ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 8, Issue – 1, January - 2025, Page No. : 26 – 34

Thrombocytopenia in Sepsis and Its Correlation with Outcome

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How to citation this article: Dr Aravind, Dr Aishwarya Gaur, Dr Rita Singh Saxena, Dr Simmi Dube, Dr. Anurag Tiwari, "Thrombocytopenia in Sepsis and Its Correlation with Outcome", IJMACR- January - 2025, Volume – 8, Issue - 1, P. No. 26 – 34.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Sepsis is a life-threatening condition that arises from a dysregulated host response to infection. Thrombocytopenia, a decrease in platelet count, is a common complication in sepsis and has been associated with increased mortality.

Methods: We conducted a prospective observational study to investigate the correlation between thrombocytopenia and sepsis outcomes. We enrolled 180 adult sepsis patients admitted to the Medical Intensive Care Unit (MICU) and monitored their platelet counts, clinical parameters, and outcomes.

Results: Thrombocytopenia was prevalent among sepsis patients, with varying severity across an 11-day observation period. Significant differences in platelet counts were found between discharged and deceased patients. Thrombocytopenia severity, duration, and reversibility were significantly associated with mortality. Day 3 platelet count and age were identified as significant predictors of mortality.

Conclusion: Our findings emphasize the importance of platelet count monitoring and trend analysis in the management of sepsis. Early identification of thrombocytopenia and its associated risk factors can aid in risk stratification and potentially lead to better outcomes for sepsis patients.

Keywords: Sepsis, Platelet, Thrombocytopenia, Outcome, Mortality

Introduction

Sepsis, a complex and life-threatening condition, arises from the body's dysregulated response to an infection[1]. The ensuing widespread inflammation and immune system activation can lead to severe complications, including organ dysfunction and even death[1,2]. Sepsis

poses a significant global health challenge, with an estimated 31.5 million cases of sepsis and 19.4 million cases of severe sepsis occurring annually, potentially resulting in 5.3 million deaths worldwide[3].

Thrombocytopenia, a hematologic disorder characterized by a low blood platelet count, is a frequent complication observed in sepsis[4]. The intricate pathophysiology of thrombocytopenia in sepsis involves a complex interplay of factors, including inflammation, coagulation abnormalities, and platelet dysfunction[5]. The inflammatory response associated with sepsis can trigger the activation and aggregation of platelets, leading to their depletion[4,5]. Additionally, sepsis can disrupt the delicate balance between coagulation and anticoagulation pathways, further contributing to platelet consumption and dysfunction[6].

The clinical implications of thrombocytopenia in sepsis are substantial. Studies have demonstrated a strong association between thrombocytopenia and increased mortality and morbidity in sepsis patients[7]. Thrombocytopenia can also increase the risk of bleeding complications, organ dysfunction, and the need for more aggressive interventions, such as blood transfusions and mechanical ventilation[7].

Despite the growing recognition of thrombocytopenia as a significant complication in sepsis, there remains a need for further research to fully elucidate the correlation between thrombocytopenia and sepsis outcomes[8]. A deeper understanding of this correlation is crucial for developing targeted strategies to prevent, monitor, and manage thrombocytopenia in sepsis, ultimately aiming to improve patient outcomes.

This study aimed to investigate the correlation between thrombocytopenia and sepsis outcomes. By examining the prevalence, severity, and temporal patterns of thrombocytopenia in a cohort of sepsis patients, we sought to gain insights into the prognostic significance of this hematologic abnormality.

Material and Methods

This was a prospective observational study conducted at the Department of Medicine, Gandhi Medical College and its associated hospital, Hamidia Hospital, Bhopal, India. The study duration was 12 months. The study included adult patients admitted to the medical Intensive Care Unit (ICU) of Hamidia Hospital with a diagnosis of sepsis, as defined by the quick Sequential Organ Failure Assessment (qSOFA) score.

