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# Thrombocytopenia in Septic Shock: Key Factors Linked to High Mortality

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***Abstract***

***Introduction:*** *Thrombocytopenia is a common complication among patients in intensive care units (ICUs), particularly those suffering from septic shock. It is strongly associated with poor outcomes, including increased mortality. This study aims to examine the epidemiological, clinical, biological, therapeutic, and prognostic characteristics of these patients to identify predictive factors for mortality*

***Methods:*** *We conducted a retrospective study of 148 patients with septic shock and thrombocytopenia admitted to the Surgical Emergency Intensive Care Unit at IBN ROCHD University Hospital, Casablanca, from January 1, 2020, to December 31, 2023. Patients with platelet counts below 150,000/µL were included. Data on demographics, clinical and biological parameters, treatments, and outcomes were analyzed. Multivariate logistic regression was used to identify factors associated with mortality.*

***Results:*** *Of the 199 patients with septic shock, 148 (74.4%) developed thrombocytopenia. The average age of these patients was 55 years, with a predominance of male patients (sex ratio of 1.4). Key findings included an average ICU stay of 4.9 days and septic shock onset averaging 2.8 days after admission. Fever, mucosal purpura, and cutaneous purpura were common clinical signs. Most patients exhibited anemia (82%), leukocytosis (84%), and coagulation abnormalities, including low prothrombin rate (89%) and prolonged aPTT (75%). The mortality rate was high at 89%. Multivariate analysis revealed that factors significantly associated with increased mortality included fever or mucosal purpura, anemia, low prothrombin rate, prolonged aPTT, elevated CRP levels (≥ 250 mg/L), and transfusions of red blood cells or fresh frozen plasma. Conversely, a lower CRP level and the use of heparin were associated with better outcomes.*

***Conclusion:*** *Thrombocytopenia in septic shock patients is a critical marker for identifying those at high risk of mortality. While transfusion of platelet concentrates was not associated with improved outcomes in this study, further research is needed to clarify its role. Identifying and addressing predictive factors can improve patient management and reduce mortality.*

**Keywords:** Septic Shock, Thrombocytopenia, ICU.

## Introduction

Thrombocytopenia is a frequent complication in critically ill patients admitted to intensive care units (ICUs) [1]. It affects approximately 22% to 58% of these patients, with 15% to 30% developing severe forms characterized by platelet counts below 50,000/µL [2]. As an independent marker of poor prognosis, thrombocytopenia is associated with an increased risk of bleeding, prolonged hospital stays, and higher mortality rates [3, 4].

Sepsis, a major risk factor for thrombocytopenia, often precedes the onset of infection by 12 to 48 hours [5]. During septic states, platelets play a central role in pathological processes, including

heightened activation, increased interaction with the endothelium, and a pro-coagulant state [6, 7]. These mechanisms contribute to reduced platelet counts, reflecting the severity of septic shock and its associated complications.

Numerous studies have established thrombocytopenia as a predictive factor for mortality in septic shock [3,5, 8-10]. However, few have explored other factors associated with mortality in this context. This study focuses on patients with septic shock and thrombocytopenia in a surgical emergency intensive care unit. Our primary objective is to analyze the epidemiological, clinical, biological, therapeutic, and evolutionary characteristics of these patients to identify predictive factors for mortality.

## Data Collection and Analysis

### Study Design

This is a retrospective descriptive and analytical study involving 148 patients who developed thrombocytopenia during septic shock over a three-year period (January 1, 2020, to December 31, 2023). The study was conducted in the Surgical Emergency Intensive Care Unit (Pavilion 33) at IBN ROCHD University Hospital, Casablanca, which specializes in managing critically ill patients, particularly those requiring surgical interventions.

### Patient Selection

The study included adult patients (≥18 years) diagnosed with septic shock, defined according to the need for vasopressor drugs to maintain a mean arterial pressure of ≥65 mmHg due to the absence of lactate measurements. Patients were eligible if they developed thrombocytopenia (platelet count <150,000/µL) during their ICU stay. Exclusion criteria included:

- Death or discharge within the first 24 hours.
- Pre-existing thrombocytopenia documented before ICU admission.
- Hematological disorders causing thrombocytopenia.
- Incomplete or unusable medical records.

