Original Article

Crit Care & Shock (2013) 16:48-57

The effect of thrombocytopenia on outcome in critically ill children

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Abstract

***Objective*: Thrombocytopenia is common in pediatric intensive care unit. We aimed to investigate thrombocytopenia and risk factors associated with mortality in the pediatric intensive care unit.**

***Design*: One year hospital records were investigated retrospectively.**

***Setting*: Present study was performed in the pediatric intensive care unit in Çukurova University, Faculty of Medicine.**

***Patients and participants*: A total of 94 patients, 50 (53.2 %) boys and 44 girls (46.8%), were included in this study. The median age was 24 months with a range from 1 to 240 months. Thrombocytopenia was defined as platelet counts <150x10^9/L. PRISM II score, mechanical ventilation (MV), use of central venous (CVC) or arterial catheters (AC), presence or absence of sepsis, coagulopathy, hemorrhage and receiving of transfusion were recorded at the time of admission. White blood cell count (WBC), aspartate aminotransferase (AST), alanin aminotransferase (ALT), total protein, albumin/globulin ratio, blood urea nitrogen (BUN), serum creatinine (Cr), total bilirubin, C reactive protein (CRP), procalcitonin (PCT) and lactate were recorded.**

***Measurements and results*: The incidence of thrombocytopenia was 59.57%. MV, CVC, coagulopathy, hemorrhage and transfusion were found to be significant factors for thrombocytopenia. Leukocytosis and leucopenia were significant in thrombocytopenic patients (p=0.024). Increased ALT, AST, BUN, total bilirubin and decreased total protein levels significantly were related to thrombocytopenia. Hospital mortality rate was 37.2%. There was a significant association between mortality and the presence of MV, CVC and AC. Sepsis, coagulopathy, hemorrhage and transfusion had strong correlation with mortality. Increased ALT, AST, BUN, bilirubin, PCT, lactate and decreased total protein levels were related to the mortality.**

***Conclusions*: The present study suggested that thrombocytopenia could be related to mortality and an indicator of poor prognosis in the pediatric intensive care unit. Therefore thrombocytopenia-associated risk factors should be closely followed up by physicians in critically ill children.**

Key words: Thrombocytopenia, outcome, children, critically care patient.

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Introduction

Thrombocytopenia is one of the most common laboratory abnormalities in pediatric intensive care unit (PICU) patients. Increased (nonimmune or immune) platelet destruction, hemodilution, platelet sequestration (as in hypersplenism), or decreased platelet production account for the reason of thrombocytopenia. (1) Platelets are the first step in coagulation cascade against bleeding, therefore

thrombocytopenia may cause to hemorrhage. Its prevalence varies between 13% and 58%, depending on the clinical features of patients. Although the highest rates have been seen in septic and trauma patients, bleeding, transfusions, certain drugs included heparin and penicillin/penicillin analogues, intravascular catheters, shock, acute respiratory distress syndrome (ARDS) or disseminated intravascular coagulation (DIC) are other risk factors associated with thrombocytopenia. (2-8)

Thrombocytopenia can be associated with decreased survival in critically ill patients because thrombocytopenia likely reflects the development of a new disorder (e.g. sepsis, disseminated intravascular coagulation) or the progression of an ongoing disease (e.g. acute respiratory distress syndrome, microvascular thrombosis, and organ failure). Thrombocytopenia should be directed towards the management of the underlying condition. In addition to proper treatment for the underlying disorder, further supportive measurements are often required to correct thrombocytopenia. When ICU patients are presented with thrombocytopenia or subsequently developed it, more severe disease or more organ failures at admission can be thought. Therefore thrombocytopenia appears to be a predictor of mortality in ICU. (9)

In this article, we aimed to evaluate whether thrombocytopenia had an association with outcome in critically ill children.

