

## Thrombocytopenia as a mortality predictor in septic patients

Anum Arshad Beg, Mirza Arshad Beg, Faisal Siddiqi, Madiha Haroon, Areeba Abdullah

### Abstract

**Objective:** To determine the association of thrombocytopenia as a predictor of mortality in septic patients.

**Material and Methods:** The study was done from November 2018 to January 2019 in all the ICU departments at Liaquat National Hospital. All patients in the ICU who had been diagnosed with sepsis at time of admission were part of the study. A daily platelet count was recorded for every patient since the time of admission until discharge or mortality occurred. Any drop of platelet count >50% compared with admission counts was also noted down.

**Results:** A sample of 168 patients were part of the study. Out of the total, 47 patients presented with sepsis and thrombocytopenia at the time of admission and discharge. Out of them, 21 patients (45%) expired. Expired patients were 14 (67%) male and 7 (33%) females with a mean age of  $60.14 \pm 13.14$  years (range 34-81 years). The mean length of hospital stay per patient was  $8.43 \pm 6.37$  days (range 1-25 days). Moreover, 9 (42.90%) of the expired patients were hypertensive and 10 (47.60%) were diabetic.

**Conclusion:** The study concludes that observing sequential platelet count in septic patients could assist health care workers in making timely intervention in high risk patients and consequently decreasing the risk of mortality associated with septic patients.

**Keywords:** Thrombocytopenia, Sepsis, Mortality

### Received

date: 6th December, 2020

### Accepted

date: 11th September, 2021

Dow University of Health Sciences, Karachi

AA Beg

Liaquat National Hospital and Medical College, Karachi

MA Beg

F Siddiqi

M Haroon

A Abdullah

### Correspondence:

Dr Mirza Arshad Beg,  
Assistant Professor,  
Deptt of Surgery, Liaquat National Hospital and Medical College, Karachi  
Cell No: +92 308-2672893  
email: doc\_mab@hotmail.com

### Introduction:

As defined by the Sepsis-3 Diagnostic Criteria, Sepsis is dys-regulated immune response leading to organ dysfunction, involving neuroendocrine, cardiovascular and metabolic systems.<sup>1</sup> Sepsis has been reported to be one of the leading cause of death in Intensive Care.<sup>2</sup> Patients with sepsis have a high risk of mortality and have therefore always been a major concern.<sup>3,4</sup> Sepsis-related mortality is linked to multiple organ failure (MOF) caused by a dys-regulated host response to infection.<sup>5</sup> This organ dysfunction is partly due to micro vascular thrombosis and endothelial dysfunction, involving thrombocytes.<sup>6</sup>

Thrombocytopenia is the most common hematologic disorder in the Intensive Care Unit (ICU)

with a prevalence of around 50%.<sup>7</sup> Considering the fundamental role of platelets in hemostasis and as markers or 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.<sup>8-10</sup> Several mechanisms contribute to sepsis associated thrombocytopenia, although the exact etiology, these include: platelet activation due to vascular injury, suppression of marrow and platelet-targeted antibodies.<sup>12-14</sup> Simply observing the platelet counts maybe very useful for assessing critical patients, especially those with sepsis. However observing one single platelet count is not as valuable as sequential platelet counts throughout the course of sepsis.<sup>7,8</sup> As reported by Venkata et al, in a retrospective study done on

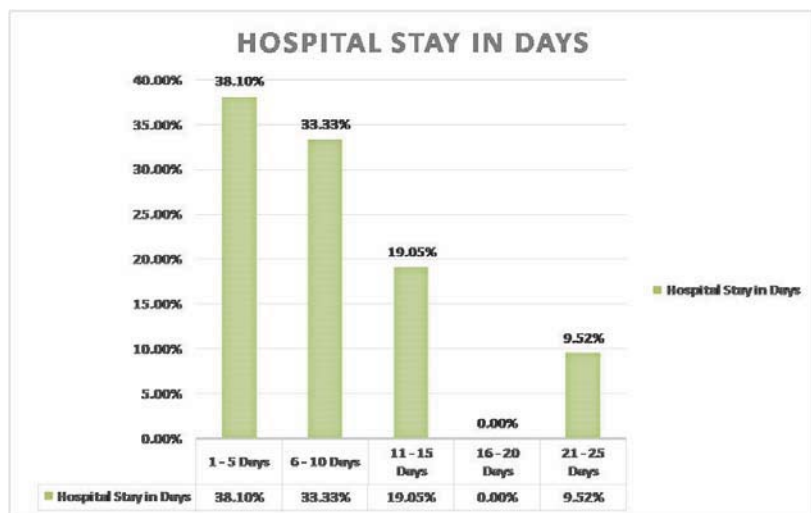


Figure 1: The length of hospital stay in days



Figure 2: Age wise distribution

ICU patients, persistence of thrombocytopenia rather than the mere presence of thrombocytopenia, lead to increased 28-day mortality.<sup>16,17</sup> Thus the aim of this study is to show an association between thrombocytopenia in relation to mortality in septic patients.

