



Relation of Systemic Inflammatory Response Syndrome (SIRS) and Pediatric End stage Liver Disease (PELD) Score with Hospital Outcome of the Paediatric Liver Cirrhosis Patients in Bangladesh

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Abstract: -

Background and Aim: Positive Systemic inflammatory response syndrome (SIRS) with a high pediatric end-stage liver disease (PELD) score may indicate a poor prognosis for children with liver cirrhosis where early interventions could reduce mortality. Our objective was to determine, for the first time in Bangladesh, the relationship between SIRS and PELD score and the hospital prognosis of children with liver cirrhosis.

Patients and Methods: This cross-sectional study was conducted between March 2018 and February 2019 at Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, among admitted children admitted with liver cirrhosis between 1 month and 12 years of age. All participants were screened for SIRS, and PELD scores were calculated. Data were analyzed to find the relationships between SIRS and PELD scores and hospital outcomes.

Results: A total of 53 patients were enrolled in this study with a mean age of 74.9 ($\pm$ 55.8) months. Among them, 26 (49.1%) patients with positive SIRS. Wilson's disease (49.1%) and biliary cirrhosis (35.8%) comprised most of the cases. Total 10 (18.9%) patients died during the hospital stay, and mortality was significantly higher among SIRS positive group ($p=0.03$). The area under the Receiver-Operator Characteristic (ROC) curve of positive SIRS and PELD was 0.691 and 0.602, respectively. A high PELD score (>24) was associated with an increased risk of death (odds ratio 2.294). Multivariate Logistic Regression analysis showed only SIRS positivity was independently associated with increased mortality ($p<0.05$).

Conclusion: Positive SIRS and high PELD scores are correlated with increased hospital mortality in pediatric liver cirrhosis patients. Early interventions can deter their imminent death.

Keywords: Pediatric liver cirrhosis, SIRS, PELD, Hospital outcome, Death.

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Introduction

Liver disorders and cirrhosis account for 23.6% of global mortality(1). However, the exact prevalence of pediatric liver disorders is unknown. According to the only available data, around 15,000 children are hospitalized annually in the United States for liver diseases(2). Paediatric End-Stage Liver Disease (PELD) is a disease severity scoring system designed to improve the transplantation organ allocation system for children younger than 12 years of age. Numerous studies demonstrated its ability to predict mortality(3). Traditionally, systemic inflammation was determined by the presence of Systemic Inflammatory Response Syndrome (SIRS), a state in which clinical and biochemical parameters are altered. Systemic inflammation has been identified to cause serious complications in patients with severe cirrhosis, including variceal bleeding, encephalopathy, and worsening of prior liver failure(4, 5). SIRS is closely linked to the severity of liver disease, as evidenced by the MELD score in adults, which has a negative impact on the in-hospital outcome of patients with liver cirrhosis(6-8). In children with liver cirrhosis, a high PELD score and a positive SIRS both indicate a poor prognosis. However, very little is known regarding their association to hospital outcomes, and no studies have been undertaken on the Bangladeshi pediatric population. Identifying the relationship between SIRS and PELD score and hospital outcomes in children with chirosis in countries with limited resources, such as Bangladesh, will improve therapeutic approaches and patient follow-up. The goal of this study is to investigate the association between SIRS and PELD scores and hospital outcomes in pediatric patients with liver cirrhosis.

Materials and methods

This cross-sectional study was conducted among 53 children with cirrhosis of the liver who were admitted at the Department of Paediatric Gastroenterology and Nutrition at Bangabandhu Sheikh Mujib Medical University Hospital (BSMMU), Bangladesh, between March 2018 and February 2019. BSMMU is a specialized tertiary care hospital and premier postgraduate medical university in Bangladesh. Cirrhosis was diagnosed if clinical symptoms of portal hypertension, poor coagulation, and/or ascites were present. SIRS was diagnosed if at least two of the following four criteria were met, with abnormal temperature or leukocyte count being one of them: 1. Core temperature of $>38.5^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, 2. Tachycardia or, for children < 1 -year-old, bradycardia, 3. Mean respiratory rate >2 SD above normal and 4. Abnormal leukocyte count for age or $>10\%$ immature neutrophils(9).

The PELD score was calculated using an online calculator (<https://reference.medscape.com/calculator/183/peld-score-age-younger-than-12-years> calculator). The outcome was defined as death or discharge following admission. Participants were selected sequentially from children admitted to BSMMU with liver cirrhosis. Exclusions were made for children with congenital heart disease and those on hepatotoxic medications. The study received ethical approval from the Institutional Review Board of BSMMU. The parents or legal guardians of every child enrolled in the study provided their written consent after being fully informed. Informed

written consent was obtained from parents or from legal guardians of each child who was in the study.

