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Variation of Platelet Indices in Sepsis

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Abstract

Introduction: Almost every organ can be affected in the case of sepsis. In fact, the hemostatic system has also been known to be adversely affected in case of sepsis. Platelet indices are cheap and readily accessible, laboratory parameters that can be used to assess the severity of sepsis.

Aims and objectives- This study was aimed at comparing the parameters of platelet indices in patients with fever and sepsis leading to multiorgan dysfunction.

Materials and methods: This was a hospital-based cross-sectional study conducted in our pathology department in patients admitted with sepsis in the medicine in-patient department over 1 year. Inclusion criteria were patients with sepsis. Two ml of blood was withdrawn from the antecubital vein of the cases and samples were collected in an EDTA vial, which was kept at room temperature on day 1 and day 7 of admission. The complete hemogram reports were analyzed. The collected data was recorded on a prestructured proforma.

Results: This study included 100 serially recruited patients having sepsis. The mean age of cases was 48.3 ± 16.3 years. While 63% of cases were male, 37% were females. The rise of PDW from day 1 to day 7 was statistically insignificant (p value= 0.24). However, the plateletcrit (PCT) fell significantly from day 1 to day 7 (p value=0.02). In our study, there were 76% survivors and 24% non-survivors. Platelet volume (MPV) rose significantly (p value=0.01), and TC fell significantly (p value<0.0001). Similarly, the platelet count also fell significantly (p value<0.05).

Conclusion: Platelet indices, especially MPV, PDW, and platelet count are reliable indicators of sepsis prognosis.

Introduction

Sepsis is one of the major health problems in debilitated patients which can affect more than a million people every year. It has been estimated that up 7,50,000 cases of sepsis per year are encountered nationwide, with a mortality rate of 85% in severe sepsis.[1] Almost every organ can be affected in the case of sepsis. In fact, the hemostatic system has also been known to be adversely affected in case of sepsis.[2]

The pathophysiological cascade experiences a major hit in sepsis, including derangement of the clotting cascade, and an upregulation of both pro-inflammatory and anti-inflammatory cytokines. These cytokines are released from mononuclear and endothelial cells, with the development of

thrombi in later stages. There is also stimulation of plasminogen and antithrombin.[2,3]

Resultantly, the fibrinolytic and profibrogenic pathways are exhausted with the activation of disseminated intravascular coagulation (DIC). Fulminant DIC results in platelet destruction, non-immune mediated destruction, development of hemophagocytic histiocytosis, along with bone marrow suppression, contributing to an unstable hemogram.[4-6] Up to 40 % of cases of severe sepsis have low platelet count.[6] Low platelet count also contributes to severe disease.[7]

Platelet indices are cheap and readily accessible, laboratory parameters that can be used to assess the severity of sepsis. Mean platelet volume (MPV) and platelet distribution width (PDW) have become widely and regularly utilized parameters globally in ICU patients to assess morbidity and mortality. Raised MPV and PDW are observed in sepsis cases.[2] Although, the role of such lab parameters in severe cases of sepsis is still not widely investigated.[8]

This study was aimed at comparing the parameters of platelet indices in patients with fever and sepsis leading to multiorgan dysfunction. We also determined the significance of platelet indices (PI) in assessing the severity of inflammation. Additionally, the role of PI as a prognostic/diagnostic marker, either individually or in combination was also assessed.

Materials and Methods

This was a hospital-based cross-sectional study conducted in our pathology department in patients admitted with sepsis in the medicine in-patient department over 1 year. Inclusion criteria were patients with sepsis. Pregnant females, cases of hematological malignancies, and renal transplant cases were excluded. The sample size was 100 samples of sepsis patients which were received by our pathology department. The following parameters were recorded: hemoglobin, red cell indices and red cell count, total and differential leukocyte counts, and platelet count.

A detailed history and demographic data were collected for all the patients who fulfilled the inclusion and exclusion criteria. Blood sample was collected after taking due aseptic precautions: 2ml of blood was withdrawn from the antecubital vein of the cases and samples were collected in an EDTA vial, which was kept at room temperature on day 1 and day 7 of admission. The complete hemogram reports were analyzed. The collected data was recorded on a prestructured proforma.

Statistical Analysis

Continuous data were summarized in the form of mean and standard deviation. Categorical data were expressed in form of proportions. test. Mean differences were analyzed using paired and unpaired t tests. The level of significance was kept at 95% for all statistical analyses, p-value <0.05 was taken as significant.