A structured proforma was used to collect comprehensive data on each enrolled patient after obtaining written informed consent. The proforma included sections for:

- Demographics: age and gender.
- Clinical history: primary diagnosis and presenting complaints.
- Physical examination findings:
  - Vital signs: temperature, pulse rate, blood pressure, and oxygen saturation.
  - General examination: icterus, clubbing, cyanosis, and oedema.
  - Systemic examination: focused on the cardiovascular, respiratory, pulmonary, and central nervous systems.
- Laboratory investigations:
  - Complete blood count (CBC): to assess blood cell counts, including platelets.
  - Peripheral smear (PS) examination: for abnormal blood cell morphology.
  - Renal function tests (RFT).
  - Liver function tests (LFT): including serum bilirubin levels.

- Coagulation tests: such as prothrombin time (PT), international normalized ratio (INR), and activated partial thromboplastin time (APTT).
- D-dimer test.
- Blood culture and sensitivity testing.
- Urine culture and sensitivity testing.
- Chest X-ray.
- Ultrasound of the abdomen.

- Thrombocytopenia assessment:
- Platelet counts were monitored on days 1, 3, 5, 7, 9, and 11.
- The severity of thrombocytopenia was categorized based on the nadir platelet count as follows[7]:

- Mild: 101-149 x 103/µL
- Moderate: 51-100 x 103/µL
- Severe: 21-50 x 103/µL
- Very severe: \leq20 x 103/µL

- The duration and trend of thrombocytopenia were also recorded.

Sepsis was defined by a quick Sequential Organ Failure Assessment (qSOFA) score of 2 or more[9]. This score is calculated based on the patient's respiratory rate, systolic blood pressure, and Glasgow Coma Scale (GCS) score[10]. Thrombocytopenia was defined as a platelet count below 150,000/µL[11].

Data were securely stored and managed to maintain confidentiality. The statistical software employed in data analysis was Jamovi. Descriptive statistics summarized patient characteristics, while inferential statistics, including the Mann-Whitney U test, Chi-square test, and logistic regression analysis, were used to analyze relationships between variables and identify predictors of mortality, with statistical significance set at a p-value less than 0.05. Ethical clearance for the study was obtained from the Institutional Ethics Committee (IEC) of Gandhi Medical College, Bhopal. Written informed consent was obtained from all participants before enrolment in the study.

Results

Of the 180 sepsis patients included in the study, 104 (57.8%) were male and 76 (42.2%) were female. The mean age of the participants was 48.5 years (SD ± 18.4), ranging from 18 to 90 years. The majority of the patients fell within the 31-45 years' age group (32.8%), followed by the ≤ 30 years' group (16.7%).

Table 1: Distribution of patients according to the age and gender

Age Group in years	Gender		Total	Chi square value P value
	Male	Female		
	N (%)	N (%)	N (%)	5.430
≤30	21 (20.2)	9 (11.8)	30 (16.7)	
31-45	30 (28.8)	29 (38.2)	59 (32.8)	0.246
46-50	17 (16.3)	14 (18.4)	31 (17.2)	
51-75	30 (28.8)	16 (21.1)	46 (25.6)	
>75	6 (5.8)	8 (10.5)	14 (7.8)	
Total	104 (100.0)	76 (100.0)	180 (100.0)	

The sepsis patients exhibited a range of physiological parameters. Systolic blood pressure averaged 88.74 mm Hg, while diastolic blood pressure averaged 59.59 mm Hg. Heart rates were elevated, with a mean of 110.69 beats/min. Oxygen saturation remained relatively stable, averaging 94.66%. Blood glucose levels fluctuated, with a mean of 153.74 mg/dl. The average temperature was 99.70 degrees Fahrenheit.

Haematological and biochemical parameters also showed variation. Haemoglobin averaged 10.39 gm/dl, and total leucocyte count was elevated with a mean of 17736.67 cells/cu.mm. Renal function was assessed through serum creatinine (mean 2.59 mg/dl) and urea (mean 109.79 mg/dl). Liver function was evaluated with serum bilirubin, which averaged 1.93 mg/dl. Coagulation parameters, including prothrombin time (mean 13.78 seconds) and international normalized ratio (mean 1.57), were also measured.