### Data Collection

Patient data were extracted from medical records and included demographics, medical and surgical history, reasons for hospitalization, clinical and paraclinical data, qSOFA score, length of stay, time to thrombocytopenia onset, treatments received, and outcomes.

### Definitions

Key terms were defined to Ensure Consistency

- **Polypharmacy:** Daily intake of more than two medications.
- **Fever:** Body temperature above 38.5°C.
- **Hypothermia:** Body temperature below 35°C.
- **Anemia:** Hemoglobin level below 130-140 g/L (13-14 g/dL) in men and below 120-130 g/L (12-13 g/dL) in women.
- **Thrombocytopenia:** Platelet count below 150,000/µL.
- **Mild thrombocytopenia:** Platelet count between 150,000 and 100,000/µL.
- **Moderate thrombocytopenia:** Platelet count between 100,000 and 50,000/µL.
- **Severe thrombocytopenia:** Platelet count below 50,000/µL.
- **Leukocytosis**: White blood cell count above 15,000/µL.
- **Leukopenia:** White blood cell count below 4,000/µL.
- Low prothrombin time (PT): Prothrombin rate below 50%.
- **Prolonged activated partial thromboplastin time (aPTT):** Patient-to-control ratio > 1.20.
- **Hepatic cytolysis:** Transaminase levels more than three times the normal value.

### Statistical Analysis

Data were analyzed using SPSS-22 and Microsoft Excel 2016. Multivariate logistic regression was employed to identify factors associated with mortality, with a significance threshold set at $p < 0.05$. Descriptive statistics summarized demographic and clinical characteristics, while appropriate comparative tests were used to evaluate associations.

## Results

Out of a total of 199 cases of septic shock recorded during the study period, 148 patients developed thrombocytopenia, representing an incidence of 74.4%. The average age of the patients was 55 years, ranging from 25 to 90 years, with a sex ratio of 1.4.

Regarding medical history, 58.1% of the patients had no comorbidities, while 10.1% had undergone major digestive surgery, 6.08% had undergone minor digestive surgery, and 1.3% had undergone cardiac surgery. Polypharmacy was reported in 4 patients (2.7%), with the previous treatments primarily consisting of antihypertensives, antidiabetics, and anticoagulants. Additionally, 24% of our patients had at least one toxic habit, with 21% being chronic smokers and 4.7% chronic alcohol users.

The length of stay for the patients ranged from 1 to 21 days, with an average of 4.9 days. The time of onset for septic shock varied between 1 and 20 days, with an average of 2.8 days.

Digestive pathologies were the primary reason for hospitalization in our series, accounting for 52% of the cases. The general characteristics of our population are detailed in Table 1.

**Table 1: General Characteristics of the Patients**

| General Characteristics | n | % |
|---|---|---|
| Age1 | 55 (25-90) | |
| Sex | | |
| Female | 61 | 41.3% |
| Male | 87 | 58.7% |
| Medical History | | |
| Diabetes | 12 | 8.1% |
| Hypertension (HTN) | 20 | 13.5% |

| | | |
|---|---|---|
| Tumor Pathologies | 4 | 2.7% |
| Surgical History | 38 | 25.7% |
| Current Treatments | | |
| Polypharmacy | 4 | 2.7% |
| Antihypertensives | 7 | 4.7% |
| Oral Antidiabetics (OAD) | 2 | 1.3% |
| Insulin | 5 | 3.4% |
| Anticoagulants | 4 | 2.7% |
| Toxic Habits | 36 | 24% |
| Length of Stay1 | 4.9 (1-21) | |
| Indications of Admission | | |
| Digestive Pathologies | 77 | 52% |
| Polytrauma | 24 | 16% |
| Neurosurgical Pathologies | 27 | 18% |
| Skin Pathologies | 7 | 5% |
| Urological Pathologies | 6 | 4% |
| Pulmonary Pathologies | 4 | 3% |

1The numbers in parentheses indicate ranges.