Upon admission, a thorough clinical evaluation of each patient was conducted. Physical examinations were done by the principal author, and the findings were recorded in a structured questionnaire. In the Department of Biochemistry, BSMMU, total WBC count, serum bilirubin, and serum albumin were measured from the venous blood of the patients using an auto analyzer. International Normalization Ratio (INR) and prothrombin time were measured by an auto-analyzer at the Department of Hematology, BSMMU. At admission, the presence or absence of SIRS was assessed. The severity of the disease was determined using the PELD score. The principal outcome variables were hospital discharge or death. Age, sex, weight, height, respiratory rate, heart rate, temperature, leukocyte count, serum bilirubin, serum albumin, and INR were independent variables. The dependent variables consisted of SIRS and PELD scores.

Data were checked manually and then analyzed using SPSS (IBM Corp. Released 2016. IBM SPSS Statistics for Windows, Version 24.0. Armonk, NY: IBM Corp.). For quantitative data, Student's t-test was done, and for qualitative data, the Chi-square test and/or odds ratio was calculated. To identify variables that were independently associated with the outcome, multivariate logistic regression analyses were performed. To predict mortality, the sensitivity, specificity, positive and negative predictive values of a positive SIRS, and a high PELD score were calculated. Receiver operating curves (ROC) were also drawn to illustrate the area under the curve. A p-value of <0.05 was considered statistically significant for all statistical tests.

Results

In this study, 53 patients with cirrhosis of the liver were selected. Table 1 shows the demographic, etiological, and clinical characteristics of the patients. A male-to-female ratio of 1.2:1 was observed among the participants, with 29 (54.7%) male and 24 (45.3%) female. The patients were between 4 months and 144 months old, with a mean age of $74.9 (\pm 55.8)$ months. All patients were evaluated for the presence or absence of SIRS using age-appropriate temperature, heart rate, respiratory rate, and WBC count. At the time of admission, 26 (49.1%) of the children were SIRS-positive, and 27 (50.9%) were SIRS-negative. Thirty-one (58.5%) children presented with jaundice and ascites; four (7.5%) with jaundice, ascites, and encephalopathy; three (5.7%) with jaundice, ascites, and upper GIT bleeding; one (1.9%) with jaundice and upper GIT bleeding; and seven (13%) with jaundice, four (7.5%) with ascites, and one (1.9%) with upper GIT bleeding. Wilson's disease and biliary cirrhosis were responsible for the majority of cirrhosis cases, with 26 (49.1%) and 19 (35.8%) cases, respectively. One patient (1.2%) was diagnosed with chronic hepatitis B, and one (1.2%) with autoimmune hepatitis. In six (11.3%) patients, the cause of cirrhosis was unidentified, and they were considered cryptogenic. Ten patients (18.9%) died during their hospital stay, while the remaining 43 patients (81.1%) were discharged with advice.

TABLE 1. Demographic, etiological and clinical characteristics of the participants (n=53)

Variables	Number	Percentage
Sex		
Male	29	54.7%
Female	24	45.3%
SIRS		
Negative	27	50.9%
Positive	26	49.1%
Reason for admission		
Jaundice and ascites	31	58.5%
Jaundice	7	13.2%
Ascites	4	7.5%
Jaundice, ascites and encephalopathy	4	7.5%
Jaundice, ascites and upper GIT bleeding	3	5.7%
Upper GIT bleeding	1	1.9%
Jaundice and upper GIT bleeding	1	1.9%
Jaundice, ascites, encephalopathy and upper GIT bleeding	1	1.9%
Causes of cirrhosis		
Willson's disease	26	49.1%
Biliary cirrhosis	19	35.8%
Cryptogenic	6	11.3%
HBV	1	1.9%
Autoimmune	1	1.9%
Hospital outcome		
Discharge	43	81.1%
Death	10	18.9%

SIRS = systemic inflammatory response syndrome; PELD = pediatric end-stage liver disease; GIT = gastrointestinal tract; HBV = hepatitis B virus.

The outcome of patients was correlated with the presence or absence of SIRS and with the high and low PELD scores in Table 2. The difference was statistically significant ($p = 0.03$) with an odds ratio of 5.556, as 8 out of 18 SIRS-positive patients and 2 out of 25 SIRS-negative patients died, respectively. Each patient's height, weight, serum bilirubin, serum albumin, and INR values were used to calculate their PELD score. The scores ranged from 0 to 48, and the mean was 24. The odds ratio for the association between a high PELD score (mean >24) and mortality risk was estimated to be 2.294. The difference, however, was not statistically significant ($p = 0.25$).

