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General Medicine

THROMBOCYTOPENIA AS THE IMPORTANT PROGNOSTIC MARKER OF SEPSIS

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ABSTRACT

BACKGROUND: Sepsis is currently a major concern globally. Assessing the prognosis of sepsis remains difficult even after the availability of several biomarkers. The simple platelet counts monitoring may be very useful for assessing the patients with sepsis. A significant drop in platelet count can be used as independent prognostic factor in sepsis.

AIM OF THE STUDY: (1) To compare the prognostic factors between the thrombocytopenic and non thrombocytopenic patients of sepsis. (2) To correlate the platelet count with APACHE II (Acute Physiology and Chronic Health Evaluation) scores during the ICU (intensive care unit) stay of sepsis patients.

MATERIALS AND METHODS: This is the prospective study done on 138 patients admitted to the ICU, diagnosed to have sepsis during the period September 2014 to June 2016 were included in this study. APACHE II score and platelet count monitored during ICU stay. Patients were divided in to two groups (with thrombocytopenia and without thrombocytopenia). Outcome of the patients in both the groups were compared.

RESULTS: Mortality rate of sepsis in the study was 54.3%. Mortality among thrombocytopenia group is 73.6% compared to patient without thrombocytopenia (33.3%). Patients with thrombocytopenia had higher mean APACHEII score (14.69) compared with other group (12.08). Among patients with low platelet count, drop in platelet >50% is associated with increased mortality (85%). Thrombocytopenia group had long duration of ICU stay compared to patient without thrombocytopenia.

CONCLUSION: Thrombocytopenia was shown to be indicator of poor prognosis. Progression of thrombocytopenia indicated by drop in platelet count >50% is associated with significant mortality, longer ICU stay and higher APACHE II score.

INTRODUCTION

Sepsis is a clinical syndrome defined by the presence of both infection and a systemic inflammatory response.[1] It is a major disease affecting millions of people worldwide each year with mortality of around 30 to 44%. In spite of availability of several biomarkers for assessing the prognosis of sepsis is difficult. Prognostic score variables have been shown to be effective for the assessment of septic patients, especially the sequential assessments provided by the Sequential Organ Failure Assessment (SOFA).[2] Several physiological and hematology parameters are used in daily practice in intensive care units. Simple parameter like the platelet counts may be very useful for assessing critical patients with sepsis. However, single platelet count is not as valuable as sequential platelet counts throughout the course of sepsis.[2]

Thrombocytopenia may be defined as a subnormal/decrease in number of platelets within the circulating blood. Almost all organs and systems are affected by sepsis. The hemostatic system is also adversely affected. Pathophysiology of thrombocytopenia in sepsis is platelet consumption, as the coagulation system activation is exacerbated due to release of many pro-inflammatory cytokines from mononuclear and endothelial cells leading to systemic microcirculation deposition of thrombi. These thrombi consumes large amounts of platelets and coagulation factors associated with disseminated intravascular coagulation (DIC).[3]

There is also peripheral non-immune destruction of platelets, hemophagocytic histiocytosis, and bone marrow suppression, all playing different roles in thrombocytopenia in sepsis patients.[3]

Considering the fundamental role in platelets in homeostasis and as biomarker of disseminated intravascular coagulation, a significant drop in the platelet is alarming in the setting of sepsis, as it is an independent factor for predicting the death.[2] The aim of this study is to correlate an association between platelet count and sepsis.

AIMS AND OBJECTIVES OF THE STUDY

(1) To compare the prognostic factors between the thrombocytopenic and non thrombocytopenic patients of sepsis.

(2) To correlate the platelet count with APACHE II scores during the ICU stay of sepsispatients.

