# Comparison between shock index and lactate as prognostic markers in severe sepsis and septic shock in PICU

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**Abstract:** Objectives: to compare shock index with lactate as prognostic markers of mortality in pediatric with severe sepsis and septic shock. **Background**: shock index is calculated from HR and SBP as vital sign and follow up of the septic patient by an easy bedside test as shock index which can affect the outcome. **Material and Methods**: This is an analytical study done at the pediatric intensive care unit (PICU) of Menoufia university Hospital from Jan 2015 to Dec 2016. We studied 50 patients who met the inclusion criteria by assessment of shock index in 0,6,12 and 24 hours from admission with measurement of lactate in same points. Patients under the study were divided into two groups according to outcome: survivors and non survivors. **Results:** As regarding shock index in our population under the study, the mean of shock index improved in survivors than non survivors after 12 and 24 hours with statistical significance of 0.04 and 0.05 respectively that not observed in HR and SBP alones. These improvement associated with normalization of lactate after 12 hours (<18 mg/dl) hours which is highly significant with p value of (<0.01) and highly correlated to PRISM score. **Conclusion**: Shock index is easily calculated and its improvement is prognostic and associated with low mortality.

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**Keywords**: lactate, prognostic value, severe sepsis, septic shock, shock index.

## 1. Introduction

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern. *(Singer et al., 2016)* In Egypt, infection accounts for 33% of deaths under 5 years of age *(WHO 2014).* Definition of sepsis had developed along last 30 years. A 1991 consensus conference developed initial definitions that focused on that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection. Sepsis complicated by organ dysfunction was termed severe sepsis, which could progress to septic shock, defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation. *(Bone et al., 1992)*. In 2014 The European Society of Intensive Care Medicine and the Society of Critical Care Medicine recognize sepsis as life-threatening organ dysfunction caused by a dysregulated host response to infection. This new definition emphasizes the primacy of the non-homeostatic host response to infection, the potential lethality that is considerably in excess of a straightforward infection, and the need for urgent recognition. *(Singer et al., 2016)*

Clinical assessment of critical ill patient includes head to toe evaluation and assessment of vital signs. Putting some vital data together or analysis of vital data from prospect other than usual may help in clinical diagnosis. Shock index (SI) is good example for this. The shock index is a bedside assessment defined as heart rate (HR) divided by systolic blood pressure (SBP), with a normal range of 0.5 to 0.7 in healthy adults. *(Berger et al., 2005)* It reflects both vascular and myocardial dysfunction and, thus, is an indicator of tissue perfusion *(*Rousseaux et al., *2013)*. Shock index in infancy and young children calculated with normal ranges above that for the adults so, in pediatric, shock index ranges is defined by age adjusted shock index (SIPA). SIPA was defined by maximum normal HR and minimum normal SBP by age *(Acker et al., 2014)* The SI was initially used to identify high-risk medical patients presenting to the emergency department but subsequently was used to discriminate outcome in in-patient settings. Shock index (SI), the ratio of heart rate to systolic blood pressure, has been found to predict shock in both settings, primarily in adult populations. Elevated SI has also been shown to predict mortality and need for critical care in adults. Studies in children have conflicting results and need more clarification. Study of shock index in pediatric trauma showing SI predictive of hemorrhagic shock and a composite measure of trauma outcomes with a few SI studies finding no predictive value. *(Rappaport et al, 2013)*

Lactate production occurs in all tissues, even at baseline and under normal healthy oxygen rich conditions. *(Uribarri et al., 1998).* In cardiogenic, hypovolemic or septic shock with tissue hypoxia there is usually an imbalance between the increased need of energy and ATP synthesis. This causes an increase in the glycolisis, resulting in a larger lactate

production. *(Megarbane et al., 1998) (koliski et al., 2005)*

A serum lactate in sepsis guidelines is one of the criteria that guide fluid therapy in shock. *(* Dellinger et al., *2013)*. In post–cardiac arrest patients who are comatose after return of spontaneous circulation, a greater percent decrease in lactate over the first 12 hours is associated with better survival and neurologic outcome. Normal lactate is up to 18-20mg/dl, lactate more than 45 mg/dl is associated with more risk of mortality in sepsis. *(*Patriawati *et al., 2014)(* Bai et al., *2014)*