Thrombocytopenia was observed in a significant proportion of patients, with the severity varying across the 11-day observation period. As shown in the table 2, on Day 1, most patients (66.1%) had mild thrombocytopenia. However, by Day 3, the majority (34.4%) had moderate thrombocytopenia, with a significant portion (37.8%) even showing normal platelet counts. This shift continues, and by Day 11, a quarter of the patients (24.4%) had severe thrombocytopenia, while over half (55.6%) had recovered to normal platelet counts.

Table 2: Distribution of Sepsis Patients by Thrombocytopenia Severity across Observation Days

Severity of Thrombocytopenia	Day 1 (%)	Day 3 (%)	Day 5 (%)	Day 7 (%)	Day 9 (%)	Day 11 (%)
Very Severe	0	0.6	1.1	0.6	1.1	1.1
Severe	5.6	1.7	5.6	13.9	17.2	24.4
Moderate	28.3	34.4	28.3	24.4	23.3	18.3
Mild	66.1	25.6	12.2	3.9	1.1	0.6
Normal Platelet Count	0	37.8	52.8	57.2	57.2	55.6
Total	100	100	100	100	100	100

The overall mortality rate in the study population was 30.6% (55 out of 180 patients).

The Mann-Whitney U test was used to compare platelet counts between patients who were discharged and those who died for each day of observation. The results revealed statistically significant differences in platelet counts between the two groups on days 3, 5, 7, 9, and 11 (all p-values < 0.05). No significant difference was found on day 1 (p-value = 0.150).

The Chi-square test was used to assess the association between thrombocytopenia severity and outcome on each day. A significant association was observed on Days 3, 5, 7, 9, and 11. (Table 3)

Table 3: Distribution of Platelet Count Categories by Day and Outcome in Sepsis Patients

Day	Platelet Count Category	Discharge (N=125)	Death (N=55)	Total (N=180)	Chi-square	p-value
Day 1	Severe	7 (5.6%)	3 (5.5%)	10 (5.6%)	1.34	0.51
	Moderate	36 (28.8%)	15 (27.3%)	51 (28.3%)		

	Mild	82 (65.6%)	37 (67.3%)	119 (66.1%)		
Day 3	Very severe	0 (0.0%)	1 (1.8%)	1 (0.6%)	11.32	0.02
	Severe	3 (2.4%)	0 (0.0%)	3 (1.7%)		
	Moderate	27 (21.6%)	35 (63.6%)	62 (34.4%)		
	Mild	37 (29.6%)	9 (16.4%)	46 (25.6%)		
	Normal	58 (46.4%)	10 (18.2%)	68 (37.8%)		
Day 5	Very severe	2 (1.6%)	0 (0.0%)	2 (1.1%)	18.21	0.00
	Severe	8 (6.4%)	2 (3.6%)	10 (5.6%)		
	Moderate	14 (11.2%)	37 (67.3%)	51 (28.3%)		
	Mild	18 (14.4%)	4 (7.3%)	22 (12.2%)		
	Normal	83 (66.4%)	12 (21.8%)	95 (52.8%)		
Day 7	Very severe	1 (0.8%)	0 (0.0%)	1 (0.6%)	15.43	0.01
	Severe	14 (11.2%)	11 (20.0%)	25 (13.9%)		
	Moderate	18 (14.4%)	26 (47.3%)	44 (24.4%)		
	Mild	5 (4.0%)	2 (3.6%)	7 (3.9%)		
	Normal	87 (69.6%)	16 (29.1%)	103 (57.2%)		
Day 9	Very severe	1 (0.8%)	1 (1.8%)	2 (1.1%)	11.89	0.02
	Severe	13 (10.4%)	18 (32.7%)	31 (17.2%)		
	Moderate	22 (17.6%)	20 (36.4%)	42 (23.3%)		
	Mild	2 (1.6%)	0 (0.0%)	2 (1.1%)		
	Normal	87 (69.6%)	16 (29.1%)	103 (57.2%)		
Day 11	Very severe	2 (1.6%)	0 (0.0%)	2 (1.1%)	23.75	0.00
	Severe	16 (12.8%)	28 (50.9%)	44 (24.4%)		
	Moderate	23 (18.4%)	10 (18.2%)	33 (18.3%)		
	Mild	1 (0.8%)	0 (0.0%)	1 (0.6%)		
	Normal	83 (66.4%)	17 (30.9%)	100 (55.6%)		