MATERIAL AND METHODS

This study is a hospital based prospective observational study conducted from October 2014 to June 2016, from tertiary care hospital. The data was collected from patients admitted to ICU diagnosed with sepsis were enrolled into the study, after taking prior informed consent during the study period. APACHE II score calculated within 24 hrs of admission. Platelet counts monitored daily until patient in ICU. The history and physical examination will be done according to a standard Proforma. Other tests such as Electrocardiogram, Arterial Blood Gas, Liver Function Tests, Renal Function Tests, Prothrombin Time, activated Partial Thromboplastin Time, International Normalized Ratio, Chest X ray, complete blood counts, serum Electrolytes, blood culture, urine culture were done for all cases. Inclusion criteria all patients admitted to ICU who meets the criteria of sepsis according to International Sepsis definition conference criteria with age more than 18yrs.[1] Exclusion criteria was other known causes of thrombocytopenia associated with sepsis and patients hospitalized for less than 24 hours. Based on the previous study [1] the present study requires a minimum of 76 subjects, 38 in each group, with 90% power, 95% confidence interval and considering a difference of 35% between the two groups in the result. Descriptive statistics of mortality in both the groups analyzed and presented in terms of percentage and its 95% confidence interval estimated. Chi square test is used to compare

mortality between two groups. The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and excel have been used to generate graphs and tables. The p value is considered as significant if 0.05<P<0.10), moderately significant P value: 0.01<P <=0.05, and strongly significant P value P<=0.01.

RESULTS

A total of 138 patients of sepsis admitted in our hospital during the period October 2014 to June2016, were included in the study. The study population divided in to two group's patients with thrombocytopenia and without thrombocytopenia. Mean age of patients studied is 58 years with standard deviation of 17 years. The age group ranged from 51-80 years. Females accounted for 43.5% and male 56.5% of study population. Out of 138 patients 72 had thrombocytopenia and 66 without thrombocytopenia. No significant difference in comorbidities between two groups. The vital parameters between the two groups showed significant difference in heart rate, respiratory rate and blood pressure among two groups were noted (Table 1). There was significant elevation of bilirubin and APTT in thrombocytopenia group. However increase in lactate and creatinine was not significant as compared to patients without thrombocytopenia. The table 2 shows cause of sepsis among the two groups. Pneumonia is the most common cause of sepsis accounting for 33.3% cases , 34.8% in non-thrombocytopenic patients, 31.9% in patients with thrombocytopenia, followed by urosepsis (18.8%). Significantly high mortality was noted in thrombocytopenic group (73.6%) compared to patient without thrombo cytopenia (33.3%),as in table 3.

Among patients with low platelet count, drop in platelet of >50% is associated with increased mortality (85%) compared to patient with drop <50% (59%). The APACHE II scoring among study population showed the high mortality associated with higher scores (Table 4). There is long duration of ICU stay in thrombocytopenia patients compared to non-thrombocytopenia patients (Table 5). There is significantly high level of procalcitonin, APACHE II score, MAP in thrombocytopenic group and the same group had increased use of mechanical ventilation and inotrope use among study groups (Table 6), which was statistically significant. p=0.031.

DISCUSSION

Sepsis and septic shock are one of the leading causes of death worldwide. Even though there are several biomarkers available to assessing the prognosis of sepsis, it remains still difficult. The decrease in platelets (thrombocytopenia) is common in severely ill patients, and several studies have reported its association with poor prognosis. Considering the fundamental role of platelets in hemostasis and as markers of disseminated intravascular coagulation, a significant drop in platelet count is alarming in the setting of septic patients, as it is an independent factor predicting death. Hence, we have conducted this study to determine thrombocytopenia and its progression in predicting of prognosis in sepsis. Mortality rate of sepsis in this study was 54.3% compared to 62.5% in study by Oliveira B T et al. [2] American and European studies report 13.5% to 53.6% mortality rates.[4-7] Mortality among thrombocytopenia group is 73.6% compared to patient without thrombocytopenia (33.3%) as compared to study by Oliveira B T et al which has 76.4%.[1] Among patients with low platelet count, drop in platelet >50% is associated with increased mortality (85%) compared to patient with drop <50% (59%). Patients with thrombocytopenia has higher mean APACHEII score (14.69) compared with other group (12.08). Mean APACHEII score among patients died was 16.29 compared to patients who survived which were 10.09, similar with study by Venkata C, et al.[8] The APACHEII score>=21 is associated with significant mortality than in patients with score<21.[8] In study by Oliveira B T et al there is no significant