Materials and Methods

One-year records, between 2009-2010, were investigated retrospectively in 94 children (50 boys and 44 girls), with critically ill children staying more than three days in intensive care unit (ICU) in Çukurova University. Parental informed consent was obtained for the study. Thrombocytopenia was defined as platelet count below $150x10^9$/L. The severity of thrombocytopenia was classified as mild, moderate, severe and very severe on the basis of below $150x10^9$/L, $100x10^9$/L, $50x10^9$/L and $20x10^9$/L, respectively. Pediatric Risk of Mortality (PRISM) II score was measured at admission to estimate the severity of illness. The data included mechanical ventilation (MV), use of central venous (CVC) or arterial catheters (AC), presence or absence of sepsis, coagulopathy, hemorrhage and receiving of transfusion were recorded at the time of admission to the PICU (**Table 1**). The laboratory data of white blood cell count (WBC), aspartate aminotransferase (AST), alanine aminotransferase (ALT), total protein, albumin/globulin ratio, blood urea nitrogen (BUN), serum creatinine (Cr), total bilirubin, C reactive protein (CRP), procalcitonin (PCT) and lactate were collected in every other day unless changing from normal limits to critical levels.

The location of the patient prior to ICU admission was recorded, with transferring from wards defined as being in the same hospital or another hospital before ICU admission. Sepsis was defined if one or more blood cultures were positive for bacteria. Patients were considered to have central lines if the femoral, internal jugular or subclavian veins were cannulated. aPTT which was 1.5 times the normal reference range for the laboratory with an associated increase in INR more than 1.5 implied coagulopathy. Hemorrhage was defined as dropping of hemoglobin level of 2 g/dL within 24 hours. Patients were grouped as survivors or nonsurvivors according to their ICU outcome.

Statistical analysis

Statistical calculations were performed by using a computer program (NCSS [Number Cruncher Statistical System], 2007 Statistical Software [Utah, USA]). Differences between groups were analyzed by the independent t test. The comparison of data was calculated by Chi-square (x^2) analysis and Fisher's exact test. A probability value of less than 0.05 was approved significant. In addition, logistic regression analysis was used to examine the independent effects of the risk factors for thrombocytopenia, which was determined to be significant by x^2 test. The risk of thrombocytopenia was determined by calculating an odds ratio with 95% confidence interval. Any independent risk factor with probability value of less than 0.05 within the regression model was considered statistically significant.

Results

A total of 94 patients, 50 (53.2%) boys and 44 girls (46.8%), were included in this study. The median age was 24 months with a range from 1 to 240 months. The median length of

the PICU stay was 8 days (range 3 to 120 days). Patients from hospital ward had higher admission than patients from emergency department and operating room. Most of patients (25.5%) had respiratory problem (**Table 1**). At least one episode of thrombocytopenia occurred in 32 (57.10%) of boys and 24 (42.90%) of girls. Platelet counts below $100x10^9$/L and $50x10^9$/L were in 15 (16%) and 7 (7.45%) patients, respectively. At the first day of admission, 24 (42.90%) of 56 patients had thrombocytopenia. The rest of patients had thrombocytopenia during PICU stay. About 57.89% of patients stayed more than 7 days had at least one episode of thrombocytopenia.

Clinical features of patients like age, gender, admission, PRISM II score, length of PICU stay, sepsis and an AC insertion showed no statistical association with the presence of thrombocytopenia. But MV and CVC were found statistically meaningful in thrombocytopenic patients. The difference was significant (p=0.002). Coagulopathy, hemorrhage and transfusion were found to be significant factors for the development of thrombocytopenia (p=0.005, p=0.002, p=0.009, respectively). The significance of mortality was high statistically in thrombocytopenic patients (p=0.002). The results of WBC, leukocytosis or leucopenia showed statistically significant difference between thrombocytopenic and non-thrombocytopenic groups (p=0.024). Increased ALT, AST, BUN, total bilirubin and decreased total protein levels were significantly related to thrombocytopenia (p=0.034, p=0.049, p=0.004, p=0.025 and p=0.015, respectively) (**Figure 1A**). Albumin/globulin ratio, creatinine, CRP, PCT and lactate levels were not associated with development of thrombocytopenia (p>0.05) (**Table 2**). Among these 12 variables, MV (OR, 9.25 [1.65-21.87]; p=0.002), WBC (OR, 4.1 [0.27-61.79]; p=0.024), ALT (OR, 3.14 [0.91-10.87]; p=0.034) and total protein (OR, 10.88 [0.83-42.48]; p= 0.015) were found to be the risk factors on logistic regression analysis in the development of thrombocytopenia (**Table 3**).

