as mode of transport and referral from another hospital affect the admission SI and mortality in children with septic shock. **Settings and Design:** Prospective observational study conducted over 1-year period in the Pediatric Emergency and Intensive Care Unit of a tertiary care teaching hospital. **Subjects and Methods:** Children <17 years of age were evaluated. Data collection included referral status, mode of transport, physiologic (SI and serum lactate), and clinical parameters. **Statistical Analysis Used:** Student’s t-test was used for analyzing continuous variables. Chi-square/Fischer’s exact test was used for analysis of categorical variables. P < 0.05 was considered as statistically significant. **Results:** Of 51 children, 21 (41%) were referred from other hospitals. Of these, less than half were transported by ambulance unaccompanied by any healthcare personnel. Twenty-six children (43%) died, of which 15 (71%) were referred. The median serum lactate, SI, and mortality were significantly higher in those referred. On multivariate analysis of factors associated with mortality, elevated SI and/or lactate >4 mmol/L and the “referral” status remained significant after adjusting for baseline variables and illness severity. **Conclusions:** Children with septic shock referred from other hospitals had higher SI, serum lactate, and mortality rates. Our study highlights the need for improving prehospital care and transportation in children with septic shock.

**Keywords:** Referrals, septic shock, serum lactate, shock index, transport

### Introduction

Acutely ill children are brought to the Pediatric Emergency Department (PED) of tertiary care centers either by their parents/relatives or are referred from other hospitals.[1] The reasons for referral may be due to lack of resources, trained personnel, diagnostic challenges, or parental pressure. Unfortunately, most referrals do not take into account – weather conditions, time to transport, or availability of specialized equipment or personnel trained in pediatric transport.[2] Many countries including India have national ambulance service or emergency response system that are equipped with lifesaving equipments and can provide basic treatment to a patient before arrival in the hospital.[3] However, few patients/facilities are reported to use these services for various reasons.

Septic shock is one of the most common causes of presentation to the pediatric emergency.[4] Many patients with septic shock either present late or are recognized late due to various reasons. Systemic inflammatory response syndrome is inaccurate in predicting the outcomes in children with sepsis.[5] Shock index (SI) (heart rate/systolic blood pressure), a rapid bedside tool, is a valuable screening tool to identify high-risk septic patients in PED.[5] Age-adjusted SI (SI pediatric age adjusted)

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has also been validated in the pediatric population as follows: >1.22 (age 4–6), >1.0 (age 7–12), and >0.9 (age 13–16).\(^6\) Effect of SI on clinical outcomes has been previously reported.\(^5\)–\(^7\) However, whether prehospital transport factors such as mode of transport and referral from another hospital affect SI and clinical outcomes has not been evaluated in acutely ill children. Our aim was to evaluate the effect of these prehospital transport factors on admission of SI values and mortality.

**Subjects and Methods**

**Design and setting**

This prospective observational study was conducted over a period of 1 year (June 2013 – May 2014) in the PED of a tertiary care teaching hospital in northern India. The annual number of patients presenting to the PED are 60,000–70,000 per year. Of these, about one-third present with sepsis and 4%–5% with septic shock. PED is well-equipped with facilities for management of sick children as per the pediatric advanced life support guidelines such as facilities for vascular access, airway management, monitoring, cardiopulmonary resuscitation, arterial blood gases, electrolytes, chest X-ray, and ultrasonography.

**Participants**

Children <17 years of age presenting to the PED with a diagnosis of septic shock\(^6\) and who survived beyond the 1st h were included in the study. Those who refused consent, had chronic underlying illness, or had a hospital stay in another hospital for >24 h before presentation to the emergency were excluded (we wanted to evaluate the effect of prehospital transport-related factors on the outcomes in children septic shock). Stay more than 24 h may affect outcomes irrespective of the transport-related factors depending on the clinical progression and treatment received by the child in that hospital. The eligible children were enrolled after obtaining informed consent from one of the parents. The study was approved by the Institute Ethics Committee.

**Objectives and outcome variables**

Our objective was to compare the following parameters such as (1) SI, (2) serum lactate at admission, and (3) mortality between children referred from other hospitals and children presenting directly to the emergency.

**Definitions**

SI defined as heart rate/systolic BP, a rapid bedside tool, is a valuable screening tool in identifying high-risk septic patients in PED. The age specific cutoffs for SI in children are 1.22 (age 4–6), >1.0 (age 7–12), and >0.9 (age 13–16).\(^5\)–\(^7\)

Septic shock was defined as per International Pediatric Sepsis Consensus Conference Criteria as sepsis with cardiovascular dysfunction.\(^4\)

**Methods**

Children were managed as per standard protocols for management of septic shock.\(^4\) All received initial fluid resuscitation at admission with monitoring for signs of fluid overload. If evidence of hypoperfusion or hypotension persisted, vasoactive drugs were added. The children were started on appropriate antibiotics within the 1st h, and any electrolyte disturbances or hypoglycemia was corrected. All the children were continuously monitored till discharge or death.

