Original Article

PRISM III Score and hsCRP as Predictors of Mortality in Patients with Sepsis, Severe Sepsis, and Septic Shock

Asif Ahmed, Qazi Iqbal Ahmad, Shahzada Saleem Yousuf

Abstract

Background: Severe sepsis and septic shock are two major causes of death in children with sepsis. The Pediatric risk of mortality (PRISM) score allows for mortality risk assessment in the pediatric ICU. It is institution-independent and can be used within limits to compare different intensive care units.

Materials and Methods: It was a prospective observational hospital based study. All patients admitted in the Paediatric Intensive Care Unit between the age group of one month to 14 years who fulfilled the inclusion criteria were prospectively observed and details were recorded in a predesigned proforma.Critical illness severity was estimated with the Paediatric Risk of Mortality (PRISM III-24) score.

Results: 30 patients (14 males & 16 females) were included in the study&mortality rate of 40.0% was witnessed.29(96.7%) patients were given pressor support. In terms of outcome, 17(94.4%) of the 18 discharged patients received pressor support and 01(5.6%) of them did not receive any pressor support. On the other hand, all 12 expired patients received pressor support (*P*=0.406). 25(83.3%) patients required mechanical ventilation. In terms of outcome, 14(77.8%) of the discharged patients required mechanical ventilation while 04(22.2%) of them did not require it. On the other hand, out of 16 patients who expired, 11(91.7%) required mechanical ventilation while 01(8.3%) did not require it (*P*=0.317). None of the patients, either from the discharged ones or from the expired ones, had a low-risk HsCRP level(<3). The mean PRISM III Score at admission in discharged patients was 20.5±3.65 and the mean PRISM III Score at admission in expired patients was 23.25±1.76 (***P*=0.01)**.The mean PRISM III score at 24 hours in discharged patients was 17.33±4.46 and the mean PRISM III score in expired patients was 22.50±1.50 (***P*=0.001)**.When analyzed in specificity versus threshold (ROC) curve, PRISM III Score was significant at both time intervals i.e., at admission (***P*=0.019)** and at 24 hours (***P*=0.003).**

Conclusion:

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Introduction

Severe sepsis and septic shock are two major causes of death in children with sepsis. Sepsis is life threatening organ dysfunction caused by a dysregulated host response to infection. Data frompediatric intensive care units (PICU) in developing countries reveals that in children the mortality rate from sepsis is higher than 50%[1-3].The reported incidence of severe sepsis and septic shock are much lower for western PICUs (2% to 8%)[4] as compared to Indian PICUs (40% to 67%).[1,2] The reported mortality rates are about 20% for children with severe sepsis and 25 to 50 % for septic shock.[1-3]

The first hours following the diagnosis of severe sepsis and septic shock are known as golden hours as it is during this period that aggressive hemodynamic resuscitation is associated with higher

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Keywords

PRISM III score, hsCRP, Pediatric, Sepsis,Severe sepsis

survival rates and reduced organ dysfunction.[5] After the golden hours, aggressive hemodynamic resuscitation is no longer effective in restoring organ dysfunction or in decreasing mortality.[5] In an Indian PICU, there was a 9-fold increase in odds of survival if the shock was corrected in the emergency department.[6] The major causes of the loss of golden hours in our country may be due to three major delays-delay in recognition, delay in transport, and delay in initiating treatment.[7]

The Pediatric risk of mortality (PRISM) score allows for mortality risk assessment in the pediatric ICU. PRISM was developed from the Physiologic Stability Index (PSI) to reduce the number of variables from 34 to 14 and the number of ranges from 75 to 23 without losing the predictive power. It is institution-independent and can be used within limits to compare different intensive care units.[8]

In 1996 physiological variables and their ranges as well as diagnostic and other risk variables reflective of mortality risk were reevaluated by Pollack et al.[9] PRISM III is widely accepted and is a standard against which other scores are compared.[8]

PRISMIII is a third-generation pediatric physiology-based score for mortality risk and it has resulted in several improvements over the original PRISM. Reassessment of physiologic variables and their ranges, better age adjustment for selected variables, and additional risk factors resulted in a mortality risk model that is more accurate and discriminates better.

