Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

PLATELET INDICES AND SEPSIS

REHAB SALAH TAHA *
Anaesthesiology, Surgical Intensive Care and Pain Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt. *Corresponding Author Email: rehabsalah2017@gmail.com

MOHAMED ELSAYED AFANDY
Anaesthesiology, Surgical Intensive Care and Pain Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt.

MOHAMED SAMIR ABD EL GHAFAR
Anaesthesiology, Surgical Intensive Care and Pain Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt.

ABDELAZIZ HAMID ELBADAWI
Anaesthesiology, Surgical Intensive Care and Pain Medicine Department, Faculty of Medicine, Tanta University, Tanta, Egypt.

Abstract

Sepsis is a significant illness that affects millions of individuals throughout the globe each year. 1 In the United States (US), sepsis affects around 750,000 people a year and kills 215,000 people. The annual economic cost of this illness to the US reached 16.7 billion dollars. Sepsis affects practically all organs and systems. A negative impact is also felt on the hemostatic system. 40% of patients suffering from severe sepsis had platelet counts under 80,000/mm3, on average. The severity of the illness is correlated with decreased platelet counts. The average size of the platelets in the blood is determined by the term "mean platelet volume" (MPV). In destructive thrombocytopenia, MPV levels are high, whereas in hypo-proliferative thrombocytopenia, MPV levels are low. Platelet size variation is shown by the platelet distribution width (PDW). PDW readings typically range from 10% to 17.9%. MPV and PDW are often used in health care settings all around the globe. Sepsis has been associated with higher MPV and higher PDW levels. The impact of these variables in severe sepsis, however, has not been studied. The purpose of our investigation was to determine if there was any connection between platelet indices (PDW, and MPV) and severe sepsis.

Keywords: Platelet Indices, MPV, PDW, Sepsis

INTRODUCTION:

Sepsis is considered one of the major causes of mortality globally and treating the seriously septic patients costs the US economy $16.7 billion annually, with expenses expected to climb by 1.5% /year. Up to 535 instances of sepsis occur per 100,000 person-years, and this number is increasing [1].

According to estimates, hospitalised patients continue to have high mortality rates, which may range from 30% to 45%. Worldwide incidence cases of sepsis were projected to be 48.9 million in 2017 (95% confidence interval 38.9-62.9), and 11.0 million (10.1-12.0)

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

fatalities from sepsis-related causes were reported, accounting for 19.7% (18.2-21.4) of all mortality globally [2]. According to the definition of sepsis, it is a "life-threatening organ malfunction brought on by an inconsistent host response to infection." Multi-organ failure (MOF), shock, and even death may result from this disproportionate reaction. Based on the updated definition of sepsis. Sepsis consequences and organ failure are primarily caused by an unbalanced immune response and stimulation of the clotting cascade [3].

The Sequential Organ Failure Assessment (SOFA) score is typically used in clinical practise to categorize the intensity of organ dysfunction. Platelets play a significant role in the SOFA score's representation of haematological function, and haematological failure is frequent in septic shock patients [4]. Platelets have a key role in the development of micro-thrombosis, disseminated intravascular coagulation, and hyperinflammation, all of which lead to the failure of various organs. Acute lung damage and acute kidney injury are sepsis-related consequences that emerge as a result of inappropriate platelet aggregation and activity [5].

SEPSIS

A life-threatening disease called sepsis may develop as a consequence of an infection. Gram-positive bacteria like Staphylococcus aureus and Streptococcus pneumoniae are the most frequent causes, followed by gram-negative bacteria like Escherichia coli [6].

Sepsis is a major worldwide health issue. In 2017, the World Health Organization adopted a resolution on sepsis encouraging all of its members to take steps to raise awareness of the condition and make investments in the creation of novel diagnostic and therapeutic approaches. It has long been known that morbidity in infection is a result of both the pathogenicity of the infecting bacterium and the associated inflammatory response of the diseased host [7]. Sepsis develops when immune response networks are unable to keep the pathogen under control and fail to sustain the inflammatory response at the infection's site. Sepsis is a very complicated illness whose aetiology gradually incorporates several elements of the immunological, clotting, and tissue homeostasis systems [8]. Sepsis is described as "life-threatening organ failure induced by a dysregulated host response to infection," according to the most current clinical recommendations (Sepsis 3), and is measured using the Sequential Organ Failure Assessment (SOFA) score. Sepsis is characterised by a dysregulated host response that initially appears as a systemic inflammatory response (SIRS), then progresses to a compensatory anti-inflammatory response (CARS), and finally to immune suppression [9].