The data were recorded on specified data collection form. The prehospital transport parameters were recorded in a structured pro forma given to parents in the ED. We recorded details such as time taken (in minutes) to reach the health facility, distance travelled, mode of transport (type of vehicle used for transport – i.e., cycle, scooter, auto-rickshaw, rickshaw, ambulance, private vehicle, by foot, metro, and train), referral status, and whether accompanied by medical personnel or not. We also recorded demographic variables such as age in years, gender, place of origin (local or from neighboring states), duration, source of infection, and preexisting chronic disease. At admission, the vital parameters such as heart rate, blood pressure (SI), respiratory rate, temperature, saturation, and variables of pediatric index of mortality (PIM-2) were also recorded. Arterial lactate was estimated at admission. About 130–150 µl of blood was obtained for estimation of lactate, and estimation was done by radiometer ABL800 Flex blood gas analyzer.

**Sample size calculation**

One-third of patients present with suspected sepsis, and 4% had septic shock at admission in the preceding 1 year before the start of this study. Assuming 4% of patients having shock in 70,000 patients, with absolute precision of 5% (95% confidence interval [CI]); the sample size required was 59 patients with shock. We screened all patients presenting during the study period of 1 year and could enroll 51 of the 67 eligible patients that fulfilled the criteria during the 1-year period.

**Statistical analysis**

Data were entered into MS Excel 2007 and analyzed using STATA, version 11.2, Stata Corp, College Station, TX, USA. Student’s t-test/rank-sum test was used for analyzing continuous variables. Chi-square/Fisher’s exact test was used for analysis of categorical variables. Relative risk (RR)/mean difference with 95% CI was calculated. \(P < 0.05\) was considered as statistically significant. We also performed a univariate and multivariate stepwise logistic regression by using mortality as the dependent variable, and the variables thought to be clinically relevant \textit{a priori} as the independent variables.

**Results**

A total of 67 children with septic shock presented to the hospital during the study period. Sixteen were excluded, and 51 children were included in the study [Figure 1]. The median (interquartile range [IQR]) age was 5 years (2, 10), and majority (59%) were males.
Forty-one percent (n = 21) were referred from other hospitals of which less than half (10/21, 47.6%) were transported in ambulance while the remaining arrived in private vehicles (52.4%). None of the children were accompanied by healthcare personnel, and no prior communication was made. All the ambulances were equipped with oxygen and pulse oximeter. Twenty-six children died (43%), of which 15 (71%) were referred. In the referred group, of 10 children transported in ambulance, 6 died; whereas, of 11 children transported by other methods, 9 died (odds ratio [OR] 0.33, 95% CI [95% CI] 0.05–2.43, P = 0.27). In the “Not referred” group, of 3 children transported in ambulance, 1 died; whereas, of 27 children transported by other methods, 10 died (OR 0.85, 95% CI 0.07–10.61, P = 0.89). The most common source of infection was pneumonia followed by skin and soft-tissue infection [Table 1].

The transport-related and physiology variables were compared between children “Referred” and those “Not referred” [Table 2]. The PIM-2 probability was comparable between the “Referred” and those “Not referred” groups. The most common method of transport in the “Referred group” was by ambulance, and in the “Not-referring” group was by auto-rickshaw. The median (IQR) duration of transport in the “Referred group” was 30 min (20, 60) as compared to 20 min (15, 30) in the “Not referred” group (P < 0.001). Most parents expressed their concern and dissatisfaction during transport in the “Referred group” (80% in “Referred” vs. 53% in “Not referred”).

On comparing children “Referred” versus those presenting directly to the emergency (Not referred), the following observations were made: the SI (1.8 vs. 1.5; P = 0.01) and arterial lactate level (mmol/L) was higher (4.5 vs. 3.1; P = 0.03) in the “Referred group” versus “Not referred” group [Table 2]. The mortality was higher (71% vs. 38%; P = 0.02) in the “Referred group” as compared to the “Not referred group.” The need for ventilation was higher as well in the “Referred group” in the first 24 h. There was no statistically significant difference in length of Pediatric Intensive Care Unit stay between the two groups.

We also compared the variables between children transported by “ambulance” and those by “other transport” [Table 3]. Except for the SI and difficulties faced by parents, there was no significant difference between the two groups.