Biomarkers have been broadly used to aid in diagnosis, prognostication, and/or therapy of many medical conditions.[10] C - reactive protein is an acute-phase protein that plays an important role in many medical conditions.Elevated CRP levels detected using highly sensitive assay (hsCRP) techniques have been associated with increased cardiovascular risk, stroke, and all-cause mortality. These levels are used as an efficient tool in the diagnosis and prognostication of pediatric sepsis and septic shock.[10,11]

PRISM III-24 score as a predictor of PICU mortality has been validated in many studies. However, hsCRP as a predictor of PICU mortality has not been studied before in many studies. Patients with a high initial PRISM score at admission, within 12 hours of admission, or within 24 hours of admission have been shown to have increased mortality. Non-survivors have shown a higher mean score compared to survivors in most of the studies. Gross mortality and adjusted PICU mortality rates have been shown to be worse with higher PRISM scores.[3,5,6,12]

In our study, we attempted to divide patients on the basis of PRISM III scores and hsCRP and see the outcome of both groups. Our study focused on ascertaining clinical or laboratory characteristics, in the form of PRISM III score and hsCRP, that would be helpful in prognosticating the outcome in pediatric patients admitted to PICU with sepsis, severe sepsis, and septic shock.

Materials and Methods

It was a prospective observational hospital based study which was conducted in the PICU of a tertiary care teaching hospital in North India.

Inclusion Criteria:

1) All children Admitted to PICU between the age group of 1 month to 14 years who met the definition of pediatric sepsis guidelines for the diagnosis of sepsis, severe sepsis, and septic shock.

2) Patients staying alive for at least 24 hours after admission.

Readmission to the PICU during the same hospitalization was analyzed as separate patients because each admission presented aseparate opportunity for an outcome.

Exclusion Criteria:

1) Children with PICU stay of<24 hours.
2) Trauma Patients.
3) Surgical Patients.
4) Children Leaving Against Medical Advice.
5) Patients with missing data.

Approach

All patients admitted in the Paediatric Intensive Care Unit between the age group of one month to 14 years who fulfilled the inclusion criteria were prospectively observed and details were recorded in a predesigned proforma.

Data Collection:

The following data was collected prospectively:

- Age.
- Gender.
- Admission diagnosis.
- Previous neonatal, paediatric intensive care or hospital admission.
- Procedures.

The following data was collected as treatment characteristics;

The need for mechanical ventilation (MV) and duration of MV in days.

- The need for inotrope use.
- Length of PICU stay (LOS).
- Need for central venous access.

Critical illness severity was estimated with the Paediatric Risk of Mortality (PRISM III-24) score. Clinical and laboratory data needed to calculate the PRISM III-24 score was reported as the worst value within 24 hours after PICU admission.Neurologic status was evaluated using the paediatric version of the Glasgow Coma Scale (GCS) and patients with GCS <8 were recorded as suffering from coma.HsCRP was recorded at admission and at 24 hrs using the QDxInstacheck test system at the point of care.

The outcome was evaluated in terms of expiration or discharge from PICU.

Categorical outcome variables were analyzed by chi-square test. All analysis was done using IBM SPSS

Microsoft Excel. A *P* value of less than 0.05 was considered significant.

Results & Observations

Initially, a total of 76 pediatric patients were scrutinized for the study. They were assessed in terms of inclusion and exclusion criteria. Out of these patients, 15 of them left against medical advice& another 10 of them had a PICU stay less than 12 hours. Refusal of consent was recorded in 12 patients and another 09 patients had missing necessary data. In our final assessment, a total of 30 patients (14 males & 16 females) were finalized for inclusion in the study.