The rate of PICU mortality was 37.2%. Seven of 38 patients (18.40%) who never became thrombocytopenic died in the ICU vs. 28 of 56 patients (50%) who were thrombocytopenic. Age, gender, admission place and PICU stay were not statistically associated with mortality. PRISM II score was found high in non-survivors than that of survivors. The difference was significant (p=0.0001). There was a significant statistical association between mortality and the presence of MV, CVC and AC (p=0.0001, p=0.005 and p=0.009, respectively). Major bleeding occurred in 19 patients who survived (32.20%) and 34 patients who died (97.14%). Sepsis, coagulopathy, hemorrhage and transfusion had strong association with mortality. The distinctive difference was seen between survivors and non-survivors (p=0.0001). In the evaluation of laboratory values, the presence of increased ALT and AST was significant statistically in non-survivors group (p=0.005 and p=0.0001, respectively). The significance of total protein (<6 g/dL) and BUN (>20 mg/dL) was high statistically in non-survivors (p=0.02 and p=0.001, respectively) than that of survivors. The results of bilirubin (>1 mg/dL), PCT (>1 mg/dL) and lactate (>2 mg/dL) were evaluated statistically different in non-survivors (p=0.002, p=0.0001 and p=0.007, respectively) compare with survivors (**Figure 1B**). White blood count, albumin/globulin ratio, creatinine and CRP were not associated with PICU mortality (p>0.05) (**Table 4**).

Only 5 variables were entered in a logistic regression analysis, PRISM II score (>8) (OR, 0.23 [0.06-0.95]; p=0.0001), hemorrhage (OR, 22.17 [4.47-43.12]; p=0.0001), transfusion (OR, 10.89 [1.41-84.12]; p=0.0001), bilirubin (>1 mg/dL) (OR, 16.72 [1.56-79.35]; p=0.002 and PCT (>1 mg/dL) (OR, 11.79 [2.47-56.28]; p=0.0001) were significantly related to PICU mortality. MV, CVC, AC, sepsis and coagulopathy were not (**Table 5**).

Discussion

Pediatric intensive care patients frequently have thrombocytopenia. Thrombocytopenia was seen in 25% of critical ill children (10,11) and ranged from 22 to 35% in neonates. (12) Various adult studies ranged the prevalence of thrombocytopenia from 8.3% to 67.6% on admission to the ICU. (10-16) Our prevalence of thrombocytopenia was 59.57% in the PICU. While comparing with previous studies performed in critically ill children, our result was high. It can be explained by our sample size and different patient group. Previous adult studies notified that thrombocytopenia was associated with a prolonged ICU stay. (6,9) Vanderschueren and colleagues presented that patients with a nadir platelet count of $<150x10^9$/L had an increased ICU stay. (1) Another

study presented that patients with thrombocytopenia had longer ICU stays than those without thrombocytopenia. (17) In our study, no such an association was observed in thrombocytopenic patients stayed longer than 14 days (37.50% vs. 23.70% in patients without thrombocytopenia; p=0.134). We thought that this result needs to be validated in a larger population. High initial PRISM score was pointed a warning signal for disease severity and a predictive value of thrombocytopenia by Agrawal et al. (10) But our PRISM II scores had no significant correlation with the development of thrombocytopenia while comparing to normal platelet count. In the same way, few numbers of patients could cause to this result.

Some invasive procedures like mechanical ventilation and the using of arterial-central line were found as an independent factor for thrombocytopenia. (5) In our study this relevance was also seen. There was a strong association with using of mechanical ventilation and central venous catheter with the presence of thrombocytopenia. In addition, mechanical ventilation was found to be a significant risk factor for the development of thrombocytopenia in our investigation. Therefore ventilatory supported patients with either respiratory or other admission problems had significantly increased risk for thrombocytopenia. In literature, intravascular catheters and mechanical ventilation were emphasized to reflect the severity of disease caused to thrombocytopenia. (13) Bonfiglio et al found that placement of a pulmonary artery catheter was significantly associated with the development of thrombocytopenia. (18) Similar observations have been made with the use of intraaortic balloon pumps in cardiac patients. (19) Our study confirmed these findings in the PICU setting.

