Platelet Indices as Prognostic Markers in Sepsis Patients

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Abstract
Introduction: Sepsis is a potentially life-threatening condition caused by the body's response to an infection. It is an extreme reaction to an infection that can, if untreated, be deadly. The objective of this research is to study the correlation of various platelet indices in sepsis patients with their prognostic implications.

Methods & Materials: Various platelet indices were taken on day 1 and day 7 of admission for a total sample size of 117 patients with sepsis and a cross-sectional observational study was carried out using their hemogram reports succeeded by statistical analysis of their mean and standard deviation.

Results: The results showed a statistically significant difference in the Platelet count (PLT) and Plateletcrit (PCT) on observation day 1 and day 7 with no considerable statistical variations in Mean Platelet Volume (MPV), Platelet Distribution Width (PDW) and Platelet Large Cell Ratio (PLCR) in the patients taken for the study.

Conclusion: The correlation of various platelet indices in patients with sepsis in the early stages of disease can be vital to plan and implement a targeted approach based on their prognostic implications.

Keywords: Sepsis, Hemogram, Prognosis, Platelet count, Plateletcrit, Mean Platelet Volume, Platelet Distribution Width, Platelet Large Cell Ratio.

Introduction
Sepsis is the body's overwhelming and life-threatening response to infection that can lead to tissue damage, organ failure, and death. Systemic Inflammatory Response Syndrome (SIRS) is defined by at least two of four defined parameters namely body temperature of >38°C or <36°C, leucocyte count of >12,000 cells / cumm or <4000 cells/cumm, heart rate >90/min, and respiratory rate of >24/min\textsuperscript{(1)}. Severe sepsis exists if there is sepsis plus sign of organ hypoperfusion or dysfunction. Septic shock exists if there is severe sepsis plus one or both of: systemic mean blood pressure is 60mmHg (or>80mmHg if the patient has baseline hypertension) despite adequate fluid resuscitation and maintaining the systemic mean blood pressure>60mmHg (or>80mmHg if the patient has baseline hypertension) requires dopamine >5mcg/kg/min, norepinephrine <0.25 mcg/kg per min, or epinephrine <0.25 mcg/kg per min despite adequate fluid resuscitation\textsuperscript{(1)}. Sepsis can be the clinical manifestation of infections acquired both in the community setting or in health care facilities. Since these infections are often resistant to antibiotics, they can rapidly lead to deteriorating clinical conditions\textsuperscript{(2)}. There are various platelet indices that work as confirmatory aspects for the prognosis of sepsis.
The current study was aimed to find the correlation and prognostic implications of five platelet indices i.e. MPV, PDW, PLCR, PLT and PCT. These had been previously supported by various other studies. An increase in MPV in patients with sepsis had been shown in a study(3). PDW and PLCR show increased trends, while PCT and PLT decrease in the non-survivor group (4).

Materials & Methods
The current research is a cross-sectional observational study carried out for a total sample size of 117 patients with sepsis who were willing to be a part of this study; fulfilled the SIRS criteria and required admission in the hospital for a period of at least 7 days. The sample size was calculated using a formula $z^2pq/d^2$ considering the prevalence rate of sepsis as 25%. Out of the total patients, 94 patients were in the survivor group and 23 in the non-survivor group. The observation of all the patients was done on day 1 (defined as day of admission) and day 7.

Procedure
A detailed case history was taken for all the patients after fulfilling the inclusion and exclusion criteria for the study. Blood sample of the patients was obtained by taking care of all the aseptic precautions; 2ml of blood was taken from the antecubital vein of the patients and the samples were collected in EDTA vials, kept at room temperature. The complete hemogram reports were thus obtained for all the patients on day 1 and day 7 of observation. The collected data was pooled in a prescribed proforma of all the experimentals and further meticulous statistical analysis was carried out.

Statistical Analysis
The pooled data was coded numerically in SPSS Windows version 22 software for statistical analysis. The data was checked for normalized distribution and independent paired t-test was used to find the mean and standard deviation (SD) of two independent groups (day 1 and day 7), otherwise non-parametric tests were applied. For testing the null hypothesis, critical value for alpha 0.05 (type I error) and 95% confidence limit was applied.

Results
MPV, PDW and PLCR showed no significant statistical difference on day 1 and day 7 of observation. PLT varied significantly in survivor group with trivial changes for the total and non-survivor groups on observation days 1 and 7. However a remarkable difference in PCT was seen in the statistical paired comparison of mean and SD values of day 1 and day 7 in the total and survivor group with no significant distinction for the non-survivor group patients (Table 1).