Amongst the 30 enrolled patients with sepsis, severe sepsis, and septic shock, a mortality rate of 40%[12/30] was witnessed, which reflects that a significant portion of pediatric patients die as a result of sepsis or septic shock.

The mean age in discharged patients was 8.67±3.46 years and the mean age of expired patients was 8.08±2.46 years(*P*=0.61).

8(44.4%) of the 14 males were discharged and 06(50.0%) of them expired. On the other hand,10(55.6%) of the 16 females were discharged &06(50.0%) of them expired (*P*=0.76).

29(96.7%) patients were given pressor support and 01(3.3%) patient did not receive any pressor support. In terms of outcome,17(94.4%) of the 18 discharged patients received pressor support and 01(5.6%) of them did not receive any pressor support.On the other hand, all 12expired patients received pressor support(*P*=0.406). Thus pressor support requirements were similar in both groups.

Out of the 30 study subjects, 25(83.3%) patients required mechanical ventilation. In terms of outcome, 14(77.8%) of the discharged patients required mechanical ventilation while 04(22.2%) of them did not require it. On the other hand, out of 16 patients who expired, 11(91.7%) required mechanical ventilation while01(8.3%) did notrequire it (*P*=0.317). Thus mechanical ventilation requirements were similar in both discharged and expired patients.

HsCRPlevel at admission in patients with septic shock was compared with their outcomes. None of the patients, either from the discharged ones or from the expired ones,had a low-risk HsCRP level(<3). Out of 18 discharged patients, 01(5.6%) had HsCRP of intermediate risk level(3-50)and the remaining 17(94.4%) had HsCRPof high-risk level(>50). All the expired patients had HsCRP of high-risk level(*P*=0.406).

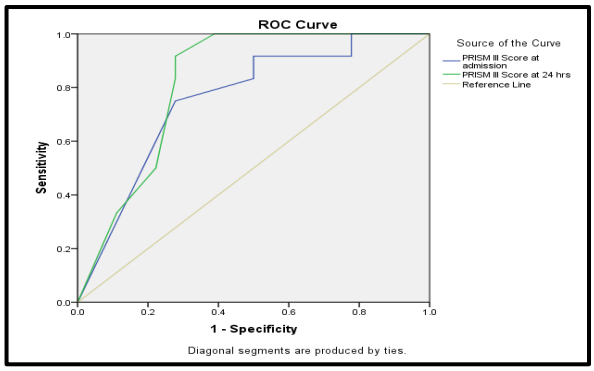
Similarly,HsCRP at 24hours in patients with septic shock was compared with their outcomes. None of the patients, either from the discharged ones or from the expired ones,had a low risk HsCRP level. 02(11.1%) of the 18 discharged patients had HsCRP of intermediate risk level and remaining 16(88.9%) of them had HsCRP of high risk level. All the 12 expired patients had HsCRP of high risk(*P*=0.232).

PRISM III score at admission in patients with septic shock was compared with their outcomes. The mean PRISM III Score at admission in discharged patients was 20.5±3.65 and the mean PRISM III Score at admission in expired patients was 23.25±1.76 (***P*=0.01)**.

The PRISM III score at 24 hours in patients with septic shock was compared with their outcomes. The mean PRISM III score at 24hours in discharged patients was 17.33±4.46 and the mean PRISM III score in expired patients was 22.50±1.50 (***P*=0.001)**.

When analyzed in specificity versus threshold (ROC) curve, PRISM III Score was significant at both time intervals i.e., at admission (***P*=0.019)** and at 24 hours **(*P*=0.003).**

Fig1. ROC Curve For PRISM III Score at Admission and at 24h.