Thrombocytopenia is mostly multifactorial and several mechanisms may contribute to thrombocytopenia in the ICU patient. It has long been recognized that thrombocytopenia may be an early warning sign of sepsis. The mechanism of thrombocytopenia occurred in sepsis is not completely clear. Hemophagocytosis consisting of active phagocytosis of megakaryocytes and also platelet consumption may play an important role in patients with sepsis. (20,21) Agrawal et al found that sepsis was significantly associated with the presence of thrombocytopenia. (10) In the present study, although 69.60% of thrombocytopenic patients had sepsis, no statistically significant difference was observed for sepsis in between thrombocytopenic and non-thrombocytopenic children. This association can be explained by small patient population. Strauss et al stated that coagulopathy was associated with thrombocytopenia. (9) Coagulopathy was seen in 41 (73.20%) of thrombocytopenic patients in our study and we found a significant correlation with the development of thrombocytopenia. Thrombocytopenia is a common cause of bleeding. (1) It was shown that transfusion was the greatest risk factor associated with the development of thrombocytopenia in critically ill trauma patients. (5) The thrombocytopenic patients accounted for 69.60% had bleeding episodes and 40 (71.40%) of patients were transfused blood products. Almost all had the platelets transfusion in our study. The meaningful association was observed for patients with low platelet count in the presence of bleeding and transfusion. Coagulation disorders may contribute to bleeding even though patients are not thrombocytopenic. Bleeding was seen in 36.80% of patients who had normal platelet count. Therefore coagulopathy should be considered in assessing bleeding risk in non-thrombocytopenic patients. Abnormal biochemical tests included increased WBC, AST, ALT, total bilirubin and decreased total protein levels had strong association with patients who had thrombocytopenia than for those who did not have it in the ICU. It could be meant that these abnormal laboratory findings might reflect the severity of disease in the development of thrombocytopenia.

The prognostic value of platelet counts has been presented in the adult literatures (1,2,18), but has not been extensively investigated in the PICU population. Various studies compared mortality rates among patients with and without thrombocytopenia. Vanderschueren and colleagues recently noted that patients with a nadir platelet count of $<150x10^9$/L had a greater ICU mortality. (1) Regardless of the cause, several studies reported that thrombocytopenia was well recognized as a poor prognostic sign. (7,10,14,22-27) In the current study, thrombocytopenia was shown to be associated with an unfavorable prognosis. Mortality was higher in thrombocytopenic patients than that of non-thrombocytopenic (50% vs. 18.40%). Therefore low platelet count could be a good indicator to estimate the mortality during ICU stay.

Patients with normal platelet counts at admission who later developed thrombocytopenia and longer length of stay

had increased mortality compared with those who did not develop thrombocytopenia. (10) Another study presented that patients with thrombocytopenia had longer ICU stays and higher ICU mortality than those without thrombocytopenia. (17) Most of our patients who survived (72.9%) stayed less than 14 days in PICU. However there was no significant difference between survivors and non-survivors in terms of longer staying than 14 days. We determined that platelet counts at the time of admission and the development of thrombocytopenia during ICU stay were predictive in terms of increased mortality in our study. Various ICU studies stated that thrombocytopenia is a determinant of death in severe sepsis. (8) Sprung et al reported that the presence of thrombocytopenia was associated with mortality in patients with sepsis syndrome. (22) We found that sepsis had a distinctive difference in non-survivors than those of survivors. In addition, high PRISM II score and the presence of MV were significantly related with mortality. Also arterial and central lines were associated with an increased risk of death in the PICU. When the risk of bleeding increased in our patients with lower platelet counts, more packed red blood cells and platelet transfusions were given. Not astonishingly, the more bleeding and subsequently transfusion of blood products and then the higher mortality rates were noticed. In addition, PICU mortality was higher in patients with increased AST, ALT, BUN, total bilirubin, PCT, lactate and decreased total protein levels than those who did not have them. As it is known, abnormal biochemical tests had the predictive dominance for the severity of underlying disease in non-survivors.

