

## A CROSS-SECTIONAL OBSERVATIONAL STUDY TO EVALUATE THE PROGNOSTIC VALUE OF BLOOD RHEOLOGICAL INDICES IN INTENSIVE CARE UNIT PATIENTS WITH SEPSIS

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### ABSTRACT

**Background:** Sepsis is a clinical illness that ranges in severity from sepsis to septic shock and is defined by systemic inflammation brought on by infection.

**Objective:** To Evaluate the Prognostic Value of Blood Rheological Indices in Intensive Care Unit Patients with Sepsis. **Materials and Methods:** The study was performed at the Government Omandurar Medical College Hospital, Chennai at Department of General Medicine in 100 critically ill patients who were diagnosed with sepsis/septic shock. **Result:** The most common source of sepsis in our study is Genitourinary infection (20%) followed by pneumonia (19%). Next most common causes are diabetic foot (14%) and cellulitis (12%). Other common causes are bronchiectasis, septic arthritis and infection like tuberculosis. Among our study population, 27 patients required ICU stay for less than 5 days, 63 patients required ICU stay for 6-10 days and rest 10 required stay for more than 10 days. Complications developed in 64 patients in our study population. Mechanical Ventilation required in 58 patients in our study. In our study, 39 patients diagnosed with sepsis or septic shock died. **Conclusion:** Absolute eosinophil count (AEC) is a simple and cost-effective marker that may be helpful in diagnosis as well as in predicting the prognosis of sepsis as evidenced by its correlation with the outcomes. The presence of elevated bands has already demonstrated utility in the initial diagnosis of sepsis, as absolute bandemia has been shown to correlate with the presence of serious infection in both the ICU and ED settings. We revealed a greater increase of MPV in non-survivors of severe sepsis and/or septic shock compared with survivors' hospitalization. So based on our study outcome above Rheological indices can be used as prognostic marker in sepsis.

## INTRODUCTION

Globally, the prevalence of septic shock and sepsis is still rising.<sup>[1]</sup> Worldwide, invasive bacterial infections are a leading cause of death, particularly for young people. If sepsis is not identified and treated right away, circulatory collapse, numerous organ dysfunction, and ultimately death will develop quickly.<sup>[2]</sup>

Patients who are diagnosed with sepsis have a 10% in-hospital death risk, and those who experience septic shock have a mortality risk of over 40%.<sup>[3]</sup> For patients to survive, sepsis severity must be identified early and treated appropriately. Numerous biochemical markers, clinical indicators, and scoring

systems are employed to evaluate the severity of sepsis and forecast death in patients.

The Sequential Organ Failure Assessment (SOFA) score, which can forecast the severity and course of multiple organ failure, is most frequently used to quantify the degree of severity. Researchers have been driven to find simple, affordable, readily accessible, and trustworthy markers in order to evaluate the severity of sepsis and forecast its prognosis.

According to recent findings, blood rheological indices can serve as a prognostic marker for sepsis, since they are significantly affected by widespread inflammation secondary to bacteraemia. As a result, CBC & other blood indices can be used to assess prognosis in patients with sepsis. Furthermore,

studies have shown that in patients who suffer from sepsis blood indices can be used as good prognostic indicators, regardless of their comorbidities.

Rheological tests of blood can provide an abundance of valuable information on blood viscosity and data on blood flow in blood vessels, and it is also worth checking the level of haematocrit and fibrinogen.

Their determination should be included in the routine examination panel in order to assess the risk of developing many diseases. Elevated aggregation of red blood cells can occur in many diseases such as myocardial infarction, stroke, diabetes, ischemia, coronary artery disease, and hypertension.

In addition, the formation of erythrocyte aggregates is favoured by a high level of fibrinogen, adipose tissue, and intense physical exercise (at which the blood viscosity increases, while erythrocyte deformability decreases). Diabetes, dehydration, and older age contribute to the increased stiffness of red blood cell membranes. Factors that may reduce blood viscosity include a lower haematocrit, greater erythrocyte deformability, and a reduced fibrinogen concentration. Based on this we have measured three blood parameters – mean platelet volume, absolute eosinophil count and band forms as rheological indices and its correlation with sepsis patients in our study.

Analyzing the CBC values, predictive significance in sepsis patients in the critical care unit is the study's justification. The study provides insight into the extent to which sepsis affects blood indices and determines whether the basic CBC is a more practical way to evaluate the prognosis of sepsis patients in intensive care units.

## MATERIALS AND METHODS

This study was conducted at Department of General Medicine, Government Medical College and Hospital, Omandurar Government Estate, Chennai. Study period was one year. Approval of the Internal Ethical Committee was obtained.

### Sample size

In this study, 100 critically ill patients are to be included with sepsis/septic shock. Informed consent was obtained from patients. Blood samples from each patient will be taken for all the rheological indices including complete blood count, peripheral smear study, creatinine, bilirubin levels, platelet count, with appropriate culture and sensitivity the source of

infection is identified at the time of admission and discharge. Investigation results will be compared with normal reference values. The severity of sepsis will be assessed using SOFA scores.

