

Evaluation of Platelet Count and Indices in Patients of Sepsis

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Abstract

Aim: To investigate the relationship between severe sepsis and platelet count, MPV, and PDW.

Methodology: This is a retrospective cohort study that was conducted for nine months in Darbhanga medical college and Hospital, Bihar. Patient medical records and the electronic patient data monitoring system were examined retrospectively. Patients diagnosed as sepsis, severe sepsis, and septic shock at the first medical examination were included. Control group/patients were selected from consecutive patients who were admitted to the outpatient clinic. The diagnosis of sepsis was made during the first examination. Sepsis was defined as SIRS with a proven or suspected source of infection. Demographic characteristics, such as age, gender, and the reason for hospitalization (medical or surgical) and laboratory results (whole blood count and CRP) at admission were obtained from patient files. Also, patient files were investigated for 28-day mortality. Patients who were discharged within 28 days after diagnosis of sepsis and who continued to have follow-up in the hospital at the 28th day of patient monitoring were accepted as survivors. Patients who died within the 28 days of patient monitoring were accepted as non-survivors.

Results: A total of 100 sepsis patients were included in this study. The study population consisted of 41% females and 59% males, of which 16% were surgical and 84% medical patients. Also, 100 patients (35% females and 65% males) were included as a control group. Thrombocytopenia was observed in 34% patients with sepsis and in 3% patients in the control group ($p < 0.001$). Age and gender were statistically similar between septic patients and the control group ($p > 0.05$). However, a statistically significant difference was found in MPV and PDW between patients with sepsis and the control group ($p < 0.05$). Among the 100 sepsis patients, 38% of them died within the 28-day follow-up. Thrombocytopenia was observed in 14 (36.8%) of the non-survivors and in 19 (30.6%) of the survivors. There was no statistical difference between survivors and non-survivors in terms of demographic characteristics and laboratory findings, except for PDW. PDW in non-survivors was significantly higher than in survivors ($p = 0.001$). MPV levels higher than 8 fl have 55.24 % sensitivity and 89.26% specificity for sepsis diagnosis.

Conclusion: It was concluded from this study that platelet indices may serve as an important tool to aid sepsis screening. Thrombocytopenia is an ominous sign that should be taken seriously in sepsis. Platelet indices and their ratios are readily available, sensitive, prognostic markers that can identify the severe sepsis patients with poorest outcome. So, we recommend platelet count, platelet indices and their ratios should be assessed in all sepsis patients upon admission.

Keywords: Sepsis, Platelets, Syndrome, Indices.

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Introduction

In sepsis pathophysiology: clotting cascades do not function, many pro- and anti-inflammatory cytokines are released from mononuclear and endothelial cells, thrombus occurs in later stages, and plasminogen stimulation and antithrombin-III activation take place in the fibrinolytic system. [1] As a result, fibrinolytic and fibrinogen substances are depleted, and formation of clots and bleeding associated with disseminated intravascular coagulation (DIC) occur at the same time. In the end, DIC results with increased platelet destruction. [2,3] There is also peripheral non-immune destruction, hemophagocytic histiocytosis, and marrow suppression, all playing different roles in thrombocytopenia in septic patients. Higher platelet counts are observed in females than in males. [4] Decreased platelet counts parallel the severity of infection. [5] Mean platelet volume (MPV) is a measurement of the average size of platelets found in the blood. There are high MPV levels in destructive thrombocytopenia and low MPV levels in hypoproliferative thrombocytopenia. [6]

Almost all organs and systems are affected by sepsis. The haemostatic system is also adversely affected [7]. In sepsis pathophysiology: clotting cascades do not function, many pro- and anti-inflammatory cytokines are released from mononuclear and endothelial cells, thrombus occurs in later stages, and plasminogen stimulation and antithrombin-III activation take place in the fibrinolytic system [8]. As a result, fibrinolytic and fibrinogen substances are depleted, and formation of clots and bleeding associated with disseminated intravascular coagulation (DIC) occur at the same time. In the end, DIC results with increased platelet destruction [9, 10].