The association between thrombocytopenia duration and outcome was assessed using a cumulative score calculated based on platelet count categories at different time points. A significant association was found between thrombocytopenia duration and outcome ($\chi 2 = 20.775$, $p < 0.001$). (Table 4)

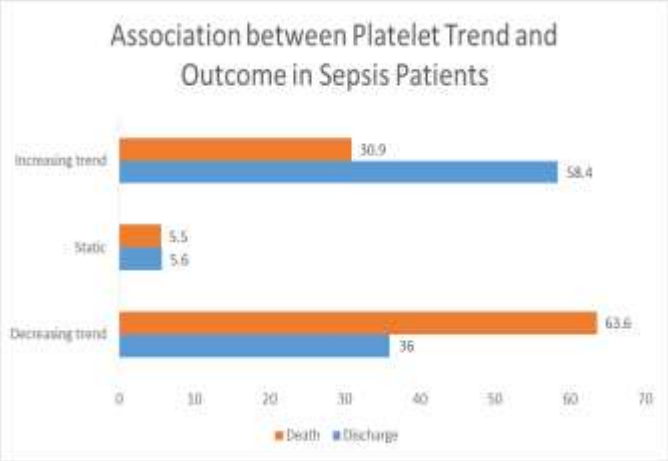
Table 4: Association between Thrombocytopenia Duration and Outcome in Sepsis Patients

Duration of thrombocytopenia	Outcome		Total	Chi square value P value
	Discharge	Death		
	N (%)	N (%)	N (%)	20.775
Short duration	50 (40.0)	8 (14.5)	58 (32.2)	

thrombocytopenia				0.000
Intermediate duration thrombocytopenia	60 (48.0)	26 (47.3)	86 (47.8)	
Long duration thrombocytopenia	15 (12.0)	21 (38.2)	36 (20.0)	
Total	125 (100.0)	55 (100.0)	180 (100.0)	

A Chi-square test was performed to examine the association between platelet trend and outcome. The results show a statistically significant relationship ($\chi 2$ = 12.338, p = 0.002). (Figure 1)

Figure 1: Association between Platelet Trend and Outcome in Sepsis Patients



Microbiological investigations revealed that Enterococcus and Acinetobacter were the most common organisms isolated from blood cultures. However, no statistically significant association was found between blood culture results and outcome ($\chi 2$ = 20.496, p = 0.001). Similarly, there was no statistically significant association between urine culture results and outcome ($\chi 2$ = 2.194, p = 0.139).

Logistic regression analyses were performed to identify predictors of mortality. The model incorporating platelet-related predictors showed that only day 3 platelet count was a statistically significant predictor of mortality (p = 0.046). In another logistic regression model, age was the only statistically significant predictor of mortality (p = 0.000). (Table 5)

Table 5: Logistic Regression Analysis of Platelet-Related Predictors of Mortality in Sepsis Patients