TABLE 2. Association of SIRS and PELD with hospital outcome

		Hospital outcome		Odds ratio	95% CI	p-value*
		Discharge	Death			
		n	n			
SIRS	Absent	25	2	5.556	1.052 - 29.328	0.03
	Present	18	8			
PELD	High (> mean value)	6	17	2.294	0.563 - 9.351	0.25
	Low (<mean value)	4	26			

*Test carried out by Chi-square test with $df=1$.

SIRS had a sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of 80%, 58%, 30.3%, and 92.6%, respectively, for predicting hospital mortality. High PELD scores to predict in-hospital death were also calculated, and the sensitivity, specificity, PPV, and NPV were 60%, 60.5%, 26.1%, and 86.7%, respectively (Table 3).

TABLE 3. Sensitivity, specificity, PPV, and NPV of SIRS and PELD

Variable	Sensitivity	Specificity	PPV	NPV
SIRS	80%	58%	30.3%	92.6%
PELD	60%	60.5%	26.1%	86.7%

PPV: Positive predictive value; NPV: Negative predictive value.

The area under the receiver-operator characteristic (AUROC) curve of positive SIRS was 0.691 (95% confidence interval 0.517 - 0.865), which is statistically significant, while the AUROC curve of high PELD score was 0.602 (95% confidence interval 0.406-0.799), which was marginally significant (Figure 1).

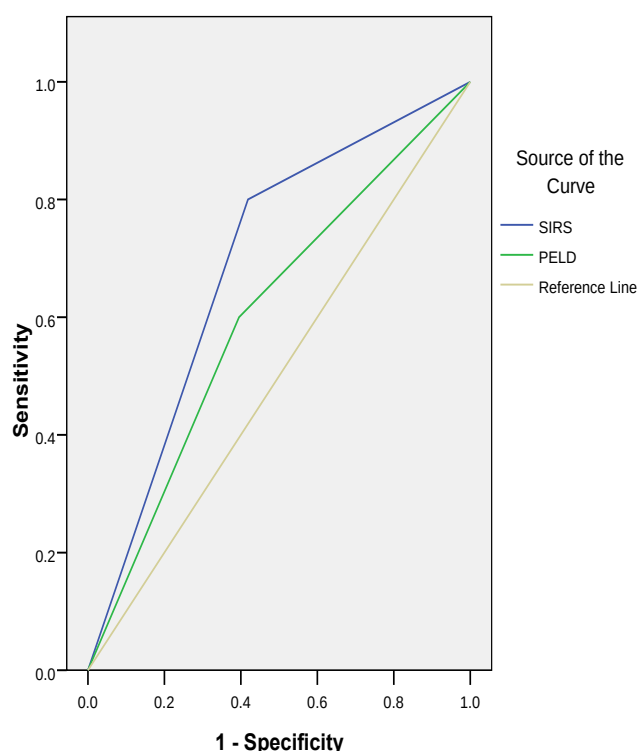


FIGURE 1. ROC curve of SIRS and PELD scores of children with liver cirrhosis

Univariate analysis of different parameters showed that a positive SIRS and a high PELD were related to death in the hospital. However, in the Multivariate Logistic Regression analysis, only positive SIRS was independently associated with increased mortality ($p < 0.05$). The mean length of hospitalization was 15 days, ranging from 3 to 56 days. For SIRS-positive patients, the mean length of hospitalization was 16.27 ± 12.56 days, while it was 13.85 ± 8.74 days for SIRS-negative patients.

Discussion

Cirrhosis of the liver is a major public health concern, and outcome prediction might assist clinicians in the treatment of cirrhotic patients, particularly children, as well as in the allocation of limited medical resources. The current most widely used clinical scoring systems in predicting outcomes are Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease (MELD), Chronic Liver Failure-Sequential Organ Failure assessment (CLIF-SOFA), Paediatric End-stage Liver Disease (PELD) in children and so on. Several studies on adults showed a negative correlation between SIRS and the outcome of liver cirrhotic patients. However, such research on the pediatric population is lacking, particularly in Bangladesh. The aim of the current study was to extrapolate the hospital outcome of children with liver cirrhosis in relation to their SIRS and PELD scores.

A total of 53 children with cirrhosis of the liver, ages ranging from 4 months to 144 months (12 years), were studied. Of them, 26 (49.1%) patients had features of SIRS. Most patients (77.4%) presented with multiple symptoms, including jaundice, ascites, encephalopathy, and upper GIT bleeding. 31 patients (58.5%) presented with both jaundice and ascites, while 12 patients (22.6%) presented with only one symptom. Bolia et al. also observed comparable presenting characteristics in children with liver cirrhosis who had several symptoms(10).