Results

This study included 100 serially recruited patients having sepsis after obtaining due ethical approval from the institute and informed consent from the patient/immediate caregiver. The age distribution of our cases ranged between 21 to 90 years. The mean age of cases was 48.3 ± 16.3 years. The most commonly affected age group was between 31-40 years with 22% cases, followed by 41-50 years with 21% cases (figure 1). While 63% of cases were male, 37% were females. The mean platelet volume on day 1 was 14.679±2.439 fL, while that on day 7 was 15.2±3.710 fL (p value=0.01). The rise of PDW from day 1 to day 7 was statistically insignificant (p value= 0.24). Similarly, the platelet-large cell ratio (P-LCR) P-LCR rose insignificantly from 33.702±9.026 on day 1 to 34.0355±9.311 on day 7 (p value=0.79). However, the plateletcrit (PCT) fell significantly from day 1 (0.143±0.07%) to day 7 (0.12±0.07%) (p value=0.02) (table 1). In our study, there were 76% survivors and 24%

non-survivors (figure 2). There was a significant fall in TLC (total leukocyte count) from day 1 to day 7 (p value<0.0001). Similarly, the platelet count also fell from day 1 to day 7 across all age groups. There were age wise variations in lab parameters (table 2).

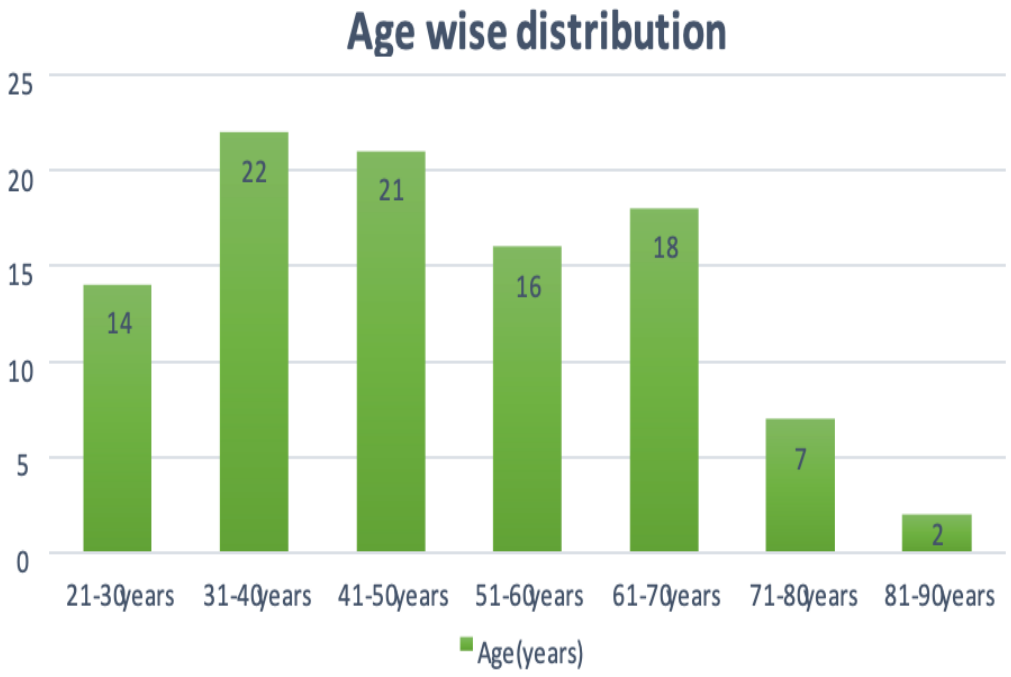

Figure 1: age wise distribution of cases

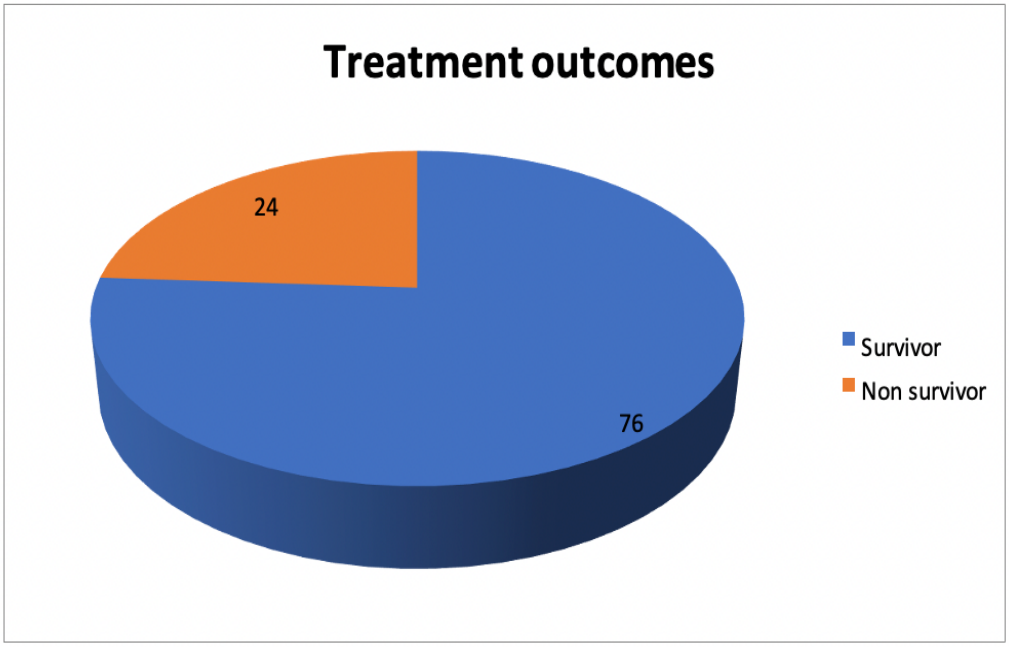

Figure 2: survivors versus non-survivors

Table 1: Kinetics of hematological parameters on day 1 and day 7

Blood Parameter	Mean± Standard deviation		P value	T value
	Day 1	Day 7		
Total Count (per microL)	17719±8056(100)	10342±3043(100)	<0.0001	8.566
Platelet count (per microL)	181946±142999(100)	147590±99522(100)	0.0500	1.972
MPV (fL)	11.196±1.330(100)	12.047±3.128(100)	0.0131	2.504
PDW (%)	14.679±2.439(100)	15.2±3.710(100)	0.2420	1.174
P-LCR	33.702±9.026(100)	34.0355±9.311(100)	0.7973	0.2572
PCT (%)	0.143±0.07518(100)	0.1199±0.07178(100)	0.0274	2.222

Table 2: variation in platelet kinetics according to age

Age group	Mean platelet count (per microL)		MPV		Mean P-LCR		Mean PDW		Mean PCT	