Clinically, fever, mucosal purpura, and cutaneous purpura were the main clinical signs observed, with an average qSOFA score of 2 at admission. Table 2 lists the main clinical parameters found in our patients.

**Table 2: Clinical Characteristics**

| Variables | n | % |
|---|---|---|
| Fever | 121 | 82% |
| Hypothermia | 7 | 5% |
| Apyrexia (absence of fever) | 20 | 14% |
| Mucosal purpura | 38 | 26% |
| Cutaneous purpura | 44 | 30% |
| Intraoperative bleeding | 10 | 7% |
| Gastrointestinal hemorrhage | 15 | 10% |

The biological parameters of our patients were mainly marked by anemia (82%), leukocytosis (84%), and a low prothrombin rate (89%).

**Table 3: Biological Variables in the Study Sample**

| Variables | n | % |
|---|---|---|
| Anemia | 121 | 82% |
| Leukocytosis | 124 | 84% |
| Leukopenia | 5 | 3% |
| Low Prothrombin Rate (TP) | 131 | 89% |
| Extended APTT (TCA) | 90 | 61% |
| CRP < 250 mg/L | 74 | 50% |
| CRP ≥ 250 mg/L | 44 | 27% |
| Hepatic Cytolysis | 27 | 18% |

Regarding therapeutic characteristics, 43% of patients received dual antibiotic therapy, while 32% received mono-antibiotic therapy, and 21% received triple antibiotic therapy. On the other hand, only 14% of patients benefited from a platelet concentrate transfusion.

**Table 4 : Therapeutic Interventions and Treatments**

| Variables | n | % |
|---|---|---|
| Mono-Antibiotic Therapy | 48 | 32% |

| | | |
|---|---|---|
| Dual Antibiotic Therapy | 63 | 43% |
| Triple Antibiotic Therapy | 31 | 21% |
| Quadruple Antibiotic Therapy | 6 | 4% |
| Sedation | 117 | 79% |
| Proton Pump Inhibitors | 137 | 93% |
| Red Blood Cell Transfusion | 86 | 58% |
| Platelet Concentrate | 20 | 14% |
| Plasma | 37 | 25% |
| Albumin | 14 | 10% |
| Heparin | 35 | 24% |
| Vitamin K | 17 | 11% |

The mortality rate in our sample was 89%. A multivariate analysis using logistic regression was conducted to identify poor prognostic factors in patients with thrombocytopenia and septic shock in intensive care settings.

Considering the characteristics measured at admission and during the course of their hospitalization, those significantly associated with mortality in patients with thrombocytopenia and septic shock in intensive care are: the onset of fever or mucosal purpura, anemia, a low prothrombin rate, an extended APTT (Activated Partial Thromboplastin Time), a CRP level greater than or equal to 250 mg/L, and the transfusion of red blood cells or fresh frozen plasma.

On the other hand, variables associated with a good prognosis in our patients were: a CRP level lower than 250 mg/L and the use of heparin.

**Table 5: Confidence Intervals and Odds Ratios for Clinical Variables**

| Variables | P Value | Odds Ratio | Lower Bound (95%) | Upper Bound (95%) |
|---|---|---|---|---|
| Fever | ≤ 0.001 | 3.98 | 2 | 7.94 |
| Mucosal Purpura | ≤ 0.01 | 2.59 | 1.02 | 6.50 |
| Anemia | ≤ 0.001 | 3.68 | 1.84 | 7.35 |
| Low Prothrombin Rate (TP) | ≤ 0.001 | 5.39 | 2.54 | 11.44 |
| Extended APTT (TCA) | ≤ 0.05 | 1.89 | 1 | 3.59 |
| CRP ≥ 250 mg/L | ≤ 0.001 | 17.89 | 2.39 | 133.99 |
| Red Blood Cell Transfusion | ≤ 0.001 | 4.05 | 1.995 | 8.242 |
| Plasma | ≤ 0.01 | 3.07 | 1.134 | 8.295 |
| Platelet Concentrate | ≤ 0.05 | 3.83 | 0.862 | 16.992 |
| CRP < 250 mg/L | ≤ 0.001 | 0.28 | 0.131 | 0.577 |
| Heparin | ≤ 0.001 | 0.48 | 0.244 | 0.946 |