Wilson's disease and biliary cirrhosis accounted for the majority of cases, with 26 (49.1%) and 19 (35.8%) cases, respectively. Other causes included infection with the Hepatitis B virus (2%) and autoimmune hepatitis (2%). In 6 (11.3%) cases, the cause was unidentifiable and considered to be cryptogenic. Alam et al. observed a nearly identical finding in which Wilson's disease (65.5%) was the major etiology(11). Hanif et al. found that 24% of Pakistani children had chronic hepatitis B infection, 16% had autoimmune hepatitis, and 16% had Wilson's disease(12). In India, Bolia et al. reported autoimmune liver disease as the leading cause of decompensated CLD in 20% of cases, followed by Wilson's disease (17.1%)(10). The differences between the results of these studies are likely attributable to differences in geographical factors, time period, and age group of the studied population. In addition, the low HBV infection incidence in Bangladesh can be connected to the addition of the hepatitis B vaccine to the Expanded Program on Immunization (EPI) schedule since 2005.

The underlying cause of SIRS in cirrhotic patients remains unclear. However, SIRS can worsen liver function and may have a serious impact on mortality and morbidity. There are limited data regarding the association between SIRS and outcomes in pediatric liver cirrhosis. Several adult studies, however, have indicated that SIRS positivity is strongly associated with mortality and portal hypertension-related complications(5-8, 13, 14). In our analysis, eight (30.8%) of the 26 patients with positive SIRS died, compared to only two (7.4%) of the 27 patients without SIRS, and this difference was statistically significant ($p=0.03$). AUROC curve with 95% confidence interval of positive SIRS to predict in-hospital death was 0.691 (Sensitivity 80%, specificity 58%), which signifies the outcome prediction. In addition, logistic regression analysis revealed that positive SIRS was independently associated with poor outcomes.

In our study, PELD scores ranged from 0 to 48, with a mean of 24. During PELD score and hospital outcome assessment, we observed

that the higher the PELD score, the greater the chance of death, as the odds ratio was 2.294. Analysis of the ROC curve of the PELD score for death yielded an AUROC curve of 0.602 (Sensitivity 60%, specificity 60.5%), indicating that the PELD score may be a marginal predictor of the in-hospital outcome of cirrhotic children. Separate investigations by Saldana et al., Shneider et al., and Bolia et al. found that the risk of death prediction by PELD scores appeared to be significantly lower and that the quantitative translation of the score into the risk of death appeared to be invalid (10, 15, 16). Several researchers, on the other hand, have suggested that a higher PELD score correlates with a more serious condition in cirrhotic patients. Studies by McDiarmid et al., Jagadisan et al., and Mazariegos et al. reported that the PELD score was significantly validated to predict outcomes (3, 17, 18). In a low-income country like Bangladesh, parents of our moribund patients usually wish to leave the hospital before death due to huge treatment costs. So many of our patients with high PELD were categorized as in the discharged group. This may cause variation in predicting death with the PELD score.

We also compared the mean PELD score to the presence or absence of SIRS and found no significant difference ($p=0.615$) between participants with and without SIRS. There are no similar data for pediatric patients, although some studies demonstrated a substantial correlation between MELD score and positive SIRS in adult patients (5-8, 13). As MELD and PELD are derived from distinct equations, it is evident that the actual numeric score for a comparable disease severity will be different for children and adults (17).

Positive SIRS and high PELD scores are associated with higher hospital mortality among children with liver cirrhosis, as demonstrated by this cross-sectional analytic study. As with adults, detecting SIRS in pediatric patients with liver cirrhosis may be a strong predictor of prognosis. In addition, SIRS may be related to infection; therefore, it is essential to pay strict attention to immunization status and the sterile clinical environment in order to provide high-quality pediatric health care.

Limitations

The primary limitation of the study was the small sample size, as time and resources for the study were limited. In addition, this study was carried out in a specialized tertiary care hospital, which may not be representative of all Bangladeshi children with liver cirrhosis.

Conclusion

Positive SIRS and a high PELD score were found to have a positive relationship with in-hospital mortality in pediatric liver cirrhosis patients. Early identification of such patients can predict short-term mortality, and timely care can improve their prognosis. This may assist pediatricians in making decisions for additional assessment and prophylactic management to prevent life-threatening outcomes. However, prospective research with a large number of patients is necessary for a more precise prediction.