## 2. Patients and methods:

**Patients**:

This Analytical study conducted on 50 critically ill children admitted to the 8 beds PICU of Menoufia University Hospital from Jan 2015 to Dec 2016. Criteria for eligibility in this study included: (1) Age beyond the neonatal period up to 18 years. (2) Admission with severe sepsis or septic shock diagnosed according to last Pediatric Sepsis Consensus Conference criteria. (3) Parental consent. The exclusion criteria included: (1) Patients in the neonatal period or those older than 18-years old. (2) Lack of parental consent. (3) Patients suffering of chronic renal or hepatic disease. (4) Known cases of metabolic diseases (5) traumatic patients.

**Methods**:

For each patient, a complete diagnostic work-up was performed including thorough history and physical examination. Physical examination included: recording heart rate, respiratory rate and blood pressure every 3 hours, pupillary reaction, and Glasgow coma scale. Laboratory Work-up included: arterial blood gases, random blood glucose, complete blood count, C-reactive protein, serum electrolytes, blood cultures, liver and kidney function tests, prothrombin. Cultures of other body fluids, like cerebrospinal fluid (CSF) and urine, were done when clinically required. Chest radiograph, brain CT, and other laboratory or radiological investigations were performed when indicated. In addition, a severity score was calculated using the Pediatric Risk of Mortality (PRISM) score from the website: http://www.sfar.org/scores2/prism2.php within 24 hours of admission.

Blood pressure measured by oscillatory method with 3 records in each time. HR measured by 5 lead ECG monitor. Age specific shock index is calculated by HR/SBP at 0,6,12 and 24 of admission. Lactate is measured at same points from peripheral venous sample. Patients were classified into 2 groups according to survival during admission (survivors and non survivors). The death is the primary outcome in this study.

**Ethical approval**:

All the procedures performed in that study were in accordance to the ethical standards of Menoufia university institutional research committee.

**Statistical analysis:**

Data entry, coding, and analysis were undergone using PSW (20), IBM Corp. Released 2011. Data of this study were of both quantitative and qualitative types. Quantitative data were expressed in Mean ($\bar{x}$), and Standard Error of Mean (SEM), while qualitative data were expressed in frequency (number), and percent (%). We used Student t test. To estimate the difference between two means of groups 1 and 2, Chi square (Chi 2) test to assess the relationship between two or more qualitative parameters and Pearson correlations to find positive and/or negative relationships between quantitative parameters of interest and other quantitative parameters of the study. Receiver operating characteristic (ROC) curve used to study cutoff value, sensitivity and specificity of SI and lactate at 12 and 24 hours of admission with PRISM score of mortality.

## 3. Results:

As regard demographic data of our population under the study, age, sex and BMI, all are non-statistical significant between two groups with mean age 0f 3.4 years among all children under the study. Hospital stay was significant with p value of 0.014 with mean of 15.9 days in non survivors and 11 days for survivors. The most common presentation on admission is Chest infection which represents 60% of total diseases under the study. We cannot identify the organism responsible for the infection in 34% of patients. Staphylococcal sp. Present by 14% which was the most common identified organism responsible of sepsis in the positive cultures. (Table 1)

Prism score between two groups is highly significant with p value of $< 0.01$ with mean of 27.4 score and 62% mortality in non survivors and 22 score and 39% mortality in survivors. (Table 1)

For the whole sample the mean of shock index was 1.74 ranged from 0.81 to 3. In opposite to HR and SBP alones, SI was significant in 0, 12 and 24 while SBP was significant only at 6hours and HR at 12 hours. Lactate was not significant on admission but after that until the end of 24 hours, lactate was highly significant with p value of $< 0.01$ (Table 2)**.**