The end consequence is potentially fatal collateral organ and tissue damage, whose origin is poorly understood. Additionally, there may be overlap between the SIRs and CARS phases, which makes identification and treatment methods more difficult.

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

Nevertheless, SIRS may be treated by reducing the immunological response, but CARS needs immune stimulation to stop subsequent infections. Antibiotic treatment of invading bacteria improves sepsis outcomes, but pharmaceutical approaches to controlling the systemic inflammatory response have not yet been successful. If alternative treatment options are not made accessible, the rising incidence of antibiotic resistance among microorganisms might have severe effects [10]. The patient population affected by sepsis is very diverse and varies based on the place of infection, the kind of pathogen, underlying host variables, and individual host reactions. Unfortunately, our increasing knowledge of sepsis aetiology has not yet resulted in improved patient classification for sepsis therapy. A lot of work is being done to understand sepsis at the molecular level throughout time. The identification of discrete sepsis phenotypes and phases based on clinical and biomarker characteristics or genomic profiling, and the targeting of certain immunomodulatory treatments to these patient populations, are essential goals [11].

PLATELET INDICES

A set of metrics known as platelet indices is utilised to calculate the quantity, shape, and proliferation kinetics of PLTs [12]. It is well knowledge that PLT indices have been used to diagnose disorders of the haematological system. These indicators have been linked in recent years to the patient's prognosis as well as the severity of their illnesses. For patients in an intensive care unit who are severely ill, a decrease in PLT count represents an independent risk factor [13].

Furthermore, thrombocytopenia is included as a separate risk factor for death in the acute physiology and chronic health evaluation II (APACHE II) criteria [14].

Numerous research teams have discovered a connection between the stimulation of the coagulation cascade, systemic inflammatory response syndrome, serious infection, trauma, and thrombotic disorders and alterations in platelet indices [15]. In several inflammatory disorders, including inflammatory bowel diseases, ankylosing spondylitis, rheumatoid arthritis, ulcerative colitis, and atherosclerosis, platelet indices have been shown to have diagnostic significance [15, 16].

Laboratory markers that may be used to determine the severity of sepsis include platelet indices, which are affordable and easily available. In ICU patients across the world, MPV and PDW are now extensively and frequently used metrics to evaluate morbidity and mortality. Sepsis patients are characterised by increased MPV and PDW. However, there hasn't been much research done on the function of these laboratory indicators in severe sepsis patients [15]. Platelet function is thought to be marked and determined by MPV, the precise measurement of platelet size. Increased MPV with larger platelets results in hemostatically greater responsiveness and increased production of the prothrombotic

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

agent thromboxane A2 (TXA2). Thrombotic problems are brought on by an increase in TXA2 production [17].

Additionally, MPV values are used as indicators of the inflammatory response. According to previous research, thrombopoietin, inflammatory cytokines including IL-1, IL-6, and TNFa, and MPV represent both prothrombotic and proinflammatory circumstances, regulating thrombopoiesis. Increased MPV readings may be a sign of a number of thrombotic conditions, such as stroke, acute coronary syndrome, and venous thromboembolism, according to previous studies [18]. Since platelet consumption in the region of inflammation is expected to be enhanced, MPV may be used to identify individuals with ongoing rheumatoid arthritis, and ankylosing spondylitis, and MPV rises with treatment in these patients [19, 20].

PDW illustrates the variance in platelet size. PDW rises as the rate of platelet breakdown rises and as the size of freshly generated immature platelets varies. As a result of the additional infections and sepsis risk, platelet production rises along with its breakdown, and fresh, immature platelets enter the bloodstream. PDW and MPV are thus also impacted [21]. The only notable laboratory measure that distinguished survivors from non-survivors was PDW. PDW used an 18% threshold for calculating mortality. Patients with septic conditions whose PDW is more than 18% are more likely to die. In a research that looked at 13,701 healthy persons in the United States, it was discovered that only PDW—not platelet count or MPV—was a reliable predictor of cardiovascular and all-cause death. PDW may thus be a measure used to estimate the mortality rate for septic patients [12].

THROMBOCYTOPENIA IN SEPSIS

An estimated 20%–40% of critically sick patients have thrombocytopenia (platelet count less than 150,000/l) at some time during their ICU stay, according to study [22]. It is known that thrombocytopenia is a separate risk factor for death in ICU patients. In adult ICU patients, both the lowest platelet count and a rapid decline in platelet count indicate a bad prognosis [23].

Additional factors that increased the risk of death were persistent thrombocytopenia and a lack of a relative rise in platelet count. Numerous research looked for important risk variables that might lead to thrombocytopenia in the ICU. In various investigations, sepsis was shown to be the most prevalent risk factor [24]. Beta lactam antibiotics, vancomycin, and heparin were also mentioned to be risk factors for thrombocytopenia; however, these findings have not been consistent across different studies. Increased illness severity was also postulated to be a risk factor, as indicated by high APACHE II and SOFA scores [25].

