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Assessment of Modified Shock Index and its association with outcome in critically ill children with septic shock

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Abstract

Background: MSI is measured as heart rate/mean arterial blood pressure (MAP). It is a non-invasive measure of the degree of hemodynamic stability in children with septic shock. The aim of the study is to determine the association between MSI and change in its values at different time intervals with outcome.

Materials and methods: This prospective observational study was carried out in PICU of a tertiary care centre over a period of 1year. First record of MSI was taken within 1 hour of presentation and recorded as 0-hour reading. Subsequent values were recorded at 0,1,2,4, and 6 hours thereafter. MSI was calculated and tabulated. Patients were divided into 2 groups according to their outcome. Association amongst various study parameters with the outcome was assessed with the help of Pearson Chi-square test and Fisher's Exact Test.

Results: Out of the 44 patients, 30(68%) survived and 14 (32%) succumbed. Trend of MSI (improving or worsening) was better association with the outcome. The difference in MAP between the survivors and non-survivors at 6 hours was found to be statistically significant (*P*= 0.019). A higher MAP and gradual improvement in MAP over time (from 1st to 6 hours) was found to be associated with a better outcome.

Conclusion: MSI may be used as an additional tool to predict the outcome of critically ill children with septic shock, thus allowing early recognition of septic shock, early activation of a rapid response team and prediction of need for aggressive treatment.

Keywords: Modified Shock index, Mean arterial blood pressure, Heart rate.

Introduction

Shock accounts to nearly 2% of all hospitalized infants, children, and adults in developed countries. Mortality rate directly relates to the aetiology and clinical circumstances (1). Incidence of Severe sepsis and septic shock is more in pediatric age group and accounts for higher rate of mortality and morbidity (2-5). Research data shows lower incidence of severe sepsis and septic shock in western pediatric intensive care units (PICU) (usually 2 to 8 %) (6,7). when it comes to developing countries like India, incidence rate rises exponentially to 40-67% (8,9). Research has shown that 20% of children with severe sepsis and 25-50% with septic shock will succumb if not intervened early (6-10). Such high mortality rates signify the importance of early diagnosis and comprehensive management of severe sepsis and septic shock to decrease mortality.

Clinical guidelines benchmarks the importance of clinical examination for early recognition of pediatric septic shock (11,12). Although early identification and prompt treatment of severe sepsis improves outcome, only a negligible number of children receive early appropriate treatment (13-18). Severe sepsis is defined as sepsis plus one of the following: Cardiovascular Organ Dysfunction OR Acute Respiratory Distress syndrome OR two or more other organ dysfunctions (2). Septic shock in a child is defined as sepsis and cardiovascular dysfunction. The initial few hours following suspicion of sepsis and septic shock are crucial and determine the survival rate, the faster the resuscitation the better the outcome hence considered as golden hours (19-21).

Modified Shock index (MSI) defined as the ratio of heart rate (HR) and mean arterial blood pressure (MAP), may be a good and non-invasive measure of the degree of hemodynamic stability (22). MSI value correlates with the degree of vascular, myocardial dysfunction and level of tissue perfusion. Central vena cava oxygen saturation (ScvO2) and lactate concentration along with other indices known to dovetail with MSI (22). In patients with post traumatic hypovolemic shock MSI was considered as reliable indicator of degree of acute circulatory collapse secondary to left ventricular dysfunction (23-25).

Based on previous studies, we expect that initial Modified shock index and its gradual worsening over time, may be used as a predictor of mortality in children with sepsis/septic shock.

Albeit there is no clear cut off value of MSI to identify risk of mortality. Risk of mortality proportionate to MSI, higher the value poorer the prognosis as evident by previous similar retrospective studies. To the best of our knowledge, this is the first prospective study of its kind, which highlights the association of Modified Shock Index with outcome in critically ill children with septic shock and proposes that children with elevated Modified shock index at presentation and worsening MSI over course of time after recognition of shock, may benefit from prompt resuscitation and prudent care.