The present study has some limitations. First, our study consisted of small patient group and the estimation of odds ratio signified the small study group. Second, we could not demonstrate a causative relationship between thrombocytopenia and PICU outcomes. The results need to be confirmed in a large study. And the last one, oncology patients may be both more likely to be thrombocytopenic and more likely to have poor prognosis when referred to the PICU. Malignancy cases were confusing in the assessment of thrombocytopenia and outcome. Therefore the underlying of disease in thrombocytopenic patients could be responsible for bad prognosis rather than the thrombocytopenia itself.

Conclusion

The present study supported recent suggestions that low platelet count could indicate a poor prognosis and also could be independently related to the mortality in critically ill children. Sequential platelet counts should be used an easy and practical method for the identifying of risk such as PRISM scoring system. Importantly, although no cause and effect relationship could be determined from these observations, close follow-up policies should be considered for thrombocytopenia associated risk factors. Low platelet count could be an important guide for physicians to determine the outcome in critically ill patients.

Acknowledgements

Authors would like to thank Ayse Menemencioglu and Recep Mutlu for providing and caring of study patients.

Table 1. Clinical features of patients in pediatric intensive care unit (n=94)

Parameters	Total
Gender (M:F)	1.13:1
Age, median (range), months	24 (1-240)
Admission	
Hospital ward	66 (70.2%)
Emergency Department	25 (26.6%)
Operation room	3 (3.2%)
Diagnosis	
Cardiovascular	21 (22.3%)
Respiratory	24 (25.5%)
Renal failure	7 (7.4%)
Hepatic failure	5 (5.3%)
Neurological	21 (22.3%)
Cardiopulmonary resuscitation	2 (2.1%)
Septic shock	14 (14.9%)
PICU stay, median (range), days	8 (3-120)
<7	37 (39.4%)
7-14	27 (28.7%)
>14	30 (31.9%)
PRISM score, median (range)	6 (0-92)
<8	51 (54.3%)
>8	43 (45.7%)
MV	72 (76.6%)
CVC	74 (78.7%)
AC	19 (20.2%)
Sepsis	61 (64.9%)
Coagulopathy	58 (61.7%)
Hemorrhage	53 (56.4%)
Transfusion	57 (60.6%)
Mortality	35 (37.2%)

Legend: MV=mechanical ventilation; CVC=central venous catheter; AC=arterial catheter.

Table 2. Clinical parameters related to thrombocytopenia

Parameters	Thrombocytopenic	Non-thrombocytopenic	P value
Age (month)	49.07±59.23	62.95±64.22	0.284
Male/female	32 (57.10%)/24 (42.90%)	18 (42.40%)/20 (52.60%)	0.351
Admission			0.563
Hospital ward	55 (98.20%)	36 (94.70%)	
Emergency Department	1 (1.80%)	2 (5.30%)	
PICU stay			0.134
<7 days	23 (41.10%)	14 (36.80%)	
7-14 days	12 (21.40%)	15 (39.50%)	
>14 days	21 (37.50%)	9 (23.7%0)	
PRISM score			0.315
<8	28 (50%)	23 (60.50%)	
≥8	28 (50%)	15 (39.50%)	
MV	49 (87.50%)	23 (60.50%)	0.002
CVC	50 (89.30%)	24 (63.20%)	0.002
AC	11 (19.60%)	8 (21.10%)	0.867
Sepsis	39 (69.60%)	22 (57.90%)	0.242
Coagulopathy	41 (73.20%)	17 (44.70%)	0.005
Hemorrhage	39 (69.60%)	14 (36.80%)	0.002
Transfusion	40 (71.40%)	17 (44.70%)	0.009
Mortality	28 (50%)	7 (18.40%)	0.002
WBC (/mm3)			0.024
>15000	20 (35.70%)	8 (21.10%)	
<5000	8 (14.30%)	1 (2.60%)	
ALT (>45 U/L)	23 (44.20%)	8 (22,20%)	0.034
AST (>45 U/L)	22 (42.30%)	8 (22,20%)	0.049
Total protein (<6 g/dL)	41 (82%)	19 (57.60%)	0.015
Albumin/globulin (<2)	39 (78%)	27 (77.10%)	0.926
BUN (>20 mg/dL)	20 (38.50%)	4 (10.80%)	0.004
Serum creatinine (>1 mg/dL)	9 (17.30%)	2 (5,40%)	0.093
Total bilirubin (>1 mg/dL)	9 (18.80%)	1 (2.80%)	0.025
CRP (>6 mg/dL)	5 (29.40%)	6 (31.60%)	0.888
PCT (>1 mg/dL)	27 (56.30%)	13 (40.60%)	0.171
Lactate (>2 mg/dL)	34 (60.7%)	19 (50%)	0.304