Discussion

Sepsis is the body's extreme response to the infection. It is a life-threatening medical emergency which develops when the already present infection triggers a chain reaction throughout the body. It often starts in the lung, urinary tract, skin, or gastrointestinal tract and delayed treatment proves fatal due to rapid damage to tissues, organ failure, and death.[13]

Severe Sepsisis sepsis associated with organ dysfunction, hypotension, or hypoperfusion. Hypoperfusion abnormalities of end organs may include hyperlactatemia, oliguria, or an alteration in mental status.[13,14]

Septic Shockissepsis associated with hypotension and perfusion abnormalities despite the provision of adequate fluid (volume) resuscitation. Perfusion abnormalities include lactic acidosis, oliguria or an acute alteration in mental status. Patients with septic shock who are receiving inotropic or vasopressor therapy might still exhibit perfusion abnormalities, despite the lack of hypotension.[13,14]

Incidence of severe sepsis is much lower in the PICU of developed countries compared to underdeveloped ones. Percentage-wise, 40%-67% of cases of sepsis or septic shock are reported in Indian PICUs compared to 2%-8% of cases in western PICUs.

The first hours following the diagnosis of severe sepsis and septic shock are known as golden hours as it is during this period that aggressive hemodynamic resuscitation has been shown to be associated with

higher survival rates and reduced organ dysfunction.[12] After the golden hours, aggressive hemodynamic resuscitation is no longer effective in restoring organ dysfunction or in decreasing mortality.[6]

Early assessment with the help of inflammatory markers, clinical signs, or with other investigations becomes essential to cultivate the golden hour period, thereby deterring the sick patient from going into shock. A number of such approaches are available and are currently being used, including the tissue oxygenation parameters such as superior vena caval oxygen saturation (ScvO2) and serum lactate, which may help to guide fluid and inotrope therapy.[15,16] Apart from ScvO2 and lactate, there are other means of evaluating regional and global tissue perfusion. Regional perfusion is evaluated using Near-infrared spectroscopy (NIRS), peripheral perfusion index, orthogonal polarization spectral, transcutaneous oxygen and CO2 measurements, peripheral to the core temperature gradient, and tissue capnometry.[8,10]The global tissue perfusion can be assessed using invasive methods like Fick's method and Thermodilution method and non-invasive methods like echocardiography, M-mode echocardiography, and doppler echocardiography.[15,16]

In our study, we analyzed the sepsis, severe sepsis, and septic shock patients based on a number of variables to predict whether these variables especially HsCRP and PRISM III Score would predict the outcome in patients with septic shock.

We recorded a mortality rate of 40.0%. The findings reflect that a significant portion of paediatric patients dies due to sepsis and septic shock.Rusmawatin-ingtyas et al[17]reported 88.2% mortality in their study. Increased mortality may be attributed to the severity of the illness or due to fluid overload which was seen in 10% of their patients.[18]

In this studymean age of the discharged patients was 8.67±3.46 years and the mean age of the expired patients was 8.08±2.46 years (p=0.61).The outcome of the patients with sepsis and septic shock had noassociation with age. Our findings are similar to the works of Kaur et al & Qui et al.[19,20]

In our study we found no association between the gender &final outcome of patients with sepsis and septic shock.08(44.4%) of the enrolled male patients were discharged and 06 (50.0%) of them expired. 10(55.5%) of the females were discharged and 06(50.0%) of them expired (p=0.76). The findings were similar to the works of Qui et al.[20]

In our study pressor support was found to be an insignificant factor in the outcome of the patients, with 29(96.66%) patients from both the groups receiving pressor support (p=0.406). This could be due to the fact that most of the patients admitted in PICU require pressor support.

In our study population mechanical ventilation was required in 25(83.33%) patients. Out of these 14(77.8%) were discharged and 11(91.7%) expired(p=0.307). Thus mechanical ventilation does not influence the outcome of patients. Our findings are contrary to the works of Kaur et al[21] who found that ventilated patients had 10.87 times more risk of mortality. Costa et al[22] have reported that mechanical ventilation significantly affected the mortality of septic shock patients. On the other hand,Ana Lila[23] and Pollack et al[9] reported that mechanical ventilation was aninsignificant variable in the outcome of septic shock patients. This difference could be attributed to the different systems involvedin presentation at different centers.