On multivariate analysis of factors associated with mortality (adjusted for age, gender, illness severity, diagnosis, mode of transport, and time taken for transport), referral status (RR [95% CI]: 1.9 [1.13–3.35]; P = 0.02), SI (1.3 [1.02–1.7]; P = 0.04), and lactate at 0 h (1.3 [1.04–2.1]; P = 0.04) remained significant [Table 4]. On analysis of factors associated with elevated SI and/or elevated lactate >4 mmol/L, the referral status remained significant (RR [95% CI]: 2.4 [1.14, 5.1]; P = 0.03).

**DISCUSSION**

In the present study, we observed median serum lactate level, SI, and mortality to be significantly higher in those “referred” from other hospitals compared to children who presented directly to the pediatric emergency.

India as a country has a huge disparity in the health system with the presence of private and government hospitals that are managed at various levels with lack of coordination within the system. The transport of patients seeking emergency care is mostly by private vehicles (e.g., bicycle, auto-rickshaw, or bullock carts, cars), and the accompanying persons include parents or relatives. The roads are poorly made, often congested that adds to the delay in reaching ED. As a result, the basic steps of emergency care (i.e., airway, breathing, and circulation) is often delayed. One study reported mean delay of around 3 h in reaching the trauma emergency, and the children were not accompanied by trained prehospital transport team similar to the present study in which none of the children were accompanied by healthcare personnel. Though some states in India have their centralized emergency ambulance system, the numbers are insufficient to meet the growing demand.

There are considerable variations reported in the modes of prehospital transport in adult patients with sepsis depending on the available infrastructure and medical system in that
In one study, patients with sepsis of any severity used public transport mode in 63%, ambulance in 29%, and mobile emergency care units in 8%.[10] The authors found no clear association between disease severity and mode of transport in the group of patients transported by ambulance, but the percentage of public transport decreased by disease severity.[10] In another study, 49%–59% of septic patients were transported via non-Emergency Medical Service (EMS) compared to EMS.[11,12] In contrast to other disease conditions, public transport is infrequently used in septic patients. In our study, majority arrived by public transport, which could be because of several factors such as lack of awareness of existing free patient transport systems in the country, financial difficulties in affording suitable private transport, and referral from remote

Table 2: Comparison of transport-related, physiologic, and outcome variables in both the groups

| Variables                          | “Referred group” (n=21) | “Not referred group” (n=30) | P     |
|-----------------------------------|-------------------------|-----------------------------|-------|
| PIM-2 score (%)                   | 74 (31)                 | 61 (24)                     | 0.2   |
| Clinical and laboratory findings  |                         |                             |       |
| Heart rate (bpm), mean (SD)       | 135 (14)                | 120 (27)                    | 0.003 |
| Respiratory rate, mean (SD)       | 37 (15)                 | 31 (16)                     | 0.77  |
| Systolic BP (mmHg), mean (SD)     | 76 (11)                 | 80 (14)                     | 0.26  |
| SI                                | 1.8 (0.35)              | 1.5 (0.44)                  | 0.01  |
| Capillary refill time (s), mean (SD)| 3 (0.7)              | 3 (0.9)                     | 0.64  |
| Lactate 0 h, mean (SD)            | 4.5 (2.5)               | 3.1 (2.2)                   | 0.03  |
| Lactate 6 h, mean (SD)            | 4 (1.8)                 | 3.5 (2)                     | 0.3   |
| Mode of transport                 |                         |                             |       |
| Auto-rickshaw                     | 6 (29)                  | 11 (37)                     | <0.001|
| Scooter/cycle                     | -                       | 6 (20)                      |       |
| Private vehicle (car/van)         | 5 (24)                  | 4 (13)                      |       |
| Ambulance                         | 10 (47)                 | 3 (10)                      |       |
| Others                            | -                       | 6 (20)                      |       |
| Transport time (min), median (IQR)| 30 (20-60)             | 20 (15-30)                  | <0.001|
| Difficulties faced during transport (as reported by parents) | 17 (80) | 16 (53) | 0.02 |
| Accompanied by healthcare personnel | 0                      | 0                            |       |
| Mortality                         | 15 (71)                 | 11 (38)                     | 0.02  |
| Need for ventilation in the first 6 h | 16 (76) | 15 (50) | 0.06 |
| Need for ventilation in the first 24 h | 18 (85) | 16 (73) | 0.01 |
| Duration of ICU stay, median (IQR)| 5 (2-7)                | 6 (3-9)                     | 0.5   |

Values in bracket indicate percentage unless specified otherwise. PIM-2: Pediatric Index of Mortality-2, IQR: Interquartile range, SD: Standard deviation, ICU: Intensive care unit, SI: Shock index