Materials and methods

This Prospective Observational study was conducted over a period of one year in the Paediatric Intensive Care Unit (PICU) of a tertiary care institution after obtaining approval from institutional ethics committee. All children aged 1 month - 12 years of either sex, admitted in PICU for monitoring and/or therapy, identified with a diagnosis of septic shock as per definitions were included in this study.

Patients having septic shock transferred to our institute on inotropic support and Patients diagnosed as Dengue with Shock Syndrome within 2 hours of admission at our institute were excluded from study. The association

between Modified Shock Index (MSI) and outcome (in terms of survival/mortality) in children having septic shock and the association between MSI at admission and MSI following admission at intervals of 0,1,2,4,6 hours, with the outcome of the patient were determined. All the children admitted in emergency room, ward or PICU, over a period of 1year, who satisfied the inclusion criteria after taking written informed consent from the parent/legal guardian were enrolled.

The sample size determined, based on the prevalence of septic shock in our settings, using software Master 1.0, with 5% precision and 95% level of confidence was 44. Baseline demographic and relevant clinical information (age, gender, vitals, day of illness, provisional diagnosis, criteria for inclusion being fulfilled) were recorded in a predesigned case record form.

Sepsis and Septic Shock: Septic Shock has been defined as Sepsis in the presence of Cardiovascular Organ Dysfunction (1). Sepsis itself is defined as Systemic Inflammatory Response Syndrome (SIRS) plus a suspected or proven infection.

SIRS: 2 of 4 criteria, 1 of which must be abnormal temperature or abnormal leukocyte count:

1) Core temperature of > 38.5oC (101.3 F) or <36oC (96.8 F),

2) Tachycardia: a) Mean Heart Rate > 2SD above normal for age in absence of external stimuli, chronic drugs or painful stimuli, Or b) Unexplained persistent elevation over 0.5 to 4 hours,

3) Respiratory Rate > 2SD above normal for age or acute need for mechanical ventilation not related to neuromuscular disease or general anesthesia,

4) Leucocyte count elevated or depressed for age (not secondary to chemotherapy) (1).

Cardiovascular dysfunction has been defined as follows:

A) Despite administration of isotonic intravenous fluid bolus of 40 mL/kg or greater in 1hour, there was a decrease in blood pressure (hypotension) lower than 5th percentile for age or SBP was less than 2 SDs less than normal for age.

AND/OR

B) The need for vasoactive drug to maintain blood pressure in normal range (dopamine > 5mcg/kg/ min or dobutamine, epinephrine, or norepinephrine at any dose).

AND/OR

C) Any 3 of the following signs of hypo perfusion:

1. Decreased pulse volume (weak or absent dorsalis pedis pulse),

2. Prolonged capillary refill of greater than 3 seconds,

3. Unexplained metabolic acidosis (base deficit >5 mEq/L),

4. Oliguria (urine output<1mL/kg/h) or

5. Core (rectal/oral)-to-peripheral (skin) temperature gap of >3˚C (1).

Modified Shock Index: Heart rate (HR) / Mean arterial pressure (MAP).

First record of Modified Shock Index was taken at 1 hour of presentation (corresponding to definition of fluid refractory shock) and recorded as 0 hour reading. Modified Shock Index was calculated at 0, 1, 2, 4, and 6 hours after admission.

Calculation

Patients were split into 2 groups based on their outcome (survival/death at PICU discharge). Results have been illustrated as median with the 25th (Q1) and 75th (Q3) percentiles for numerical variables. The quantitative data has been presented with the help of mean, standard deviation, median and interquartile range.