	Day 1	Day7	Day 1	Day7	Day 1	Day7	Day 1	Day7	Day 1	Day 7
21-30 years	185571.43	166214.29	10.43	12.86	35.42	30.29	13.5	12.86	0.143	0.143
31-40 years	140181.82	102636.36	11.27	17.36	35.3	38.82	15	17.36	0.136	0.091
41-50 years	189857.14	164428.57	11.23	14.38	30.92	28.05	14.95	14.38	0.143	0.143
51-60 years	150162.5	120750	11.69	16.94	34.75	38.19	15.56	16.94	0.125	0.063
61-70 years	251722.22	205555.56	11.22	14.28	34.31	33	14.72	14.28	0.11	0.11
71-80 years	184285.714	108000	10.57	14.71	30.73	37.86	13.14	14.71	0.143	0.143
81-90 years	151000	166500	13.5	13	29.9	33.5	13.5	13	0.175	0.17

Table 3: Comparative analysis of our work with previously conducted studies

Study	Mean PDW	Mean PLCR	Mean PCT	Mean PLV	Mean PLT
Current (7^{th} day)	15.2	34.0	0.11	12.0	147(10^3/ml)
Yanxia's study (survivor group)	11.7	26.8	0.18	10.3	164(10^3/ml)
Sayed's study (survivor group)	14.9	-	0.22	7.9	265(10^3/ml)
Guclu's study (cases)	18.2	-	-	8.4	201 (10^3/ml)
Choudhary's study(cases)	20.62	-	-	11.82	107 (10^3/ml)

Discussion

In this study, 100 patients of sepsis were recruited to assess the role of platelet indices as prognostic markers of disease severity. In our study, the most encountered age group was between 31 to 40 years, with the mean age being 48.32±16.3 years. Similar observations were made by Guclu et al.,[8] Yanxia Gao et al.[9] and Gracelene Wegrzyn et al.[10] In their study Guclu et al.[8] reported the mean of patients to be 69 years. In the study conducted by Yanxia Gao et al.[9], they included 124 sepsis patients, with the mean age being 61 years. Similarly, in Gracelene Wegrzyn et al's study, the mean age was 57.1±18.6 years.[10]

However, while both Yanxia et al.[9] and Gracelene et al.[10] have reported a female preponderance, in our study a majority of cases were males (63% males and 37% females). Similar to our work in Guclu et al.'s[9] study as well a majority of cases were males (57.9%). This gender variation could be attributed to the fact that both our study and Guclu's study included predominantly younger populations.

