Original Article

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Paediatrics Section

Sequential Shock Index as a Prognostic Marker in Children with Septic Shock-A Cohort Study

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ABSTRACT

Introduction: Shock Index (SI), is a simple ratio of Heart Rate (HR) and Systolic Blood Pressure (SBP) and a good marker of haemodynamic stability than HR or SBP individually.

Aim: To assess the prognostic value of sequential SI and to compare whether higher SI at admission or worsening SI since admission predicts higher mortality in children.

Materials and Methods: The present cohort study included 50 children between 1-5 years who presented in the Paediatric emergency with shock. The HR, SBP and SI were calculated at 0 and 6 hours of admission. According to the changes in SI over time, the children were divided into four groups, Group 1 (normal SI at 0 and 6 hours), Group 2 (normal SI at 0 hours and abnormal SI at 6 hours), Group 3 (abnormal SI at 0 hours and normal SI at 6 hours), Group 4 (abnormal SI at 0 and 6 hours). They were followed to their condition at discharge and were further subdivided into two groups (survived/died). The relative risk of death was compared among the groups.

Results: Taking the first group as the reference, the relative risk of mortality was 1.442 (Group 2), 1.026 (Group 3), 2.712 (Group 4) i.e., the risk of mortality was highest in the children with worsening SI since admission. Difference in SI at 0 and 6 hours was statistically significant between survivors and non survivors (p=0.001, p<0.001, respectively). In the ROC, SI at 0 hours (0.877) had more sensitivity than SI at 6 hours (0.863).

Conclusion: The SI is a simple, non invasive, cost-effective and a quick tool to detect patients with high risk of mortality and can be used as a quick non invasive method for prompt identification and categorisation of critical illness in Emergency Department. It should be added to HR and SBP, thereby assisting in early identification of septic shock and also the need for aggressive management. Sequential SI values can have a better prognostic value than single admission SI.

Keywords: Haemodynamic parameters, Mortality, Sepsis, Survival

INTRODUCTION

In children younger than 5 years, approximately 29,000 die every day and more than 70% of these deaths are attributed to diarrhoea, severe malaria, neonatal infection, pneumonia, premature birth, or neonatal asphyxia. The majority of these cases are infectious in origin which often lead to sepsis and even septic shock [1]. Sepsis is defined as the systemic response to infection. In a recent systematic review and meta-analysis of epidemiology of paediatric sepsis done by Fleischmann-Struzek C et al., group, the incidence of sepsis in children was reported as 48 cases per 100,000 persons/year and that of severe sepsis as 22 cases per 100,000 persons/year with an approximate incidence of 1.2 million cases of paediatric sepsis per year [2]. Sepsis therefore being a very common cause of death among children. Mortality from paediatric sepsis ranges from 9-35% [3].

Cardiac output is dependent on stroke volume and heart rate. In a young child, change in heart rate is a quick and an early response than change in stroke volume [4]. Hence during hypovolemia in children, tachycardia is an early sign and alteration in Blood Pressure (BP) a late manifestation. As the vascular tone begins to decrease, the change in Diastolic Blood Pressure (DBP) is early as compared to Systolic Blood Pressure (SBP) which is well maintained initially and begins to fall only once haemodynamic stability is severely compromised.

As children often will maintain their BP until they are severely ill, shock may occur long before hypotension occurs in children [5]. Therefore, using BP alone as a reliable indicator to assess the severity of shock and its management may not be adequate enough. Hence it becomes important to have a parameter which can detect children with shock in compensated stage thereby facilitating early aggressive treatment. Having a simple, non invasive marker which can help in predicting prognosis of these children will enable in better triaging and management as well.