## Discussion

Thrombocytopenia is a frequent and serious complication in critically ill patients with septic shock, as observed in 74.4% of our study population. This incidence is notably higher than the 55% reported by B. Sharma et al. and the 50–65% range described in broader ICU studies [11, 12]. The discrepancy could be attributed to differences in study populations, disease severity, and definitions of thrombocytopenia. For instance, our study included patients in a surgical emergency intensive care unit, where trauma and post-surgical conditions might predispose patients to more severe thrombocytopenia.

The pathophysiology of thrombocytopenia in septic shock is multifactorial. Platelets play a crucial role not only in hemostasis but also in modulating inflammatory and immune responses [13]. During sepsis, platelet activation and consumption are exacerbated by endothelial dysfunction, disseminated intravascular coagulation (DIC), and cytokine storms, leading to rapid platelet depletion [14]. De Stoppelaar et al. highlighted that thrombocytopenia triggers the release of pro-inflammatory mediators such as TNF-α and IL-6, which amplify septic inflammation and worsen patient outcomes [15]. Consistent with these findings, we observed a significant association between severe thrombocytopenia and elevated inflammatory markers, including CRP levels ≥ 250 mg/L.

### Predictors of Mortality

Our multivariate analysis identified several key predictors of mortality, including fever, mucosal purpura, anemia, low prothrombin rate, extended APTT, elevated CRP levels, and transfusions of red blood cells or plasma. These results align with the findings of Thiery-Antier et al., who demonstrated that thrombo-

cytopenia within the first 24 hours of septic shock is a strong predictor of mortality in ICU patients [16]. Furthermore, persistent thrombocytopenia or a significant drop in platelet count during the ICU stay has been linked to increased mortality, corroborating the importance of monitoring platelet dynamics over time [17].

Interestingly, our study also identified protective factors such as CRP levels < 250 mg/L and the use of heparin. The latter finding supports previous studies suggesting that anticoagulation therapies, particularly low-dose heparin, may mitigate the risk of thrombotic complications in septic patients while preserving platelet counts [18]. However, the role of heparin in improving outcomes remains controversial, as other studies have not consistently demonstrated survival benefits [19]. Further randomized trials are needed to clarify its efficacy in this context.

**Comparison of Therapeutic Interventions**

Transfusions of red blood cells and plasma were associated with poorer outcomes in our cohort. This finding aligns with previous research indicating that transfusion-related complications, including immunomodulation and pro-inflammatory effects, may worsen septic shock outcomes [20]. Despite this, transfusions are often unavoidable in patients with severe anemia or coagulopathy, highlighting the need for stringent transfusion protocols and individualized patient assessments.

Interestingly, only 14% of our patients received platelet concentrate transfusions, and this intervention was not significantly associated with improved outcomes. Similar results have been reported in other studies, where platelet transfusions failed to reduce mortality or prevent bleeding in septic patients [21]. This may reflect the complex balance between thrombocytopenia, coagulation abnormalities, and the pro-thrombotic state seen in sepsis.

**Limitations and Future Directions**

Our study has several limitations that must be acknowledged. The retrospective design and reliance on medical records may introduce selection and information biases. The absence of advanced diagnostic tools, such as peripheral blood smears or platelet function tests, limits our ability to differentiate between true thrombocytopenia and pseudo thrombocytopenia. Additionally, variations in treatment protocols and patient severity across different ICUs may affect the generalizability of our findings.

Despite these limitations, our study provides valuable insights into the epidemiological, clinical, and therapeutic aspects of septic shock with thrombocytopenia. The high mortality rate (89%) observed in our cohort underscores the critical need for early identification and targeted management of high-risk patients. Future research should focus on validating these findings in larger, multicenter studies and exploring the potential benefits of novel therapies, such as platelet-sparing agents or personalized anticoagulation strategies.