In our study, the mean total leukocyte count, mean platelet count, PCT, PDW, and P-LCR were compared in sepsis patients on day 1 and day 7. There were 76% survivors and 24% non-survivors in the current study. Similarly, there were 88 survivors and 15 nonsurvivors out of 103 patients in Gracelene's73 study. However, in Yanxia et al.'s[9] study, only 29% of patients had survived the episode of sepsis. In fact, even in Samira Sayed et al.[11] study, there were 19 survivors and 41 non-survivors.

In their study, Yanxia et al.[9] compared the various platelet parameters between survivors and non-survivors. They observed that MPV was significantly higher in non-survivors than survivors. Additionally, they also found that PDW and PLCR rose in non-survivors while PLT decreased in non-survivors. A similar observation was also made in our study. In Samira Sayed et al.'s[11] study as well, the PLT and PCT were significantly higher in survivors compared to nonsurvivors.

However, in the current study, we did an age-wise comparison of sepsis patients. As compared to other studies, in our study the mean platelet count and PCT were significantly lower. However, in Choudhary et al's[12] study, the platelet count was even lower than in our study. The mean PLV and PDW of our patients were comparable with other similar studies.

In our study, the total platelet count decreased from day 1 to day 7 across all age groups. While the mean platelet distribution width also

increased from day 1 to day 7 in our study in patients between 31-40 years, 51-60 years, 71–80-year age group, but decreased in 21-30 years, 41-50 years, 61-70 years and 81-90 years. However, the study by **Choudhary et al.**[12] had found that platelet count was low in cases (culture-positive or sepsis screen positive) against controls. Both Choudhary et al. and Mittal et al.[13] et al.observed that platelet indices were comparable between males and females and across all ages.

Higher values of mean platelet volume were seen in early sepsis (60.64% cases) than in late sepsis (78.64% cases) in Choudhary's[12] study. They also observed that increased MPV was seen in later stages of sepsis compared to early stages, with a significant difference. In the current study as well, the mean platelet volume increased from day 1 to day 7 in a majority of study participants with a highly significant difference. Choudhary's study had concluded that increased MPV is observed in late-onset sepsis than in early onset.[12] The findings of our study were comparable to theirs. Another similar study was done by **Mangalesh et al.[13]** also found that MPV and PDW were significantly higher in late-onset sepsis (table 3).

In our study, the mean total leukocyte count, mean platelet count, mean platelet volume, mean P-LCR and mean PCT were used as laboratory parameters to assess the prognosis in sepsis patients. We found that a rise in MPV, PDW, P-LCR, TLC, and fall in platelet count and PCT could be utilized as effective tools to label the poor prognosis of sepsis. Other platelet-marker which could predict the prognosis of sepsis patients included markers like fibrinogen binding to platelets which were assessed by **Laiyos et al.**[14] The authors had observed that D dimer and platelet-Fg get significantly elevated in cases with sepsis who are admitted into ICU. It is therefore pertinent to consider platelet indices while assessing the grade of organ dysfunction following sepsis.

Antiplatelet therapy in sepsis cases could combat the contribution of platelets toward organ dysfunction.[16,17] Therefore, utilizing antiplatelet agents, namely, clopidogrel prior to induction of sepsis downregulates the plasma markers of liver damage and organ dysfunction.[18-21] A few limitations of our study included the absence of a case-control setup and no comparative analysis of parameters between survivors and non-survivors.

Conclusion

Platelet indices, especially MPV, PDW, and platelet count are reliable indicators of sepsis prognosis. 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.[22] Studies to be conducted in the future must concentrate on identifying the novel molecular mechanisms which could play a cardinal role in platelet phenotypical variations and the tendency to develop infection should concentrate on identifying molecular mechanisms behind platelet phenotypes in various infections, and amidst the different stages of sepsis.

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