Shock Index (SI), calculated as the ratio of HR and SBP may be a quick, promising non invasive measure of degree of haemodynamic status than HR or SBP alone [6], thereby helping in early recognition of severe sepsis and improving the outcome. The concept of SI was first introduced by Allgöwer M and Buri C in 1967 as a simple tool for assessing hypovolemia in patients with haemorrhagic and septic shock states [7]. It can be used as a proxy marker for tissue perfusion since it reflects dysfunction in both, vascular and myocardial status [8]. Studies also suggest it to correlate with other markers of end organ perfusion such as central venacava oxygen saturation ($scvO_2$) and lactate levels [9]. The utility of SI in adults have been well studied and reported. It has been studied as a tool for assessing hypovolemic shock in adult trauma patients [10], shown to predict mortality in conditions such as sepsis, pulmonary embolism [11], traumatic injuries [12], community acquired pneumonia [13], rupture of ectopic pregnancy [14]. The SI was also used to assess early acute hypovolemia in healthy blood donors where SI was found to be high even after five minutes of giving blood, whereas no clinically significant difference were found in HR and SBP [15].

There are fewer studies in children [8,16] which suggest SI to be a better measure of hypovolemic status than HR and SBP to indicate the present haemodynamic condition. With limited studies available, there is no clear cut-off SI to prognosticate/identify the mortality risk. However, as indicated by the studies that increasing SI predicts higher mortality, children with elevated SI should be managed aggressively and referred early, if the need arises. Hence the present study is designed to expand the utility of SI as an early non invasive marker of prognosis in children with septic shock.

MATERIALS AND METHODS

This is an observational cohort study conducted from July 2014 to April 2015 at the Department of Paediatrics, Dr. Baba Saheb Ambedkar Hospital, Delhi, India after the Institutional Ethics Committee approval (DNB/08/2014). The study included 50 children between 1-5 years of age.

Inclusion criteria: All children, between the age of 1-5 years, admitted or diagnosed with septic shock were enrolled for the study. The International Consensus Conference on Paediatric Sepsis 2005 proposed guidelines are used as the criteria for defining sepsis or septic shock [17].

Exclusion criteria: Children with severe acute malnutrition, major congenital anomalies, any chronic illness (e.g., tuberculosis, HIV/AIDS), any form of neoplasm, previously existing co-morbidities (e.g., cerebral palsy), causes of shock other than sepsis (e.g., dengue), trauma patients were excluded. Children on long term medications or who received any inotrope or fluid bolus before coming to our hospital were also excluded from the study.

Study Procedure

The cut-offs for HR, respiratory rate, and SBP used are as proposed in Advanced Paediatric Life Support Manual 2005 [18]. The value of SI for each class of age, was calculated from the normal values of HR and SBP (SI=HR (highest value)/SBP (lowest value). The SI threshold were, 1 to <2 years 1.9, between 2 to <5 years 1.75.

Along with demographic data, the following variables were recorded at 0 and 6 hours of admission: HR, SBP, SI. Other optional investigations which were also recorded at 0, 6 hours of admission were DBP, Lactate Concentration and pH.

The enrolled children were divided into four groups according to the changes in SI over time:

Group 1: SI normal at 0 and 6 hours;

Group 2: Normal SI at 0 hours, Abnormal at 6 hours;

Group 3: Abnormal SI at 0 hours, Normal SI at 6 hours;

Group 4: Abnormal SI at 0 and 6 hours.

The patients were followed to their condition at discharge and were subdivided into two groups according to their outcome (survival/death). The mortality risk among the four groups based on SI changes was compared using appropriate statistical tests. The relative risk of dying was compared among the four groups taking the first as the reference.

STATISTICAL ANALYSIS

Qualitative variables/categorical variables were presented in number and percentage (%) and quantitative variables/continuous variables were presented as mean±SD. The clinical profile of patients was analysed by Chi-square test for qualitative variables. Paired t-test, Student t-test and one-way ANOVA were performed for comparison of quantitative variables. A 5% probability level was considered as statistically significant. The ROC curve was plotted for calculating sensitivity. All the statistical analysis was performed using SPSS version 20.0.

RESULTS

A total of 50 paediatric patients were enrolled in the study. Out of the total 50 children, 33 were male and the mean age was 32.46±16.79 months. The mortality rate was 28%. The SI was calculated in all the children at 0 and 6 hours of admission. Number of children in each group was 36 (group1), seven (group 2), five (group 3), two (group 4). [Table/Fig-1] shows the SI in the four groups. In Group 4, p-value could not be calculated because of the small sample size.