Comparison amongst study parameters has been done with the help of Unpaired T-test and Qualitative data has

been presented with the help of frequencies and percentage tables. Association amongst various study parameters with the outcome of patient, has been assessed with the help of Pearson Chi-square test and Fisher's Exact Test. Outcome (survival vs mortality) has been compared between the 2 groups (Survivors/Non-survivors) for – MSI at 0 hours (at admission) at 1hour and at 6 hours after admission: p-value of <0.05 has been considered as significant, and Changes in SI between admission and 6 hours and likelihood ratio with mortality, has been calculated with a 95% confidence interval.

Results

A total of 44 patients were prospectively enrolled comprising 16(36.36%) females and 28(63.64%) males over a period of 1year. Table I illustrates the distribution of study participants according to outcome, 14 of these patients did not survive (Mortality 31.82%) while 30 of them survived (Survival 68.18%). On comparing Gender difference with outcome, we found that in survival group 63.3% (19) were males and 36.7% (11) were females and in mortality group 64.3% (9) were male and 35.7% (5) were females.

Table 1 : Distribution of study participants according to Outcome

Outcome	Frequency	Percentage
Mortality	14	31.82%
Survival	30	68.18%
Grand Total	44	100.00%

Table II and Figure 1 illustrates that there was no significant difference seen between the mean parameters of HR, MAP and MSI at 1st hour and 6 hours between Mortality group and Survival group. The difference between MSI over 6 hours was Positive among survival group and difference between MSI over 6 hours was Negative among mortality group, showing an increase in MSI over time amongst non-survivors. For systematic analysis of the study, Pearson Chi-Square and Fisher's Exact Test were applied as shown in table III and results showed that the *P*-value for both these tests were > 0.05 indicating that the association between MSI and outcome in critically ill children with septic shock were statistically not significant. On applying Unpaired T test, we found that the difference in MAP between the survivors and non-survivors at 6 hours was statistically significant (*P*=0.019) and Improvement in MAP over time (from 1st to 6 hours) was significantly associated with a better outcome.

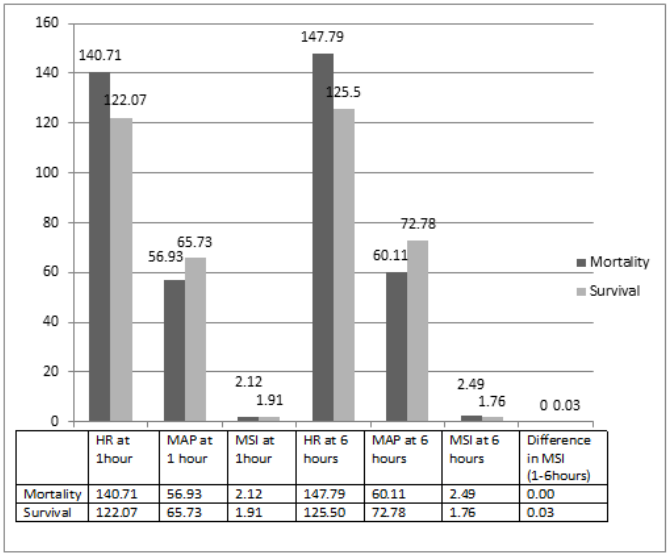

Figure 1: Comparison based on the outcome. HR, Heart Rate; MAP, Mean Arterial blood Pressure; MSI, Modified Shock Index.

Table 2 : Comparison based on the outcome

Study Parameter	Mortality (n=14)				Survival (n=30)				Un-paired T test	P Value
	Mean	Std Dev	Median	IQR	Mean	Std Dev	Median	IQR		
HR at 1st hour	140.71	32.66	140.00	102.00	122.07	37.13	126.00	172.00	0.80	0.43
MAP at 1st hour	56.93	20.67	61.50	82.00	65.73	21.73	66.33	112.00	-1.25	0.22
MSI at 1st hour	2.12	0.78	2.00	3.17	1.91	0.78	1.78	3.50	0.75	0.46
HR at 6 hours	147.79	29.02	146.00	92.00	125.50	28.17	125.00	117.00	0.32	0.75
MAP at 6 hours	60.11	10.48	59.00	40.40	72.78	11.84	70.00	56.00	-1.28	0.21
MSI at 6 hours	2.49	0.55	2.49	2.14	1.76	0.47	1.80	1.71	0.95	0.35
Diff in MSI (1^{st}-6 hours)	0.00	0.38	0.09	1.30	0.03	0.97	-0.06	4.58	0.05	0.52

Abbreviations: HR, Heart rate; IQR, Inter quartile range; MAP, Mean Arterial blood Pressure; MSI, Modified shock index; Std Dev, Standard Deviation.