It was considered that the sole cause of thrombocytopenia in sepsis was reduced platelet production, particularly in patients with severe sepsis, which might induce nutritional

Xi'an Shiyou Daxue Xuebao (Ziran Kexue Ban)/
Journal of Xi'an Shiyou University, Natural Sciences Edition
ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

deficits and bone marrow failure, leading to extensive pancytopenia [26]. Segre et al. discovered the opposite, proving that a septic episode may result in thrombopoiesis rather than decreasing platelet production [27].

In their study of newborn patients with sepsis, Eissa et al. discovered that while this group has a high rate of thrombopoiesis, platelet consumption is higher than creation. In order to demonstrate that the platelet creation rate was high, they employed the reticulated platelet percentage (RP%) and thrombopoietin (TPO), both of which were elevated in septic patients [28]. According to study, severe endotoxemia in sepsis raises thrombopoietic pro-inflammatory indicators such tumour necrosis factor (TNF), interleukin (IL)-1, IL-6, and IL-8, which are known to promote platelet formation. Middleton et al. investigated the natural history of sepsis and platelets and concluded that there are many alterations in the expression of translations and transcripts in platelets, the majority (64%) of which are upregulated [29].

PLATELET ACTIVATION IN HUMAN SEPSIS

Patients with sepsis have been shown to have increased platelet activation, although the sample sizes in these investigations are often quite small. Enhanced surface-bound thrombospondin and platelet-leukocyte complex formation in the ex vivo platelet population are correlated with organ failure [30].

Platelet activation has taken place in vivo if there is a reduction in platelet aggregation in consequence to ex vivo activation. Compared to patients with gram-negative sepsis, patients with gram-positive sepsis had more upregulation of P-selectin to the activated platelet surface and higher platelet-monocyte complex formation, which may indicate that different platelet morphologies are linked to different infections. It's interesting to note that a subset of sepsis patients had higher levels of TF protein production and platelet procoagulant action [31].

The platelet translatome and transcriptome were examined in sepsis in a recent elegant work. After CLP, mouse platelets also showed an upregulation of the glycoprotein (GP) IIb/IIIa gene, which codes for the integrin complex's IIb component. It is clear that platelet activation happens in cases of human sepsis, and additional research into the specific causes and effects of this activation might help in the creation of new, perhaps more sensitive platelet function indicators in cases of inflammation and sepsis [29].

CONCLUSION

The platelet indices PDW, MPV, and platelet count are particularly accurate predictors of the prognosis of sepsis. When determining a sepsis diagnosis or making a distinction

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

between mild and severe sepsis, MPV and PDW are important factors. PDW is a crucial factor in calculating the mortality rate for septic patients. Patients with sepsis should have their MPV and PDW values closely monitored during whole blood counts, which are done on practically all patients admitted to healthcare institutions. A better understanding of platelet phenotypes in sepsis patients could perhaps help in the early identification of inflammatory biomarkers of patients suffering from sepsis who could benefit from antiplatelet therapy while revealing new antiplatelet targets at the same time.

References

1. Walkey AJ, Lagu T, Lindenauer PK. Trends in sepsis and infection sources in the United States. A population-based study. Ann Am Thorac Soc. 2015; 12:216-20.

2. Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020; 395:200-11.

3. Huang M, Cai S, Su J. The Pathogenesis of Sepsis and Potential Therapeutic Targets. Int J Mol Sci. 2019; 20.

4. Zhao L, Zhao L, Wang Yy, Yang F, Chen Z, Yu Q, et al. Platelets as a prognostic marker for sepsis: A cohort study from the MIMIC-III database. Medicine. 2020; 99:e23151.

5. Greco E, Lupia E, Bosco O, Vizio B, Montrucchio G. Platelets and Multi-Organ Failure in Sepsis. Int J Mol Sci. 2017; 18.

6. Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. N Engl J Med. 2003; 348:1546-54.

7. Casadevall A, Pirofski LA. The damage-response framework of microbial pathogenesis. Nat Rev Microbiol. 2003; 1:17-24.

8. Angus DC, van der Poll T. Severe sepsis and septic shock. N Engl J Med. 2013; 369:840-51.

9. Hotchkiss RS, Monneret G, Payen D. Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy. Nat Rev Immunol. 2013; 13:862-74.

10. Assinger A, Schrottmaier WC, Salzmann M, Rayes J. Platelets in Sepsis: An Update on Experimental Models and Clinical Data. Front Immunol. 2019; 10:1687.