Shock Index (SI) changes	Mortality		Total	p-value
	No	Yes		
Group 1	32	4	36	<0.001
Group 2	1	6	7	<0.059
Group 3	3	2	5	0.655
Group 4	0	2	2	-----
Total	36	14	50	<0.001

[Table/Fig-1]: Comparison of Shock Index (SI) in the four groups*.
*Group 1 taken as the standard group, Chi-square test applied

[Table/Fig-2] shows the relative risk of mortality in each group, considering the first group as the reference. The table shows that the mortality risk was highest (2.712) in the group 4 which had abnormal SI throughout.

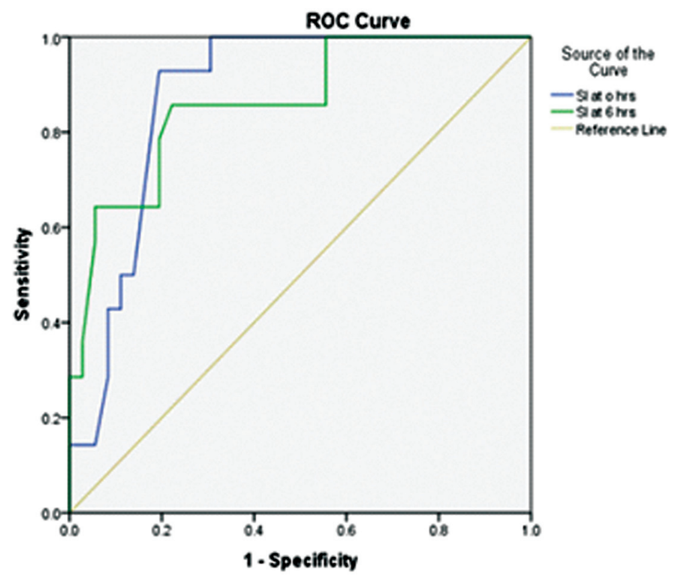
S. No.	Groups (Survivors/Non survivors)	Relative risk (95% Confidence interval)
1	Normal SI at 0 and 6 hours (32/4)	Reference group
2	Normal SI at 0 and Abnormal SI at 6 hours (1/6)	1.442 (1.12-1.84)
3	Abnormal SI at 0 and Normal SI at 6 hours (3/2)	1.026 (0.74-1.28)
4	Abnormal SI at 0 and 6 hours (0/2)	2.712 (2.23-3.04)

[Table/Fig-2]: Relative risk of mortality.

The SI's were different between the two groups (survivors and non survivors) at 0 and 6 hours. Out of the 36 patients that survived, 35 had normal SI (97.3%) and one had abnormal SI (2.7%) at 6 hours. Out of the 14 children that died, at 6 hours of admission, 6 had normal SI (42.85%) and 8 children had abnormal SI (57.15%). The relation of the variables analysed, with respect to survival/non survival of the children are shown in the [Table/Fig-3]. The ROC curve [Table/Fig-4] shows SI at 0 hours (0.877) more than SI at 6 hours (0.863) hence sensitivity of SI at 0 hours has more sensitivity than SI at 6 hours.

Variables	Mortality	Mean±SD	p-value
HR at 0 hours	No	145.77±26.19	0.550
	Yes	150.71±25.52	
HR at 6 hours	No	136.77±23.45	0.015
	Yes	155.21±22.18	
SBP at 0 hours	No	103.72±11.22	<0.001
	Yes	86.07±17.88	
SBP at 6 hours	No	102.77±11.19	0.013
	Yes	93.0000±14.21	
SI at 0 hours	No	1.41±.25	0.001
	Yes	1.81±.54	
SI at 6 hours	No	1.35±.25	<0.001
	Yes	1.74±.24	
DBP at 0 hours	No	67.58±14.33	<0.001
	Yes	51.21±7.86	
DBP at 6 hours	No	62.27±10.28	0.009
	Yes	52.64±13.54	
pH at 0 hours	No	7.30±.14	<0.001
	Yes	7.11±.18	
pH at 6 hours	No	7.31±.08	0.005
	Yes	7.22±.10	
Lactate at 0 hours	No	1.96±1.12	0.092
	Yes	2.70±1.85	
Lactate at 6 hours	No	1.71±.86	0.121
	Yes	2.39±2.18	

[Table/Fig-3]: Characteristics of the variables analysed.
Survived n=36, died n=14



[Table/Fig-4]: ROC curve showing SI at 0 hours and SI at 6 hours.