The contribution of thrombocytopenia in severe sepsis has not been clearly established [7, 11]. The normal range of platelet counts in adults is 150,000 – 400,000/ μ L. Higher platelet counts are observed in females than in males [12]. Approximately 40 % of patients with severe sepsis have platelet counts less than 80,000/mm³ [11]. Decreased platelet counts parallel the severity of infection [13]. Mean platelet volume (MPV) is a measurement of the average size of platelets found in the blood. There are high MPV levels in destructive thrombocytopenia and low MPV levels in hypoproliferative thrombocytopenia [14,15]. Platelet distribution width (PDW) is an indicator of variation in platelet size. Normal values of PDW are between 10 % and 17.9 % [16].

Platelet indices are a group of parameters that are used to measure the total amount, morphology and proliferation kinetics of platelets. The commonly used platelet indices include platelet count, mean platelet volume (MPV), platelet distribution width (PDW), and Plateletcrit (PCT). Mean platelet volume is a measure of the average size of platelets. Platelet Distribution width is an indicator of volume variability in platelets size and is increased in the presence of platelet anisocytosis. Plateletcrit is the volume occupied by platelets in the blood as a percentage. [17] Originally, these indices have been applied in the diagnosis of hematological diseases. Recently, it has been discovered that these indices are related to the severity of illness and patient's prognosis. A reduction in platelet count is an independent risk factor for critically ill patients in intensive care unit. [18] In addition, Acute Physiology and

Chronic Health Evaluation II (APACHE II) System also includes thrombocytopenia as an independent risk factor for mortality. [19]

These studies have measured platelet count, mean platelet volume (MPV), and platelet distribution width (PDW). It has been shown by these studies that platelet count decreases and MPV and PDW increases in neonates with sepsis [17]. Other studies demonstrated the important role platelet play in synthesis and release of vascular endothelial growth factors that is involved in tumor angiogenesis in addition to inflammation in tumor pathogenesis [20]. In recent years, the number of studies suggesting that the platelet and their indices can be used as inflammatory markers in cancer cases in addition to cardiovascular, cerebrovascular, inflammatory and thromboembolic diseases is increasing by the time [21]. In this study, we aimed to investigate the relationship between severe sepsis and platelet count, MPV, and PDW.

Methodology

This is a retrospective cohort study that was conducted for nine months in Darbhanga medical college and Hospital, Bihar. Patient medical records and the electronic patient data monitoring system were examined retrospectively. Patients diagnosed as sepsis, severe sepsis, and septic shock at the first medical examination were included. Control group/patients were selected from consecutive patients who were admitted to the outpatient clinic. The diagnosis of sepsis was made during the first examination. Sepsis was defined as SIRS with a proven or suspected source of infection. SIRS was defined as two or more of the perturbations in Table 1 [22]. Patients who had organ dysfunction and/or hypoperfusion abnormalities were defined as severe sepsis [23]. Thrombocytopenia was defined as a platelet count lower than 150,000/mm³.

Table 1: Criteria of systemic inflammatory response syndrome and severe sepsis

Systemic inflammatory response syndrome criteria [22]	Severe sepsis criteria [23]
1. Temperature (>38° C or <36° C)	1. Arterial hypoxemia (PaO ₂ / FiO ₂ < 300)
2. Heart rate (> 90 beats/minute) least 2 hours)	2. Acute oliguria (urine output < 0.5 mL/kg/h for at
3. Respiratory rate > 20 breaths/minute or PaCO ₂ <32 mmHg	3. Creatinine (increase > 0.5 mg/dL)
4. White blood cell count > 12.000 cells/mm ³ or < 4000 cells/mm ³ or > 10 % immature band forms	4. Coagulopathy (INR > 1.5 or PTT > 60 sec)
	5. Ileus
	6. Thrombocytopenia (platelet count < 100,000 mm ³)
	7. Hyperbilirubinemia (bilirubin > 4 mg/dL)

Demographic characteristics, such as age, gender, and the reason for hospitalization (medical or surgical) and laboratory results (whole blood count and CRP) at admission were obtained from patient files. Also, patient files were investigated for 28-day mortality. Patients who were discharged within 28 days after diagnosis of sepsis

and who continued to have follow-up in the hospital at the 28th day of patient monitoring were accepted as survivors. Patients who died within the 28 days of patient monitoring were accepted as non-survivors.