| PARAMETER | GROUP       | Day 1 MEAN±SD | Day 7 MEAN±SD | P VALUE |
|-----------|-------------|---------------|---------------|---------|
| MPV       | Total       | 10.51±1.71    | 11.36±8.00    | 0.260   |
|           | Survivor    | 10.39±1.76    | 11.49±8.90    | 0.243   |
|           | Non survivor| 10.98±1.57    | 10.83±1.73    | 0.562   |
| PDW       | Total       | 16.30±0.87    | 16.33±0.65    | 0.116   |
|           | Survivor    | 16.24±0.61    | 16.32±0.65    | 0.304   |
|           | Non survivor| 16.02±1.64    | 16.40±0.59    | 0.236   |
| PLCR      | Total       | 41.15±10.78   | 42.07±11.75   | 0.357   |
|           | Survivor    | 40.52±10.22   | 42.03±11.67   | 0.180   |
|           | Non survivor| 43.70±12.73   | 42.25±12.41   | 0.524   |
| PLT       | Total       | 258.23±168.75 | 278.44±172.30 | 0.200   |
|           | Survivor    | 262.30±179.89 | 291.09±182.92 | 0.045   |
|           | Non survivor| 241.61±114.59 | 226.78±107.76 | 0.603   |
| PCT       | Total       | 2.61±1.50     | 2.87±1.43     | 0.003   |
|           | Survivor    | 2.54±1.59     | 2.96±1.49     | 0.002   |
|           | Non survivor| 2.40±1.10     | 2.50±1.17     | 0.772   |
Figure I: Sex wise distribution of survival (54.25% male and 45.74% female); non survival (65.21% male and 34.78% female), and total (56.41% male and 43.58% female) patients with sepsis included in the study.

![Sex wise distribution of survival, non survival, and total patients with sepsis](image1)

Figure II: Age wise distribution of the total patients in the study.

![Age wise distribution of total patients](image2)

Discussion

An observation could be made regarding male : female ratio of sepsis in this study as the overall admission rates in our setup are higher for males than females. The observation made through this study was clearly evident with 66 males (56.41%) and 51 females (43.58%) out of the total patients taken for the study (Figure 1). According to a
study by Gupta et al, in Indian rural setup exposure to environmental and other factors which will directly or indirectly facilitate sepsis process is more for males than females. However there can be other factors responsible for this such as co morbid conditions in males and immunological factors that need to be studied\(^5\).

In the study of Padkin et al, there was a predominance of men (58.8%) in their cohort of patients with severe sepsis. Similarly, there were 59.6% men in the Australian and New Zealand study \(^6\). In a study by Sinha M et al male patients were more with male-female ratio of 28:12\(^7\).

The occurrence of sepsis was observed to be the most in the age range of 46 to 60 years i.e. 32 patients (27.35%) (Figure 2). The age distribution is similar to studies done around the world. The mean age in an epidemiological study of sepsis in India was 54.9 years\(^8\). In another study by Meynaar IA, mean age of patients with sepsis was 65 and those with SIRS were 62 years\(^9\).

MPV values showed no significant changes on day 1 and day 7 but an overall increase could be noticed in the non-survivor group as compared to that of survivor group. This is consistent with the results of a study by Chan ho Kim (2015) in which MPV increased significantly during the first 72 hours in non-survivors (\(P = 0.001\)) and survivors (\(P < 0.001\)); however, the rate of MPV increase was significantly higher in non-survivors (\(P = 0.003\))\(^3\). A study by Gao Y et al, (2014) showed that MPV in the non survivor group was higher than that of the survivor group\(^4\).

There was no statistically significant difference in PDW for the total, survivor and non-survivor groups. These results were contradictory with the findings of a study by Guclu E et al (2013) where MPV and PDW were significantly different between sepsis patients and control group (\(P<0.05\)). PDW was the unique significantly different parameter between survivors and non-survivors (\(P=0.001\))\(^10\).

The PLT count a significant variability between mean and SD of day 1 and day 7 in the survivor group but not in the total and non-survivor groups. A study by Guclu E et al (2013) showed that platelet count in sepsis patients was lower than control group but the difference was not significant\(^10\).

PLCR resulted to be a poor prognostic factor for sepsis patients with no significant changes in day 1 and day 7 of observation for all the three groups taken for the study. A remarkable changeability was observed for PCT in the total and survivor patients groups without any variations of values for the non-survivor group on observation day 1 and day 7. A study by Gao Y et al in 2014 concluded that different change trends of platelet parameters can be seen between the non-survivors and survivors of septic shock patients. If PDW, PLCR and MPV show increased trend while PLT and PCT show decreased trend, a poor prognosis maybe indicated\(^4\).

**Conclusion**

Sepsis occurs when chemicals released in the bloodstream to fight an infection trigger inflammation throughout the body. This can cause a cascade of changes that damage multiple organ systems, leading them to fail, sometimes even resulting in death. It is a major cause of admissions in hospitals. Although various guidelines are available for the management of sepsis patients, but still high mortality rates can be observed. It is very important that the existing biomarkers of sepsis should be clinched early to look for the prognosis. Hemogram, however, is an easily available, cost effective and accessible way to decide upon the prognosis of sepsis. The various platelet indices are known to be the reliable aspects for the early diagnosis and hence for the implementation of an effective intervention plan in patients with sepsis.

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