Table 3. Risk factors associated with thrombocytopenia

Parameters	OR (95% Confidence Interval)	
	Unadjusted	Adjusted
MV	4.56 (1.64-12.72)	9.25 (1.65-21.87)
CVC	4.86 (1.66-14.22)	
Coagulopathy	3.38 (1.41-8.07)	
Hemorrhage	3.93 (1.64-9.40)	
Transfusion	3,09 (1.30-7.32)	
Mortality	4.43 (1.67-11.72)	
WBC≥15000 (/mm3)	3.20 (0.34-29.92)	4.1 (0.27-61.79)
ALT (>45 U/L)	2.78 (1,06-7.23)	3.14 (0.91-10.87)
AST (>45 U/L)	2.57 (0.98-6.70)	
Total protein (<6 g/dL)	0.30 (0.11-0.81)	10.88 (0.83-42.48)
BUN (>20 mg/dL)	5.16 (1.59-16.76)	
Total bilirubin (>1 mg/dL)	8.08 (0.97-67.04)	

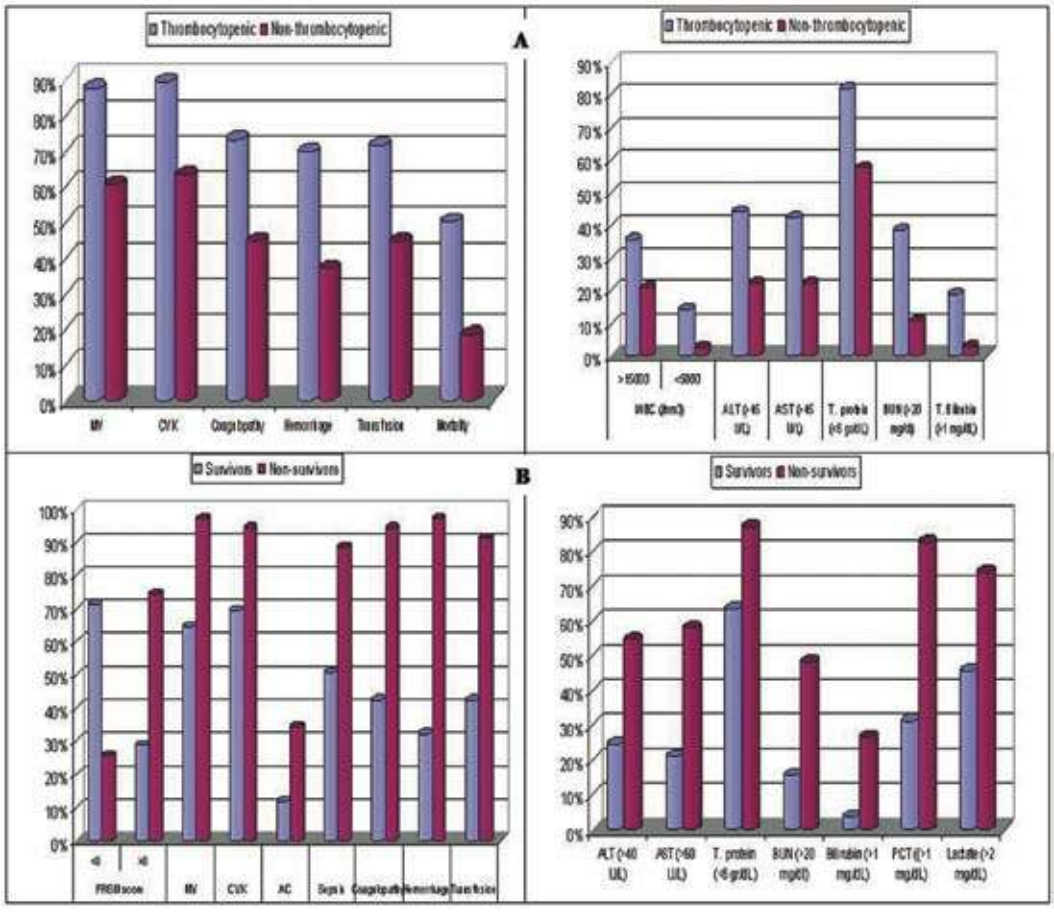
Table 4. Clinical parameters related with outcome