difference in mortality.[2] Pneumonia is the most common cause of sepsis accounting for 33.3%, followed by urosepsis (18.8%). In study by Oliveira B T et al sepsis was due to respiratory (55.4%) and abdominal (25%) foci in majority of cases[2]. Thrombocytopenia group have long duration of ICU stay compared to patient without thrombocytopenia. Significant number of patients in thrombocytopenia group required inotropic support than in patients without thrombocytopenia. No significant difference in requirement of ventilator support in two groups. Study by Venkata C, et al showed significant increase in serum creatinine and lactate levels in thrombocytopenia group.[8] In our study there is increase in creatinine and lactate levels in thrombocytopenia group but did not reach statistical significance. In our study there is significant elevation of bilirubin and APTT in thrombocytopenia group as compared to study by Venkata C, et al where there is no significant difference between two groups.[8] There is also significant high procalcitonin level among thrombocytopenia group compared to patient without thrombocytopenia.

CONCLUSION

Thrombocytopenia was shown to be an indicator of poor prognosis in sepsis. Progressive drop in platelet, indicated by drop in platelet count >50% is associated with significant mortality and also associated with longer ICU stay compared to patients without thrombocytopenia. Patients with thrombocytopenia have higher APACHEII score. Considering the results of this study, platelet counting can be used as a simple and affordable method, in assessing prognosis of sepsis patients.

Table 1

Vitals	Platelet Count		P value
	No Thrombocytopenia	Thrombocytopenia	
Heart Rate (bpm)	99.52±10.69	105.46±10.54	0.001**
RR	21.65±5.25	24.97±4.71	<0.001**
SBP (mm Hg)	108.91±16.13	98.92±15.36	<0.001**
DBP (mm Hg)	68.58±13.99	63.06±13.34	0.019*
Temp	100.41±1.11	100.52±1.19	0.564

Student t test

Table 2

Diagnosis	Platelet Count		Total
	No Thrombocytopenia	thrombocytopenia	
Pneumonia	23(34.8%)	23(31.9%)	46(33.3%)
Urosepsis	11(16.7%)	15(20.8%)	26(18.8%)
Gastro enteritis	6(9.1%)	8(11.1%)	14(10.1%)
Cellulitis	5(7.6%)	8(11.1%)	12(8.7%)
cholangitis	6(9.1%)	6(8.3%)	12(8.7%)
CNS INFECTIONS	2(3.03%)	3(4.2%)	9(6.5%)
Post surgery	6(9.09%)	4(5.6%)	7(5.1%)
No definite cause	7(10.6%)	5(6.9%)	12(8.6%)
Total	66(100%)	72(100%)	138(100%)

Table 3

Outcome	Platelet Count		Total
	No Thrombocytopenia	Thrombocytopenia	
DEATH	22(33.3%)	53(73.6%)	75(54.3%)
SURVIVED	44(66.7%)	19(26.4%)	63(45.7%)
Total	66(100%)	72(100%)	138(100%)

P<0.001**, significant, Chi-Square test

Table 4

Outcome	APACHE		Total
	<21	≥21	
Death	58(50%)	17(77.2%)	75(54.3%)
Survived	58(50%)	5(22.7%)	63(45.7%)
Total	116(100%)	22(100%)	138(100%)

P<0.001**, significant, chi-square test

Table 5

Duration of Stay	Platelet Count		Total
	No Thrombocytopenia	Thrombocytopenia	
<6	25(37.9%)	1(1.4%)	26(18.8%)
6-14	39(59.1%)	63(87.5%)	102(73.9%)
>14	2(3%)	8(11.1%)	10(7.2%)
Total	66(100%)	72(100%)	138(100%)

P<0.001**, significant, Fisher Exact test

Table 6:

variables	Platelet Count		P value
	Not Thrombocytopenia	thrombocytopenia	
Apache	12.08±5.36	14.69±6.30	0.010**
GCS	13.17±2.35	12.49±3.25	0.164
Procalcitonin	11.13±17.83	17.69±20.68	0.049*
MAP	81.80±13.70	74.82±13.33	0.003**

Student t test

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