Table 1. Characteristics of patients, clinical parameters and PRISM score

| | Total n(50) | Non survivors n(30) | survivors (20) | P |
|---|---|---|---|---|
| **Age, mean (range) years** | 3.49 (.3-14) | 3.1 (.3-9) | 4.0 (.67 – 14) | .306 |
| **Sex, Male( %)**<br>**Female (%)** | 30(60%)<br>20(40%) | 18(60%)<br>12(40%) | 12(60%)<br>8(40) | 1.00 |
| **BMI mean(range)** | 17.2 (12.3-27) | 16.8(12.3-23.8) | 17.9(12.3-27) | .291 |
| **Hospital stay, mean**<br>**(range) days** | 14<br>(5-34) | 15.96<br>(5-34) | 11<br>(6-15) | .014 |
| **TLC mean** | 19.14 | 18.5 | 20 | .558 |
| **Need for MV Yes %**<br>**NO %** | 28%<br>72% | 26.7%<br>73.3% | 30%<br>70% | .797 |
| **Culture positive**<br>**Negative** | 64%<br>34% | 70%<br>30% | 60%<br>40% | .851 |
| **PRISM score**<br>**Mortality%** | 25.34<br>53.38% | 27.43<br>62.8% | 22.2<br>39.2% | .000 |
| BMI: body mass index, TLC: total leucocytic count /mm$^3$, MV: mechanical ventilation | | | | |

Table 2. Comparison of HR, SBP, Shock index and Lactate

| | | Non survivors | survivors | p |
|---|---|---|---|---|
| **Heart rate (b/m)** | **H0** | 139.6(80-205) | 154.7(130-184) | .086 |
| | **H6** | 127.3(100-185) | 130.5(110-150) | .579 |
| | **H12** | 127.1(95-170) | 116.3(95-150) | .081 |
| | **H24** | 128.96(90-160) | 109.5(80-140) | .002 |
| | | | | |
| **SBP mmHg** | **H0** | 87.6(60-110) | 81(60-115) | .133 |
| | **H6** | 99.1(80-120) | 93.5(80-110) | .045 |
| | **H12** | 100.6(85-118) | 102(95-110) | .521 |
| | **H24** | 98.2(80-120) | 105(90-120) | .068 |
| | | | | |
| **Shock index** | **H0** | 1.6(.81-2.5) | 1.96(1.47-3) | .004 |
| | **H6** | 1.28(.83-2) | 1.4(1-1.87) | .095 |
| | **H12** | 1.29(.77-1.9) | 1.14(.86-1.5) | .041 |
| | **H24** | 1.2(1-1.9) | 1.0(.72-1.4) | .050 |
| | | | | |
| **Lactate mg/dl** | **H0** | 37.2(21-62) | 35(24-45) | .493 |
| | **H6** | 33.4(19-57) | 20.3(9.3-30) | .000 |
| | **H12** | 35.1(15.5-63.2) | 12(4-18) | .000 |
| | **H24** | 31.7(18-53.3) | 11.1(6.9-19.6) | .000 |
| | | | | |
| Mean (range), (b/m) beats per minute, SBP: systolic blood pressure, HR heart rate, H0: hour zero of admission. | | | | |

Table 3. Area under the curve for Shock index, lactate and PRISM

| Test Result Variable(s) | Area | Std. Error[a] | Cutoff value | Sensitivity | spacificity | Asymptotic Sig.[b] | Asymptotic 95% Confidence Interval | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | | Lower Bound | Upper Bound |
| PRISM score | .872 | .053 | 22.5 | 90% | 70% | .000 | .769 | .975 |
| PRISM mortality % | .933 | .046 | 37% | 93% | 70% | .000 | .844 | 1.000 |
| Lac12 | .987 | .012 | 19.8 | 87% | 10% | .000 | .964 | 1.000 |
| Lac24 | .987 | .012 | 18.2 | 93% | 10% | .000 | .964 | 1.000 |
| SI12 | .700 | .076 | 0.97 | 83% | 90% | .017 | .551 | .849 |
| SI24 | .705 | .073 | 0.88 | 83% | 70% | .015 | .562 | .848 |
| Lac12: lactate at 12 hours, Lac24:: lactate at 24 hours, SI12: shock index at 12hours, SI24: shock index at 24 hours | | | | | | | | |

Examine of SI and lactate with PRISM score by Receiver operating characteristic (ROC) curve show a near sensitivity and specificity of shock index to PRISM at 12 hours, (83% (SI) and 93% PRISM) sensitivity, (90% (SI)

and 70% PRISM) specificity (Fig. 1). The cut of value of the SI at 12 hours in all sample found to be 0.97. Lactate found to be highly sensitive and equal to PRISM (93%) at 24 hours but with low specificity with cutoff value of 18.2mg/dl. (Table 3). The mortality rate represented by PRISM is positively correlated with delta shock index with high significance at 12 hours and with lactate level at 12 and 24 hours. (Table 4**).**