Parameters	Survivors	Non-survivors	P value
Age	62.95±64.22	49.07±59.23	0.284
Male/female	29 (49.20%)/30 (50.80%)	21 (60%)/14 (40%)	0.308
PRISM score			0.0001
<8	42 (71.20%)	9 (25.70%)	
>8	17 (28.80%)	26 (74.3%0)	
Admission			0.291
Hospital ward	3 (5.10%)	0 (0%)	
Emergency Department	56 (94.90%)	35 (100%)	
MV	38 (64.40%)	34 (97.10%)	0.0001
CVC	41 (69.50%)	33 (94.30%)	0.005
AC	7 (11.90%)	12 (34.30%)	0.009
Sepsis	30 (50.80%)	31 (88.60%)	0.0001
Coagulopathy	25 (42.40%)	33 (94.30%)	0.0001
Hemorrhage	19 (32,20%)	34 (97.10%)	0.0001
Transfusion	25 (42.40%)	32 (91.40%)	0.0001
PICU stay			0.431
<7 days	25 (42.40%)	12 (34.30%)	
7-14 days	18 (30.50%)	9 (25.70%)	
>14 days	16 (27.10%)	14 (40%)	
WBC (/mm3)			0.125
≥15000	17 (28.80%)	11 (31.40%)	
<5000	3 (5.10%)	6 (17.10%)	
ALT (>45 U/L)	14 (24.60%)	17 (54.80%)	0.005
AST (>45 U/L)	12 (21.10%)	18 (58.10%)	0.0001
Total protein (<6 g/dL)	33 (63.50%)	27 (87.10%)	0.02
Albumin/globulin (<2)	46 (83.70%)	20 (66.70%)	0.073
BUN (>20 mg/dL)	9 (15.50%)	15 (48.40%)	0.001
Serum creatinine (>1 mg/dL)	5 (8.60%)	6 (19.40%)	0.143
Bilirubin (>1 mg/dL)	2 (3.70%)	8 (26.70%)	0.002
CRP (>6 mg/dL)	8 (29.60%)	3 (33.30%)	0.835
PCT (>1 mg/dL)	16 (31.40%)	24 (82.80%)	0.0001
Lactate (>2 mg/dL)	27 (45.80%)	26 (74.30%)	0.007

Table 5. Risk factors for outcome

Parameters	OR (95% Confidence Interval)	
	Unadjusted	Adjusted
PRISM score>8	7.14 (2.77-18.36)	0.23 (0.06-0.95)
MV	18.79 (2.40-147.31)	
CVC	7.24 (157-33.50)	
AC	3.88 (1.35-11.12)	
Sepsis	7.49 (2.35-23.90)	
Coagulopathy	22.44 (4.92-102.42)	
Hemorrhage	71.58 (9.10-563.13)	22.17 (4.47-43.12)
Transfusion	14.51 (3.99-52.78)	10.89 (1.41-84.12)
ALT (>45 U/L)	3.73 (1.47-9.45)	
AST (>45 U/L)	5.19 (1.99-13.51)	
Total protein (<6 g/dL)	0.26 (0.08-0.85)	
BUN (>20 mg/dL)	5.10 (1.88-13.89)	
Bilirubin (>1 mg/dL)	9.45 (1.86-48.16)	16.72 (1.56-79.35)
PCT (>1 mg/dL)	10.5 (3.39-32.53)	11.79 (2.47-56.28)
Lactate (>2 mg/dL)	3.42 (1.37-8.55)	

Figure 1. Clinical and laboratory features found to be significant factors associated with the presence of thrombocytopenia (A) and PICU mortality (B)



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