Results

A total of 100 sepsis patients were included in this study. The study population consisted of 41% females and 59% males, of which 16% were surgical and 84% medical patients. Also, 100 patients (35% females and 65% males) were included as a control group. Thrombocytopenia was observed in 34%

patients with sepsis and in 3% patients in the control group ($p < 0.001$). Age and gender were statistically similar between septic patients and the control group ($p > 0.05$). However, a statistically significant difference was found in MPV and PDW between patients with sepsis and the control group ($p < 0.05$).

Table 2: Demographic characteristics and laboratory findings of patients with sepsis and control groups

Characteristics	Patients with sepsis (n=100)	Control group (n=100)	p-value
Gender (Male)	59%	65%	0.174
Age (years)	67,5 [48.0–80,0]	61.0 [50.0–78.0]	0.836
Platelet (K/uL) ⁵	225000 ± 135000	245000 ± 70000	0.183
Mean Platelet Volume (fl) ³	8.6 ± 1.8	7.0 ± 1.5	<0.001
Platelet Distribution Width (%) ⁴	18.9 [17.0–19.5]	17.1 [16.8–18.0]	<0.001

Out of 100 sepsis patients, 64% of them were diagnosed as having severe sepsis. Thrombocytopenia was observed in 42% severe sepsis patients and in 24% non-severe sepsis patients ($p = 0.01$). While a statistical difference was not found

between sepsis and severe sepsis patients in terms of demographic characteristics, CRP, leukocyte, and neutrophil count, there was a meaningful statistical difference in platelet count and their indices present.

Table 3: Demographic and laboratory findings of patients with sepsis and severe sepsis

Characteristics	Patients with sepsis (N=36)	Patients with severe sepsis (N=64)	p-value
Gender (Male)	21 (58.3%)	35 (54.7%)	0.874
Age (years)	62.6 ± 20.7	64.0 ± 19.3	0.792
C-Reactive Protein (mg/L)	153.5 [48.0–235.0]	142 [65.5–282.6]	0.883
Leukocyte (K/uL)	13700 ± 8200	14300 ± 9000	0.747
Neutrophil (K/uL)	11570 ± 7800	12300 ± 8400	0.636
Platelet (K/uL)	262000 ± 134500	205000 ± 131000	0.007
Mean Platelet Volume (fl)	7.0 [7.0–8.0]	8.0 [7.0–9.0]	0.001
Platelet Distribution Width (%)	17.2 [17.0–18.6]	17.8 [17.0–19.0]	0.028

Among the 100 sepsis patients, 38% of them died within the 28-day follow-up. Thrombocytopenia was observed in 14 (36.8%) of the non-survivors and in 19 (30.6%) of the survivors. There was no statistical difference between survivors and non-survivors in terms of demographic characteristics and laboratory findings,

except for PDW. PDW in non-survivors was significantly higher than in survivors ($p = 0.001$).

MPV levels higher than 8 fl have 55.24% sensitivity and 89.26% specificity for sepsis diagnosis. The results of ROC curve analysis are shown in table 4.