11. Scicluna BP, van Vught LA, Zwinderman AH, Wiewel MA, Davenport EE, Burnham KL, et al. Classification of patients with sepsis according to blood genomic endotype: a prospective cohort study. Lancet Respir Med. 2017; 5:816-26.

12. Guclu E, Durmaz Y, Karabay O. Effect of severe sepsis on platelet count and their indices. Afr Health Sci. 2013; 13:333-8.

13. Sezgi C, Taylan M, Kaya H, Selimoglu Sen H, Abakay O, Demir M, et al. Alterations in platelet count and mean platelet volume as predictors of patient outcome in the respiratory intensive care unit. Clin Respir J. 2015; 9:403-8.

14. Akavipat P TJ, Thikhamrop B, Sriraj W. . . Acute physiology and chronic health evaluation (APACHE) II score–the clinical predictor in neurosurgical intensive care unit. Acta Clin Croat. 2019; 58:50-5.

ISSN: 1673-064X
E-Publication: Online Open Access
Vol: 65 Issue 12 | 2022
DOI 10.17605/OSF.IO/FK6S9

15. Thachil J. Platelets in Inflammatory Disorders: A Pathophysiological and Clinical Perspective. Semin Thromb Hemost. 2015; 41:572-81.

16. Margetic S. Inflammation and haemostasis. Biochem Med (Zagreb). 2012; 22:49-62.

17. Shimodaira M, Niwa T, Nakajima K, Kobayashi M, Hanyu N, Nakayama T. Correlation between mean platelet volume and fasting plasma glucose levels in prediabetic and normoglycemic individuals. Cardiovasc Diabetol. 2013; 12:14.

18. Sarkar RN, Das CK, Bhattacharjee U, Banerjee M. Platelet Indices as a Marker of Severity in Non-diabetic NonHypertensive Acute Ischemic Stroke Patients. J Assoc Physicians India. 2018; 66:40-2.

19. Kim DA, Kim TY. Controversies over the interpretation of changes of mean platelet volume in rheumatoid arthritis. Platelets. 2011; 22:79-80.

20. Yazici S, Yazici M, Erer B, Erer B, Calik Y, Bulur S, et al. The platelet functions in patients with ankylosing spondylitis: anti-TNF-alpha therapy decreases the mean platelet volume and platelet mass. Platelets. 2010; 21:126-31.

21. Gao Y, Li Y, Yu X, Guo S, Ji X, Sun T, et al. The impact of various platelet indices as prognostic markers of septic shock. PLoS One. 2014; 9:e103761.

22. Drews RE, Weinberger SE. Thrombocytopenic disorders in critically ill patients. Am J Respir Crit Care Med. 2000; 162:347-51?

23. Vanderschueren S, De Weerdt A, Malbrain M, Vankersschaever D, Frans E, Wilmer A, et al. Thrombocytopenia and prognosis in intensive care. Crit Care Med. 2000; 28:1871-6.

24. Shalansky SJ, Verma AK, Levine M, Spinelli JJ, Dodek PM. Risk markers for thrombocytopenia in critically ill patients: a prospective analysis. Pharmacotherapy. 2002; 22:803-13.

25. Venkata C, Kashyap R, Farmer JC, Afessa B. Thrombocytopenia in adult patients with sepsis: incidence, risk factors, and its association with clinical outcome. Journal of Intensive Care. 2013; 1:9.

26. de Stoppelaar SF, van't Veer C, van der Poll T. The role of platelets in sepsis. Thromb Haemost. 2014; 112:666-77.

27. Segre E, Pigozzi L, Lison D, Pivetta E, Bosco O, Vizio B, et al. May thrombopoietin be a useful marker of sepsis severity assessment in patients with SIRS entering the emergency department? Clin Chem Lab Med. 2014; 52:1479-83.

28. Eissa DS, El-Farrash RA. New insights into thrombopoiesis in neonatal sepsis. Platelets. 2013; 24:122-8.

29. Middleton EA, Rowley JW, Campbell RA, Grissom CK, Brown SM, Beesley SJ, et al. Sepsis alters the transcriptional and translational landscape of human and murine platelets. Blood. 2019; 134:911-23.

30. Wang Y, Ouyang Y, Liu B, Ma X, Ding R. Platelet activation and antiplatelet therapy in sepsis: A narrative review. Thromb Res. 2018; 166:28-36.

31. Rondina MT, Schwertz H, Harris ES, Kraemer BF, Campbell RA, Mackman N, et al. The septic milieu triggers expression of spliced tissue factor mRNA in human platelets. J Thromb Haemost. 2011; 9:748-58.