Table 3: Analysis of study

Chi-Square Tests	Value	Df	*P* Value	Association is
Pearson Chi-Square	0.004	1	0.951	Not Sig
Fisher's Exact Test			0.612	Not Sig

Abbreviations: df, Degrees of freedom; Not sig, Not Significant; P-Value < 0.05 is significant.

Discussion

Various clinical parameters including heart rate (HR), pulse rate (PR), blood pressure (BP), shock index (SI), and modified shock index (MSI) have been analysed to predict the severity of serious patients at an emergency room in various retrospective studies (7,8).

The studies have found that patients with MSI more than 1.3 had a greater mortality rate (8-10). It has been

reported that in addition to SBP, diastolic blood pressure (DBP) is also vital to predict the severity of these patients (10). It was observed that HR more than 120 beats per minute, SBP less than 90 mmHg and DBP less than 60 mmHg correlated with mortality rates of emergency patients (8). They recommended incorporation of DBP in the assessment of these patients.

In contrast to the traditional beliefs, they found a non-significant correlation of shock index (SI) of 0.5-0.9 with mortalities of these emergency patients (10). In another study, SI has been shown to assist in identification of shock states in poly trauma patients (26). MSI was considered as a better marker for assessing the severity of shock than HR and BP alone. Thus, in clinical practice, MSI has been used to assess the severity of emergency patients.

They also found that MSI correlates with hospital stay, duration of stay in ICU, duration of ventilatory support, and use of blood. In our study, we prospectively enrolled 44 patients of septic shock over duration of 1year. To the best of our knowledge, ours is the first prospective study of its kind, which evaluates the association of Modified Shock Index with outcome in critically ill children of age group 1 month-12 years with septic shock, in a tertiary care centre in India.

Out of the 44 patients enrolled, 16(36.36%) females and 28(63.64%) males with a F:M ratio of 1:1.75. Mortality amongst females was found to be much less (35.7%) as compared to that amongst males (64.3%). Rosseaux et al, in his study on 'Prognostic value of shock index in children with septic shock' retrospectively enrolled 146 patients over a period of 9 years, out of which 86 were males (60%) and 60 were females (40%) (5). M:F ratio was 1.43. Almost half of the patients in our study (45%) were infants (less than 1 year of age).

In the study by Rosseaux et al, there was no significant difference regarding age, weight, and sex in the 2 study groups (5). There was no significant difference in mortality between the different genders in any of the studies.

30 (68%) of the 44 cases enrolled in our study survived while 14 (32%) succumbed to septic shock. Overall mortality was 32%. This was comparable with the mortality found by Rosseaux et al in their study (35%) (5). Yasaka et al found an overall mortality of 23% in their study (2).

Our study reveals that in the 1st hour of admission, the non-survivors had a higher mean HR (140.71) compared to survivors (122.07) and survivors had a higher MAP (65.73) compared to the non-survivors (56.93).

After 6 hours since admission, the non-survivors again had a higher value of mean HR (147.79) and low MAP (60.11) as compared to the survivors (125.50 & 72.78 respectively). It was found that, this difference in HR and MSI between the survivors and non-survivors, in 1st hour and after 6 hours and the difference in MAP between the survivors and non-survivors at 1st hour was not statistically significant (*P* value >.05).

However, the difference in MAP between the survivors and non-survivors after 6 hours was found to be statistically significant (*P*=.019).