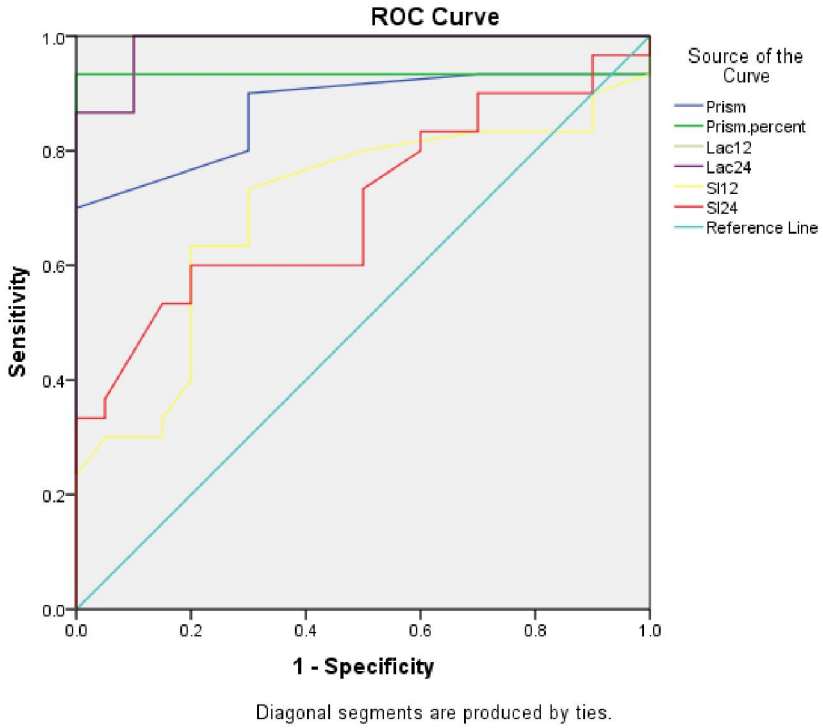


Table 4. Correlation between PRISM, lactate and delta shock index

| | | Delta.SI.12 SI12-SI0 | Delta.SI.24 SI24-SI0 | Lactate 12 | Lactate 24 |
|---|---|---|---|---|---|
| **PRISM** | r | .360 | -.102- | .318 | .339 |
| | p | .010 | .482 | .025 | .016 |
| **PRISM percent** | r | .439 | -.135- | .455 | .514 |
| | p | .001 | .350 | .001 | .000 |
| SI: shock index | | | | | |

**4. Discussion:**

Shock index in our study as vital sign was significant at 0,12 and 24 hours and its improvement is correlated with low mortality at 12 hours, in comparison with HR which was only significant at 24 and SBP which only significant at 6 hours. *Rousseaux et al 2013* who study the shock index among septic patient and end to shock index is statistically significant between survivors and non survivors on admission and could be better measure of hemodynamic when compared to HR and SBP alone. *Yasaka et al 2013* that find that improvement of hourly shock index in the 1st 6hours not linked to outcome when studied in all patients but when stratified by age, it associated with low mortality in 1-3 and above 12 years age groups only.

our results about lactate show that improvement of serial lactate in septic patient is highly significant predictor of low mortality and vice versa, *Koliski et al 2005* who found that normalization or reduction of lactate levels at and after 24 hours of admission was significantly related with higher chances of survival. In our results normalization of lactate occur at 12 hours and persist for the 24 hours, But in non survivors no normalization even after 24 hours. These appear brightly in high positive correlation between lactate and PRISM score.

From our results Lactate was better than shock index from two points of concern; the 1st is lactate became significant earlier than shock index and 2$^{nd}$ is the degree of significant of lactate is of higher value than shock index. But in studying ROC curve, the

shock index is near to PRISM than lactate and has better specificity.

**Limitations:**

Our study data is limited by the number of patients included in the study and may the data be more clarified if the sample expand. Also effect of vasopressor and stratification of the sample by age may affect the data of shock index.

**Conclusion:**

Shock index is easily calculated vital sign better than SBP and HR and its improvement in 1st 12 hours of admission is associated with low mortality especially if that improvement accompanied by normalization of lactate which is strong prognostic biomarker for sepsis in pediatric.

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