There is a dearth of literature on given subjects and most of the studies are of retrospective nature. In most of the studies, recommendation is made for a prospective study and whereby doing so will contribute towards local data as well. The various scoring systems in vogue for ICU patients are pretty comprehensive but platelets separately have not been studied as sole markers of mortality. Thus the objective of this study was to determine the association of thrombocytopenia as a predictor of mortality in septic patients.

**Material and Methods:**

The study was conducted after approval from ethical review committee. This was a single center, prospective cohort study conducted in the ICU Department of Liaquat National Hospital. The study population included all septic patients admitted in ICU department from November 2018 to January 2019.

The study included patients of either gender, above age of 13 years with hospital stay of more than 12 hours. All the septic patients were diagnosed according to the international sepsis definitions conference<sup>11</sup> criteria. These patients had sepsis either at admission or at any time during hospitalization. The study excluded any patient who was discharged or expired within first 12 hours of admission. A non-probability convenience sampling was used for data collection. All the demographics were recorded with case number, date of admission, cause of sepsis, initial platelet count, any drop of platelet count >50% compared with admission count and platelet count at time of discharge or expiry. All the relevant data was retrieved from the medical charts of the patient along with daily platelet count during hospitalization until the patient expired or was discharged.

Sample size calculation was done using WHO software for sample size. With prevalence of mortality (P) =62.5%, margin of error (d) = 8%, and a 95% confidence level, the calculated sample size was 141. For this study a larger sample size of 168 patients was taken into account.

After data collection, patient’s data was compiled and analyzed through statistical package for social sciences (SPSS) Verizon 21. Frequency and percentage were used for qualitative variables like gender, mortality, mean ± SD was calculated for quantitative variables like age, hospital stay, platelet count at admission and platelet count at time of discharge/expiry. Chi square test was applied to determine the association of age, gender, hospital stay, platelet count at admission and platelet count at time of discharge/expiry

with respect to outcome i.e. mortality.  $P < 0.05$  was considered as significant.

#### Results:

A sample consisting of 168 patients were recruited; all of whom fulfilled the inclusion criteria. From the recruits, 47 (27.98%) patients presented with sepsis and thrombocytopenia at the time of admission and discharge. Out of them, 21 patients (45%) expired when they were followed through the course of time. The expired patients were 14 (67%) male and 7(33%)female with a mean age of  $60.14 \pm 13.14$  years (range 34-81 years). The mean length of hospital stay per patient was  $8.43 \pm 6.37$  days (range 1-25 days). Moreover, 9(42.90 %) of the expired patients were hypertensive and 10(47.60%) were diabetic.

#### Discussion:

Thrombocytopenia due to sepsis is a major cause of mortality in ICU;<sup>18,19</sup> therefore, it is crucial to detect patients at high risk of death in order to improve their management.

In a study done in 2019,<sup>4</sup> it was concluded that the mortality rate was higher in people who were thrombocytopenic (57.4% expired) which was relatively close to our result with a mortality rate of 45%. The study only took people at time of discharge while our study incorporated both time intervals (i) at time of discharge and (ii) at time of discharge and admission both.

In a Brazilian study done recently, it was found that mean age was 65.2 years (49-76) which is conjunction with our results of mean of 60.14 years (34-81) and the mean was a hospital stay of 2 days while our study had a mean of 8.43 days stay. Our study incorporated the most prevalent comorbid in our part of the world which was not highlighted in other studies.<sup>10</sup> Vander-schueren et al, conducted a similar study on 329 ICU patients, where overall mortality was 19.5%, whereby 41.3% of the total patients had a platelet count  $< 150,000/L$ .<sup>20</sup>

The limitations of our study include a smaller

sample size, being a single center study, thus the results cannot be generalized to a wide population. Another limitation was that the baseline platelet level of patients before admission was unknown.

#### Conclusion:

The study concludes a significant relation between thrombocytopenia as a marker to assess the prognosis of septic patients. It also highlights the importance of observing sequential platelet count in septic patients which would assist health care workers in making timely intervention and consequently decreasing the high risk of mortality associated with septic patients.

Acknowledgement: none

Disclaimer: This article has not been presented or published elsewhere, nor is it currently under consideration for publication elsewhere. This manuscript was not part of a research, PhD or thesis project.