In other words, improvement in MAP over time (from 1st to 6 hours) was found to be significantly associated with a better outcome. Conversely, a low value of MAP at presentation and its gradual worsening or failure to improve over time with therapeutic interventions, is significantly associated with a worse outcome.

Rosseaux et al observed that, HR was significantly different between survivors and non-survivors only at 6 hours and SBP, at 0 & 6 hours but SI was significantly

different between survivors and non-survivors at 0,4 and 6 hours (5).

This study shows that for the survivors, the median MSI at 0 and 6 hours ranged from 1.78 to 1.80 while for the non- survivors, this range was 2 to 2.49. In the study by Rosseaux et al, the median MSI at 0 and 6 hours ranged from 1.63 to 1.70 for the study population as a whole (5). Age adjusted MSI values were then calculated in their study and median MSI computed for each age group and compared between the survivors and non-survivors. Yasaka et al also used MSI values stratified by age (2). Acker et al and Ray et al too utilized pediatric age adjusted SI (SIPA) values for comparison (3,4).

Acker et al concluded that a pediatric specific shock index (SIPA) more accurately identifies children who are most severely injured, have intraabdominal injury requiring transfusion, and are at highest risk of death when compared to shock index unadjusted for age (3). Due to limitation of sample size and very few numbers of cases in each age group in our study, Age adjusted MSI values were not computed.

In our study, the value of MSI at the time of admission was not very different between the survivors and the non-survivors (2 &1.78 respectively).

This indicates that a single point value of MSI is not predictive of the outcome. But this value of MSI improved over time (from 1st to 6 hours since admission) for the survivors while it worsened (increased) over time for the non-survivors, thus indicating clinical worsening followed by mortality in this group.

The improvement or worsening of MSI over time was not significantly different between the survivors and non-survivors and hence MSI was not independently related to outcome. Yasaka et al found that, even though higher MSI was in harmony with mortality, there was no cut off value with adequate positive or negative likelihood ratios to identify mortality in any age group of children (2). When all participants analysed simultaneously the improvement of MSI in the initial 6 hours of hospitalisation was not associated with outcome.

Although, among patients whose MSI were above the 50th percentile at ICU admission for each age group, improvement of MSI was associated with lower ICU mortality in children between 1-3 and more than or equal to 12 years old (P=0.02 and P=0.03, respectively).

In the study by Rosseaux et al, MSI was significantly different between survivors and non-survivors at 0,4 and 6 hours (P=0.02, 0.03 and 0.008 respectively) and was predictive of death (5). Children with higher Age-adjusted MSIs at 0 and 6 hours had a significantly higher Relative Risk (RR) of death.

From our study we found that the difference in Modified Shock Index (MSI) at presentation and after a period of 6 hours between survivors and non-survivors, was not statistically significant (p = 0.084) and hence, not related to outcome. Similarly, Rosseaux et al observed that changes in MSI between admission and 6 hours were not related to outcome (P=0.59) (5).

Ray et al observed that the predictive value of a change in MSI for mortality was no better than either a change in HR or blood pressure and concluded that the absolute or change in MSI does not predict early death any more than HR and SBP individually in children with sepsis (4).

Limitations of study

The usefulness of MSI alone as a prognostic marker in septic shock could not be proven by this study. It may have value as an additional tool to predict outcome in septic shock, in concordance with other parameters. In our study Sample Size was small and it requires more

studies with large sample size to conclude the usefulness of modified shock index.

Conclusions

The study indicates that a single point value of MSI is not a predictor of outcome. Trend of MSI (improving or worsening over time) are better association with the outcome.

A higher MAP and gradual improvement in MAP over time (from 1st to 6 hours) is significantly associated with a better outcome. A low value of MAP at presentation, gradual worsening or failure to improve with therapeutic interventions: significantly associated with a worse outcome.

Informed Consent: Taken from Parents/ Guardian.

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