Variable	B	S.E.	Wald	df	Sig.	Exp(B)
Day 1 Platelet count	0.52	0.404	1.661	1	0.197	1.682
Day 3 Platelet count	-0.848	0.425	3.971	1	0.046	0.428
Day 5 Platelet count	-0.406	0.362	1.258	1	0.262	0.666
Day 7 Platelet count	0.903	0.472	3.665	1	0.056	2.468
Day 9 Platelet count	-1.117	0.571	3.821	1	0.051	0.327
Day 11 Platelet count	-0.184	0.451	0.167	1	0.683	0.832
Duration of Thrombocytopenia	-0.586	0.666	0.774	1	0.379	0.556
Trend of platelet count change	0.222	0.38	0.341	1	0.559	1.249
Constant	4.304	3.66	1.383	1	0.24	73.979

Discussion

Our study confirms the high prevalence of thrombocytopenia in sepsis and highlights its significant association with patient outcomes. We found that the severity and persistence of thrombocytopenia are crucial determinants of mortality in sepsis. Patients with moderate to severe thrombocytopenia, particularly those experiencing a decreasing trend in platelet counts over time, exhibit a higher likelihood of adverse outcomes. These results underscore the importance of close monitoring of platelet counts and trends in the management of sepsis, as advocated by Vandijck et al.[12] and Koyama et al[13].

Our findings are consistent with several previous studies on thrombocytopenia in sepsis. Sharma et al.[14] reported a 55% prevalence of thrombocytopenia in septic shock patients, which is comparable to the prevalence observed in our study. Similarly, Venkata et al.[7]found that 47.6% of their ICU patients with sepsis developed thrombocytopenia, further supporting the notion that thrombocytopenia is a frequent occurrence in this patient population. The overall trend observed in our study indicates that while thrombocytopenia is common in sepsis, its severity and persistence appear to be critical determinants of patient outcomes.

However, our study also differs from some previous research in several aspects. For instance, Tsirigotis et al.[15] reported a higher prevalence of sepsis in older populations, while our findings suggest that sepsis can affect individuals across a wide age spectrum, including younger adults. This difference could be attributed to variations in healthcare access, socioeconomic factors, and the prevalence of predisposing conditions in the local population.

The dynamic changes in platelet counts observed in our study emphasize the importance of considering the trend of platelet counts, rather than relying solely on single measurements, when assessing the prognosis of sepsis patients. This observation aligns with the findings of Venkata et al.[7], who reported that patients who did not recover from thrombocytopenia had a significantly higher mortality rate compared to those who did recover.

The clinical implications of our findings are substantial. Early recognition and close monitoring of thrombocytopenia in sepsis patients can aid in risk stratification and guide clinical decision-making. This can help clinicians identify patients at higher risk of adverse outcomes and tailor treatment strategies accordingly.

Our study has several limitations that need to be acknowledged. The single-center nature of the study limits the generalizability of the findings to other populations and healthcare settings. The moderate sample size may have limited the power to detect subtle associations and increased the risk of type II errors. Additionally, the observational design limits our ability to establish definitive causal relationships between thrombocytopenia and outcomes.

Future research should focus on prospective studies with larger sample sizes and multicentre designs to confirm our findings and further explore the complex interplay of factors contributing to thrombocytopenia in sepsis. Studies evaluating the impact of interventions, such as rhTPO as suggested by Zhou et al.[16] and Liu et al.[17], on thrombocytopenia and patient outcomes are also warranted. Furthermore, research exploring the underlying mechanisms of thrombocytopenia in sepsis, including the roles of inflammation, coagulation abnormalities, and impaired platelet production, is

crucial for developing targeted therapies. By improving our understanding of thrombocytopenia in sepsis, we can strive to improve outcomes for this vulnerable patient population.

Conclusion

This study underscored the significant association between thrombocytopenia and outcomes in sepsis patients. The severity, duration, and reversibility of low platelet counts are key predictors of patient outcomes in sepsis. A decreasing trend in platelets and prolonged thrombocytopenia were linked to increased mortality, emphasizing the importance of platelet count monitoring and trend analysis in sepsis management. By identifying thrombocytopenia early and understanding its associated risk factors, healthcare providers can make more informed decisions, potentially leading to better outcomes.

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