In our study majority of our patients were admitted due to gastroentrological illnesses (45.2%) followed by respiratory illnesses (29.5%), cardiovascular illnesses (9.3%), and miscellaneous illnesses (4.6%) in that order,as against other studies in which surgical patients represented a big proportion of PICU patients ranging from 16%-60%.[18,24,25] The majority of our patients were admitted due to pediatric medical emergencies.

In our study,hsCRPlevels were higher in the majority of the cases at both time intervals.In 18 discharged patients, except for a single patient,hsCRPat admission was found to be of higher value (>50).In all12 expired patients hsCRPwas higher invalue (p=0.406). Similarly at 24 hours, in 10 out of 12 discharged patients,hsCRP was of higher value & it was of lowervalue in only 2 cases.Inall expired cases,hsCRPwas of higher value (p=0.232). The findings indicate overall elevated levels of hsCRP in sepsis and septic shock patients.Wu et al[26] found that hsCRP levels in the expired patients were significantly higher than in the discharged ones (p<0.001).

In our study, PRISM III score was measured at admission and at 24 hours. At both intervals,the mean PRISM III score was higher in expired patients than indischarged patients. At admission mean PRISM III scorein dischargedpatients was 20.50±3.6and in expired patients, it was 23.25±1.76(p=0.01). A net increase of 2.75 was present in the PRISM III score in expired patients compared to discharged ones. At 24 hours mean PRISM III score in discharged patients was 17.33±4.46 and in expired patients,it was 22.50±1.50(p=0.001). A net increase of 5.17 in PRISM III score at 24 hours in expired patients compared to discharged ones also reflects an increased distinction in the PRISM III score at 24 hours compared to the score at admission. Our findings indicate that the PRISM III score is significantly higher in patients who expired with sepsis and septic shock and this difference is more pronounced at 24 hours compared to the admission time scores. In specificity and threshold analysis (ROC curve) our results were again similar, with strong statistical significance at 24 hours (p=0.019) compared to admission time (p=0.003). Kaur et al[19] reported that the PRISM III score was significantly higher among expired patients compared

to those who were discharged.However in multivariate logistic regression, they found that mortality was not significantly predicted bythe PRISM score at admission (p=0.07). Hassan et al[27] found that PRISM score >8 was a significant predictor of mortality (p<0.001). The odds ratio for dying in the presence of a PRISM score >8 was 9.28 and Cox regression analysis showed that a PRISM score >8 was an independent predictor of mortality in patients with septic shock. Our results are also similar to those of Bellad et al,[16] who found that the mean PRISM score was lower in discharged patients as compared to the expired patients (6.5±3.6 vs 15.5±7; p<0.001). Further, they mentioned that with an increase in PRISM score by 1, the child's odds of death increased by 36%, and using the logistic model they were able to correctly classify 89.2% of patients. Qui et al[20] noted the median probability of mortality for PRISM, PIM, and PIM2 scores to be 6.20% (3.06%-12.25%), 2.54% (1.90%-6.92%) and 2.20% (1.59%-5.78%) respectively. Also, they were found to be significantly higher in the expired group than in the discharged group for the 3 scores(p<0.05).

Overall, in our study, while the rest of the variables were found to be either similar orstatistically insignificant, the PRISM III score was significant in predicting the mortality in patients with sepsis and septic shock.

Our study faces the limitations of being monocentric with limited infrastructure. Moreover, the sample size for this study was very small. Broader sample sizes and multicentric studies are needed to infer fromthe results obtained with this study.

Conclusion:

Among the variables analysed in this study including HsCRP at admission and at 24 hours, except for PRISM III score rest of the variables proved insignificant in predicting the mortality of patients with sepsis and septic shock.

PRISM III score in expired patients at both time intervals remained higher when compared with the discharged patients.

PRISM III score was more distinctive between the expired and discharged patients at 24 hours and hence carries a reliable value in predicting the mortality associated with aforementioned illness.

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