Conflict of interest: None

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References

1. Majethia, N. K., Patil, M. V., & Kalgutkar, A. D. (2016). A Histo-Pathological Study of Liver in 118 Cases of Cirrhosis. *J Liver*, 5(193), 2167-0889.
2. Arya, G., & Balistreri, W. F. (2002). Pediatric liver disease in the United States: epidemiology and impact. *Journal of gastroenterology and hepatology*, 17(5), 521-525.
3. Mazariegos, G. V., Anand, R., & McDiarmid, S. V. (2002). Validation of PELD severity score in a pediatric transplant candidate database. *Am J Transplant*, 2(3), 251.
4. Tandon, P., & Garcia-Tsao, G. (2008, February). Bacterial infections, sepsis, and multiorgan failure in cirrhosis. In *Seminars in liver disease* (Vol. 28, No. 01, pp. 026-042). © Thieme Medical Publishers..
5. Thabut, D., Massard, J., Gangloff, A., Carbonell, N., Francoz, C., Nguyen-Khac, E., ... & Moreau, R. (2007). Model for end-stage liver disease score and systemic inflammatory response are major prognostic factors in patients with cirrhosis and acute functional renal failure. *Hepatology*, 46(6), 1872-1882.
6. Behroozian, R., Bayazidchi, M., & Rasooli, J. (2012). Systemic inflammatory response syndrome and MELD score in hospital outcome of patients with liver cirrhosis. *Middle East journal of digestive diseases*, 4(3), 168.
7. Mahassadi, A. K., Nguieguia, J. L. K., Kissi, H. Y., Awuah, A. A. A., Bangoura, A. D., Doffou, S. A., & Attia, A. K. (2018). Systemic inflammatory response syndrome and model for end-stage liver disease score accurately predict the in-hospital mortality of black African patients with decompensated cirrhosis at initial hospitalization: a retrospective cohort study. *Clinical and Experimental Gastroenterology*, 143-152.
8. Abdel-Khalek, E. E., El-Fakhry, A., Helaly, M., Hamed, M., & Elbaz, O. (2011). Systemic inflammatory response syndrome in patients with liver cirrhosis. *Arab Journal of Gastroenterology*, 12(4), 173-177.
9. Goldstein, B., Giroir, B., & Randolph, A. (2005). International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics. *Pediatric critical care medicine*, 6(1), 2-8.
10. Bolia, R., Srivastava, A., Yachha, S. K., & Poddar, U. (2018). Pediatric CLIF-SOFA score is the best predictor of 28-day mortality in children with decompensated chronic liver disease. *Journal of Hepatology*, 68(3), 449-455.
11. Alam, R., Karim, A. B., Rukunuzzaman, M., Yasmin, A., Hossen, K., & Benzamin, M. (2019). Non-endoscopic predictors of esophageal varices in children with chronic liver disease and their utility in resource-constrained countries. *Indian Journal of Gastroenterology*, 38, 310-316.

12. Hanif, M., Raza, J., Qureshi, H., & Issani, Z. (2004). Etiology of chronic liver disease in children. *JPMA. The Journal of the Pakistan Medical Association*, 54(3), 119-122.
13. Cazzaniga, M., Dionigi, E., Gobbo, G., Fioretti, A., Monti, V., & Salerno, F. (2009). The systemic inflammatory response syndrome in cirrhotic patients: relationship with their in-hospital outcome. *Journal of hepatology*, 51(3), 475-482.
14. Yang, D., Xie, Y., Pan, H., Huang, Y., Dai, Y., Tong, Y., & Chen, M. (2017). Clinical characteristics and prognostic factors of liver cirrhosis patients with systemic inflammatory response syndrome. *Hepatology Research*, 47(11), 1174-1185.
15. Saldaña, R. S., Schrem, H., Barthold, M., & Kaltenborn, A. (2017). Prognostic abilities and quality assessment of models for the prediction of 90-day mortality in liver transplant waiting list patients. *PloS one*, 12(1), e0170499.
16. Shneider, B. L., Neimark, E., Frankenberg, T., Arnott, L., Suchy, F. J., & Emre, S. (2005). Critical analysis of the pediatric end-stage liver disease scoring system: a single center experience. *Liver transplantation*, 11(7), 788-795.
17. McDiarmid, S. V., Anand, R., & Lindblad, A. S. (2002). Development of a pediatric end-stage liver disease score to predict poor outcome in children awaiting liver transplantation1. *Transplantation*, 74(2), 173-181.
18. Jagadisan, B., Srivastava, A., Yachha, S. K., & Poddar, U. (2012). Acute on chronic liver disease in children from the developing world: recognition and prognosis. *Journal of pediatric gastroenterology and nutrition*, 54(1), 77-82.