Table 3: Comparison of transport-related, physiologic, and outcome variables in ambulance versus other transported group

| Variables                          | “Ambulance group” (n=13) | “Other transport group” (n=38) | P     |
|-----------------------------------|-------------------------|-----------------------------|-------|
| PIM-2 score (%)                   | 64 (22)                 | 70 (28)                     | 0.36  |
| Clinical and laboratory findings  |                         |                             |       |
| Heart rate (bpm), mean (SD)       | 130 (15)                | 122 (26)                    | 0.24  |
| Respiratory rate, mean (SD)       | 36 (16)                 | 32 (15)                     | 0.62  |
| Systolic BP (mmHg), mean (SD)     | 78 (10)                 | 76 (16)                     | 0.49  |
| SI                                | 1.7 (0.48)              | 1.5 (0.44)                  | 0.01* |
| Capillary refill time (s), mean (SD)| 3 (0.8)              | 3 (0.7)                     | 0.68  |
| Lactate 0 h, mean (SD)            | 4.4 (2.6)               | 3.4 (2.4)                   | 0.53  |
| Lactate 6 h, mean (SD)            | 4.1 (1.2)               | 4.5 (2.2)                   | 0.47  |
| Transport time (min), median (IQR)| 22 (16-42)             | 28 (14-44)                  | 0.08  |
| Difficulties faced during transport (as reported by parents) | 9 (69) | 31 (82) | 0.02* |
| Mortality                         | 7 (54)                  | 19 (50)                     | 0.74  |
| Need for ventilation in the first 6 h | 9 (69) | 28 (73) | 0.66 |
| Need for ventilation in the first 24 h | 10 (77) | 31 (82) | 0.28 |
| Duration of ICU stay, median (IQR)| 5 (2-8)                | 6 (210)                     | 0.45  |

Values in bracket indicate percentage unless specified otherwise. *P value significant. PIM-2: Pediatric Index of Mortality-2, IQR: Interquartile range, BP: Blood pressure, SD: Standard deviation, ICU: Intensive care unit
Prehospital transport factors in children with septic shock

Prehospital transport factors can expose the severely ill pediatric patients to additional physiologic stressors that can cause further deterioration and pose difficulties in successfully resuscitating these children. This has been demonstrated in both pediatric and studies in adult patients.[2,14–18] The additional crude mortality rates in critically ill children because of interfacility transport in developed countries are reported to be in the range of 4%–10%.[19–21] We also found increased mortality and worsened SI as well as high serum lactate at admission in this group of children.

In the present study, we observed that in children who travelled by ambulances to our centre and who were referred, there was no clear communication to the treating team at our hospital. This is a common occurrence in developing countries, as many private hospitals fail to admit poor patients because of high cost incurred for treatment and failure of parents to afford the same.[22] Many critically children are usually referred in a hurry to government hospitals for further treatment. This poses a challenge in treatment of these children destabilizing them further in the process of transfer.

Unlike trauma, conditions including sepsis and septic shock in pediatric population have drawn less attention regarding patient transport practices.[10] The awareness is less among the public as well as the healthcare personnel. Besides this, sepsis often presents with nonspecific signs and symptoms, and patient may go into shock quickly without development of any clear-cut prewarning signs. This results in increasing morbidity and mortality in this group of patients.

An interesting observation made in our study was that the ambulance service was underutilized. There could be various reasons for such underutilization such as less number of ambulances per population, delay in arrival of the ambulance, and lack of awareness about ambulance transport service among others. However, the ambulance-transported patients did not have any significant difference from those transported by other methods except the SI and difficulty faced by parents. This may be because of availability of less-equipped ambulances and lack of trained personnel accompanying the patients.

The Joint Working Group of the Academic College of Emergency Experts in India recently has provided a detailed elaboration of current pediatric emergency services in India and recommendations to improve the same that include prehospital transport and care of sick children.[22]

Our study adds to the scarce literature on prehospital transport practices and their effects on hemodynamic variables such as SI, serum lactate levels, and clinical outcomes in children with septic shock. As our study is from a resource-limited setting, the findings would be more generalizable to children from similar settings. The major limitation is that it is from a single centre of a government institute offering free services to patients, and the numbers are small. The results may vary in patients presenting to tertiary care corporate hospitals from similar countries and need further evaluation. The other important limitation is we did not have detailed information on the treatment received in the patients referred from other hospitals as there was no prior communication before referral. This might have affected the outcomes but we tried to limit the same by excluding children with hospital stay more than 24 h.

**Conclusions**

Children with septic shock referred from other hospitals had higher SI, serum lactate, and mortality rates. Less than half were transported in ambulance unaccompanied by any healthcare personnel. Our study highlights the need for improving prehospital care and transportation in children with septic shock.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

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