## Conclusion

Thrombocytopenia is a common and critical complication in patients with septic shock, as demonstrated in our population, and is associated with a notably high mortality rate. The identification of predictive factors such as fever, mucosal purpura, anemia, coagulation abnormalities, and elevated CRP levels can provide valuable tools for early risk stratification. This approach enables clinicians to prioritize intensive monitoring and targeted interventions for patients at the highest risk of poor outcomes.

Although some studies suggest that platelet transfusions may improve outcomes in septic shock our findings did not confirm this association [22, 23]. This discrepancy highlights the complexity of thrombocytopenia's role in sepsis and underscores the need for further prospective studies to better understand the potential benefits and limitations of transfusion strategies in this context.

Our results emphasize the importance of integrating thrombocytopenia monitoring into routine sepsis management protocols. By recognizing the clinical and biological markers associated with increased mortality, healthcare providers can adopt more personalized approaches to treatment, potentially improving survival rates.

Future research should focus on validating these findings in larger, multicenter cohorts and exploring novel therapeutic strategies, including the role of platelet-sparing agents or anticoagulation therapies, in improving outcomes for patients with septic shock and thrombocytopenia [15, 18]. By advancing our understanding of these critical associations, we can contribute to reducing the global burden of sepsis-related mortality.

## Authors contribution

All the authors have read and agreed to the final manuscript.

- Anass ERRAGH, Safia CHAABI, and Ibtissam NABIH contributed equally to this work and are co-first authors.
- Anass ERRAGH: writing, data collection, and design; Ibtissam NABIH: writing and editing; Safia CHAABI: writing and editing; Afak NSIRI and Rachid ALHARRAR: editing and final approval.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.


## Financial Disclosure

No financial or non-financial benefits have been received or will be received from any party related directly or indirectly to the subject of this article.


## Consent for Publication

Written informed consent was obtained from all patients for publication of this study and accompanying images.

## Data Availability Declaration

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

All relevant raw data will be made available to any researcher wishing to use them for non-commercial purposes, without breaching participant confidentiality.

## References


1. Hui, P., Cook, D. J., Lim, W., Fraser, G. A., & Arnold, D. M. (2011). The frequency and clinical significance of thrombocytopenia complicating critical illness: a systematic review. Chest, 139(2), 271-278.