Table 4: Results of ROC analysis for various biomarkers in predicting sepsis compared to control

	Cut-off point	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive of Value	AUC	CI 95% AUC
Platelet (K/uL)	<=155	36.27	96.72	89.5	59.8	0.597	0.540–0.655
Mean Platelet Volume (fl)	>8	55.24	89.26	80.8	65.0	0.750	0.690–0.800
Platelet distribution Width (%)	>17.9	59.28	76.05	71.5	65.2	0.731	0.680–0.780

Discussion

Easily accessible, inexpensive, and widely used laboratory tests that show the severity of sepsis are important. MPV and PDW are widely and routinely used in clinical practice worldwide. Higher MPV and increased PDW have been found in sepsis [7]. However, the role of these parameters in severe sepsis have not been investigated. Mean platelet volume (MPV) is a measurement of the average size of platelets found in the blood. There are high MPV levels in destructive thrombocytopenia and low MPV levels in hypoproliferative thrombocytopenia [14, 15]. Platelet distribution width (PDW) is an indicator of variation in platelet size. Normal values of PDW are between 10 % and 17.9 % [16].

The prevalence of thrombocytopenia in sepsis is variable and different values have been reported by workers across the globe. Abdulla *et al.* in their study showed that 42.8% babies with sepsis developed thrombocytopenia [24]. In another study by Ahmad *et al.*, it was seen that mortality rate was higher among children with thrombocytopenia and its prevalence was 24.7% in sepsis [25]. This variation may be attributed to the fact that in this study we considered a cut-off of platelet counts of less than 1.5 lakhs/mm³ and other contemporary studies considered a cut-off of 1 lakhs/mm³. The sensitivity and specificity of thrombocytopenia in detecting sepsis were found to be 83.08%

and 20.33%, respectively, when compared with other studies where sensitivity was 24.7% [25]. Many other investigators have demonstrated thrombocytopenia as an important marker of sepsis which this study reinforces [24].

On comparing the platelet indices with the gold standard, the blood culture, thrombocytopenia (platelet count < 1.5 lakhs/mm³) was the most sensitive marker for sepsis, (83.08%). Previous studies have shown the sepsis screen to have variable sensitivity and specificity, because the timing of sample collection may affect its results. If sample is drawn several hours after illness or after starting antibiotics, sensitivity and specificity of sepsis screen will change. Moreover, CRP increases in other inflammatory conditions as well [26].

Our findings indicated that greater MPV levels higher than 8 fl have moderate (53.47 %) sensitivity and good (87.41%) specificity for sepsis diagnosis. Therefore, MPV may be used as an auxiliary test in the diagnosis of sepsis. A high positive predictive value of this test (81.1 %) supports this hypothesis too. Moreover, in multivariate logistic regression analysis, the independent laboratory parameters in sepsis diagnosis were MPV [OR:2,05 (1,5 – 2,7)], and PDW [OR:1,8 (1,3 – 2,5)]. Patients with severe sepsis have lower platelet count, higher MPV, and increased PDW compared to patients with sepsis. On the other hand, leukocyte count, neutrophil

count and CRP are not useful in a differential diagnosis of sepsis and severe sepsis. Therefore, platelet count and their indices can be used as a direct indicator of organ dysfunction.

The present study conducted in adults demonstrated that PDW was higher in sepsis patients, as were MPV levels. Moreover, PDW and MPV levels in severe sepsis patients were higher than in patients with sepsis. It has been demonstrated that coagulation and platelet activation/hyper aggregation can occur in an early phase of sepsis [7]. In order to obtain a larger surface, platelets change their discoid shape to a spherical shape during activation. At the same time, pseudopodia formation occurs. Platelets with increased number and size of pseudopodia may affect the PDW [27]. Platelet volume is related to platelet function and activation as well. Generally, platelet production increases as platelet count decreases. An increased number of young platelets is also functionally more active than older platelets [28]. The low level of thrombocytopenia in patients with severe sepsis can explain the high levels of MPV and PDW. [29,30]

Conclusion:

It was concluded from this study that platelet indices may serve as an important tool to aid sepsis screening. Thrombocytopenia is an ominous sign that should be taken seriously in sepsis. Platelet indices and their ratios are readily available, sensitive, prognostic markers that can identify the severe sepsis patients with poorest outcome. So, we recommend platelet count, platelet indices and their ratios should be assessed in all sepsis patients upon admission.

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