**Conflict of interest:** None

**Funding source:** None

#### Role and contribution of authors:

Anum Arshad Beg, Synopsis writing, data analysis

Mirza Arshad Beg, manuscript writing and result compilation

Faisal Siddiqi, Final editing of manuscript

Madiha Haroon, data Collection and Result tabulation

Areeba Abdullah, collected the data and references and helped in discussion writing

#### References:

1. Wu X, Li Y, Tong H. Research Advances in the Subtype of Sepsis-Associated Thrombocytopenia. *ClinApplThrombHemost.* 2020 Jan-Dec;26:1076029620959467.
2. Zhou Z, Feng T, Xie Y, Zhang X, Du J, Tian R, Qian B, Wang R. Prognosis and rescue therapy for sepsis-related severe thrombocytopenia in critically ill patients. *Cytokine.* 2020

- Dec;136:155227.
3. Biason L, Teixeira C, Haas JS, Cabral CDR, Friedman G. Effects of Sepsis on Morbidity and Mortality in Critically Ill Patients 2 Years after Intensive Care Unit Discharge. *Am Journal Crit Care*. 2019 Nov; 28(6):424-432.
  4. Teixeira C, Kern M, Rosa RG. What outcomes should be evaluated in critically ill patients?. *Rev Bras TerIntensiva*. 2021;33(2):312-319.
  5. Bullock B, Benham MD. Bacterial Sepsis. [Updated 2021 Jun 26]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK537054/>
  6. Bounes FV,Ruiz S,Gratacap MP,Garcia C,Bernard Payrastre B,Minville V. Platelets Are Critical Key Players in Sepsis.*Int JMol Sci*. 2019 Jul; 20(14): 3494. doi: 10.3390/ijms20143494
  7. BounesFN,GratacapMP,Groyer S,Ruiz S,Georges B, SeguinT,et al. Kinetics of mean platelet volume predicts mortality in patients with septic shock. *PLOS ONE*. 2019; 14(10): e0223553.
  8. Bernard GR, Vincent JR , Laterre PF, LaRosa SP, Dhainaut JF, Lopez-Rodriguez A, et al. Recombinant human protein C worldwide evaluation In severe sepsis (PROWESS) study group. Efficacy and safety of recombinant human activated protein C for severe sepsis. *The NewEngl JMed*. 2001;344(10):699709.
  9. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal directed therapy in treatment of severe sepsis and septic shock. *The N Engl J Med*.2001; 345(19):1368-77.
  10. Silva E, Pedro Mde A, Sogayar AC, Mohovic T, Silva CL, Janiszewski M, et al. Brazilian sepsis epidemiological study (BASES) study. *Critical Care*. 2004; 8(4):R251-60
  11. Boechat TO, Fernanda M, Silveria BB, Faviere W, Macedo GL. Thrombocytopenia in sepsis: an important prognosis factor. *Rev Bras TerIntensiva*. 2012; 24(1):35-42.
  12. Vincentt JL, Yaghusi A, Pradier O. Platelet function in sepsis. *Critical Care Med*. 2002; 30(5) S313-7.
  13. Dewitte A, Lepreux S, Villeneuve J, et al. Blood platelets and sepsis pathophysiology: A new therapeutic prospect in critically [corrected] ill patients? [published correction appears in *Ann Intensive Care*. 2018 Feb 28;8(1):32]. *Ann Intensive Care*. 2017;7(1):115. Published 2017 Dec 1. doi:10.1186/s13613-017-0337-7
  14. Angus DC, van der Poll T. Severe sepsis and septic shock. *N Engl J Med*. 2013;369(21):2063.
  15. DeutschmanCS, Tracey KJ. Sepsis: current dogma and new perspectives. *Immunity*. 2014;40(4):463–475.
  16. Venkata C, Kashyap R, Farmer JC, Afessa B. Thrombocytopenia in adult patients with sepsis: incidence, risk factors, and its association with clinical outcome. *J Intensive Care*. 2013;1(1):9.
  17. Akca S, Haji-Michael P, de Mendonca A, Suter P, Levi M, Vincent JL. Time course of platelet counts in critically ill patients. *Crit Care Med*. 2002;30:753–756
  18. Shannon O. The role of platelets in sepsis. *Res PractThromb-Haemost*. 2021;5:27–37.
  19. Moreau D, Timsit JF, Vesin A, Garrouste-Orgeas M, de Lassen-ceA, Zahar JR, et al. Platelet count decline: an early prognostic marker in critically ill patients with prolonged ICU stays. *Chest*. 2007 Jun;131(6):1735-41.
  20. Vanderschueren S, De Weerd A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, et al. Thrombocytopenia and prognosis in intensive care. *Crit Care Med*. 2000 Jun;28(6):1871-6.