2. Venkata, C., Kashyap, R., Farmer, J. C., & Afessa, B. (2013). Thrombocytopenia in adult patients with sepsis: incidence, risk factors, and its association with clinical outcome. Journal of intensive care, 1, 1-10.
3. Williamson, D. R., Lesur, O., Tétrault, J. P., Nault, V., & Pilon, D. (2013). Thrombocytopenia in the critically ill: prevalence, incidence, risk factors, and clinical outcomes La thrombocytopénie chez les personnes gravement malades: prévalence, incidence, facteurs de risque et pronostics cliniques. Can J Anesth/J Can Anesth, 60, 641-651.
4. Strauss, R., Wehler, M., Mehler, K., Kreutzer, D., Koebnick, C., & Hahn, E. G. (2002). Thrombocytopenia in patients in the medical intensive care unit: bleeding prevalence, transfusion requirements, and outcome. Critical care medicine, 30(8), 1765-1771.
5. Thiery-Antier, N., Binquet, C., Vinault, S., Meziani, F., Boisramé-Helms, J., & Quenot, J. P. (2016). Is thrombocytopenia an early prognostic marker in septic shock?. Critical care medicine, 44(4), 764-772.
6. Dewitte, A., Lepreux, S., Villeneuve, J., Rigothier, C., Combe, C., Ouattara, A., & Ripoche, J. (2017). Blood platelets and sepsis pathophysiology: a new therapeutic prospect in critical ill patients? Annals of intensive care, 7, 1-18.
7. Gando, S., Levi, M., & Toh, C. H. (2016). Disseminated intravascular coagulation. Nature reviews Disease primers, 2(1), 1-16.
8. Tsirigotis, P., Chondropoulos, S., Frantzeskaki, F., Stamouli, M., Gkirkas, K., Bartzeliotou, A., ... & Dimopoulou, I. (2016). Thrombocytopenia in critically ill patients with severe sepsis/septic shock: prognostic value and association with a distinct serum cytokine profile. Journal of critical care, 32, 9-15.
9. Semeraro, N., Ammollo, C. T., Semeraro, F., & Colucci, M. (2012). Sepsis, thrombosis and organ dysfunction. Thrombosis research, 129(3), 290-295.
10. Vandijck, D. M., Blot, S. I., De Waele, J. J., Hoste, E. A., Vandewoude, K. H., & Decruyenaere, J. M. (2010). Thrombocytopenia and outcome in critically ill patients with bloodstream infection. Heart & Lung, 39(1), 21-26.
11. Sharma, B., Sharma, M., Majumder, M., Steier, W., Sangal, A., & Kalawar, M. (2007). Thrombocytopenia in septic shock patients—a prospective observational study of incidence, risk factors and correlation with clinical outcome. Anaesthesia and intensive care, 35(6), 874-880.
12. Vanderschueren, S., De Weerdt, A., Malbrain, M., Vankersschaever, D., Frans, E., Wilmer, A., & Bobbaers, H. (2000). Thrombocytopenia and prognosis in intensive care. Critical care medicine, 28(6), 1871-1876.
13. Wagner, D. D., & Burger, P. C. (2003). Platelets in inflammation and thrombosis. Arteriosclerosis, thrombosis, and vascular biology, 23(12), 2131-2137.
14. Levi, M., Toh, C. H., Thachil, J., & Watson, H. G. (2009). Guidelines for the diagnosis and management of disseminated intravascular coagulation. British journal of haematology, 145(1), 24-33.
15. Shannon, O. (2021). The role of platelets in sepsis. Research and practice in thrombosis and haemostasis, 5(1), 27-37.
16. Wang, C., Chi, C., Guo, L., Wang, X., Guo, L., Sun, J., ... & Li, E. (2014). Heparin therapy reduces 28-day mortality in adult severe sepsis patients: a systematic review and meta-analysis. Critical care, 18, 1-9.
17. Patanwala, A. E., Seaman, S. M., Kopp, B. J., & Erstad, B. L. (2018). Heparin dosing for venous thromboembolism prophylaxis in obese hospitalized patients: an observational study. Thrombosis Research, 169, 152-156.
18. Rohde, J. M., Dimcheff, D. E., Blumberg, N., Saint, S., Langa, K. M., Kuhn, L., ... & Rogers, M. A. (2014). Health care–associated infection after red blood cell transfusion: a systematic review and meta-analysis. Jama, 311(13), 1317-1326.
19. Kaufman, R. M., Djulbegovic, B., Gernsheimer, T., Kleinman, S., Tinmouth, A. T., Capocelli, K. E., ... & Tobian, A. A. (2015). Platelet transfusion: a clinical practice guideline from the AABB. Annals of internal medicine, 162(3), 205-213.
20. Semple, J. W., Italiano, J. E., & Freedman, J. (2011). Platelets and the immune continuum. Nature Reviews Immunology, 11(4), 264-274.
21. He, S., Fan, C., Ma, J., Tang, C., & Chen, Y. (2022). Platelet transfusion in patients with sepsis and thrombocytopenia: a propensity score-matched analysis using a large ICU database. Frontiers in Medicine, 9, 830177.
22. Anthon, C. T., Pène, F., Perner, A., Azoulay, E., Puxty, K., Van De Louw, A., ... & Russell, L. (2024). Platelet transfusions in adult ICU patients with thrombocytopenia: A substudy of the PLOT-ICU inception cohort study. Acta Anaesthesiologica Scandinavica.
23. Cardenas, J. C., Zhang, X., Fox, E. E., Cotton, B. A., Hess, J. R., Schreiber, M. A., ... & Holcomb, J. B. (2018). Platelet transfusions improve hemostasis and survival in a substudy of the prospective, randomized PROPPR trial. Blood advances, 2(14), 1696-1704.