DISCUSSION

Severe sepsis culminating into septic shock is frequent in children and is often associated with high morbidity and even mortality rates [2,19,20]. In various prehospital settings and in the emergency department, a simple, quick non invasive tool like SI can be used as an indicator of measure of the degree of haemodynamic stability, however, there is paucity of data with this regard in children. It is also suggested that improvement in the subsequent SI values can be used as an evidence for the effectiveness of the resuscitation measures taken in children with septic shock [21], SI as a predictor of outcome of children with severe sepsis has not been evaluated though. Thus, the present study was designed to assess the prognostic significance of sequential SI, if any.

The study shows that abnormal SI at admission or worsening SI since admission predicts a higher mortality. Patients who did not survive had significantly had low SBP and high SI at 0 hours than the survived patients. After 1 hour, only SI was significantly different between two groups. However, HR, SBP and SI at 6 hours were significantly different between the survived and the expired patients.

Shock index may be a better measure of the degree of haemodynamic stability than HR or SBP alone [6] and therefore can predict haemodynamic compromise early, prior to changes in HR or BP alone. The results of the present study are in concordance with that of Rousseaux J et al., wherein they reported that HR was significantly different between survivors and non survivors only at 6 hours ($p=0.04$) and SBP at 0 hours ($p=0.002$) and 6 hours ($p=0.045$), whereas SI was significantly different between survivors and non survivors at 0, 4 and 6 hours ($p=0.02$, $p=0.03$, $p=0.008$) [8]. In the present study, among the various parameters studied, HR was significantly different between survivors and non survivors at 6 hours ($p=0.015$), SBP at 0, 6 hours ($p<0.001$, $p<0.013$, respectively), SI at 0 and 6 hours ($p=0.001$, $p<0.001$, respectively).

The DBP has not been analysed in studies done so far, however it was statistically different between the survivors and non survivors in the present study at 0 and 6 hours ($p<0.001$, $p<0.009$, respectively). The pH at 0 hours was also significant ($p=0.005$). However, contrary to Rousseaux J et al., lactate concentration was not found to be statistically significant with p-value at 0, 6 hours 0.092, 0.121, respectively [8].

In the present study, children with persisting abnormal SI from the beginning or worsening SI since admission had higher chances of mortality. The results were similar to that of Rousseaux J et al., and Yasaka Y et al., where also sequential values of SI over time were analysed, indicating that a persistent abnormal or worsening SI predicted an unfavourable outcome [8,16].

Studies with large adult population suggest that the use of SI is indeed very useful to do a quick and better triaging [22,23], thereby ending in favourable outcomes for the patients [24]. The SI is an easy, fast, inexpensive, and secure tool that can be used in the pre-hospital and hospital settings for early recognition of critical states, its severity as well as means to assess the adequacy of resuscitative measures undertaken and also to predict mortality [25, 26].

Limitation(s)

The present study had a small sample size, involving a smaller cohort of age group and included children with septic shock only, it is therefore recommended that the usefulness of SI should be explored and tested in large cohorts of children with shock of different etiologies to validate and improve the outcome prediction and also to standardise the age adjusted values of SI.

CONCLUSION(S)

From the results of the present study, it may be concluded that SI is a clinically relevant tool to predict mortality. In addition to other established methods for identification of sick children, SI can be used as a quick, non invasive emergency tool to risk stratifies patients. The SI, however has been poorly studied in children. In this study, probably the first of its kind in India, it was observed that SI, if added to HR and SBP, can help in early recognition of septic shock and prediction of the need for aggressive treatment. The SI could be used either in the Emergency Department as well as in the wards for prompt medical management or even in prehospital settings for early referral.

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