### Inclusion Criteria

- Patients treated in intensive care unit
- All patients meet the criteria for sepsis. (sepsis-3 criteria: Suspicious /Unknown infection/Increase of more than or equal to 2 SOFA)
- Gender – males /females
- Age group -18 years and above

### Exclusion Criteria

- Age less than eighteen Year
- Pregnancy
- Blood Transfusion in Past 3 Months
- Hematological Malignancy
- Bone Marrow Infiltrating Malignancies
- Auto Immune Blood Diseases
- Hypersplenism
- Granulocyte Stimulating Factor Users
- Chemotherapy and Radiotherapy, Acute Blood Loss
- HIV/Adrenal Insufficiency and Exogenous Steroids

### Methodology

Blood cultures gathered prior to the administration of broad-spectrum antibiotics. For the purpose of researching the in-hospital outcome, the SOFA score was noted during admission in the emergency room or intensive care unit.

**Statistical Analysis:** Microsoft Excel was used to enter the data. The statistical software SPSS 24.0 version was used. The Chi-Square test for categorical variables. A p value of less than 0.05 is regarded as the significant. When comparing means, the unpaired t test is used. To assess the relationship between numerical variables, Pearson correlation was employed.

## RESULTS

In our study population of 100 patients only 40 patients were below 40 years, rest all were above 40 years with 51-60 years being most common age. In our study population, 45 were males and 55 were females.

We analysed QSOFA score in 40 patients it was two, in 59 patients it was three.

**Table 1: QSOFA Score Among Study Population**

| QSOFA DAY 1 | NO OF PATIENTS | PERCENTAGE |
|-------------|----------------|------------|
| ONE         | 1              | 1%         |
| TWO         | 40             | 40%        |
| THREE       | 59             | 59%        |

We calculated PAO<sub>2</sub>/FIO<sub>2</sub> ratio to assess ARDS severity, around 33 patients had value less than 300 among which mild was 16, moderate was 11 and

severe ARDS was 6. Vasoactive agents were used in 52 patients in our study. Urine output was reduced in 39 patients in our study.

**Table 2: Prevalence of ARDS among study population**

| PAO2/FIO2 | NO OF PATIENTS | PERCENTAGE |
|-----------|----------------|------------|
| < 100     | 6              | 6%         |
| 101-200   | 11             | 11%        |
| 201-300   | 16             | 16%        |
| 301-400   | 18             | 18%        |
| > 400     | 49             | 49%        |

Coming to comorbidities in our study population Diabetes mellitus was present in 87 patients, 69 patients had hypertension, 16 had CAD, 9 patients had CKD and 4 patients had CAD.

The most common source of sepsis in our study is Genitourinary infection (20%) followed by

pneumonia (19%). Next most common cause are diabetic foot (14%) and cellulitis (12%). Other common causes are bronchiectasis, septic arthritis and infection like tuberculosis.

**Table 3: Distribution of various foci of sepsis among study population**

| SOURCE OF SEPSIS                | NO OF PATIENTS | PERCENTAGE |
|---------------------------------|----------------|------------|
| GENITOURINARY INFECTION         | 20             | 20%        |
| PNEUMONIA                       | 19             | 19%        |
| DIABETIC FOOT                   | 14             | 14%        |
| CELLULITIS                      | 12             | 12%        |
| BRONCHIECTASIS                  | 7              | 7%         |
| SEPTIC ARTHRITIS                | 5              | 5%         |
| BEDSORE                         | 5              | 5%         |
| PNEUMONIA -ILD                  | 3              | 3%         |
| LUNG ABCESS                     | 3              | 3%         |
| LIVER ABCESS                    | 2              | 2%         |
| CELLULITIS-NECROTISING FASCITIS | 2              | 2%         |
| CNS-TB MENINGITIS               | 2              | 2%         |
| CNS - TB GRANULOMA              | 2              | 2%         |
| INGUINAL ABCESS                 | 1              | 1%         |
| PANCREATITIS                    | 1              | 1%         |
| INVASIVE FUNGAL INFECTION       | 1              | 1%         |
| GLUTEAL ABCESS                  | 1              | 1%         |

Culture was done and was positive for organisms in 98 patients.

Among our study population, 27 patients required ICU stay for less than 5 days, 63 patients required ICU stay for 6-10 days and rest 10 required stay for more than 10 days. Complications developed in 64 patients in our study population.

Mechanical Ventilation required in 58 patients in our study. In our study 39 patients diagnosed with sepsis or septic shock died.

In our study, increase in SOFA score had a negative correlation with AEC and band form on both day 1 and day 5, on day 5 this correlation was statistically significant too, which mean increase in SOFA score has a fall in AEC and BAND forms, while for Mean platelet volume there is positive correlation which is statistically significant on Day 5.

**Table 4: Descriptive Statistics of Vitals**

| PARAMETERS | MEAN    | SD     |
|------------|---------|--------|
| SBP day 1  | 98.1    | 16.311 |
| DBP day 1  | 55.5    | 12.822 |
| PR D1      | 119.8   | 11.813 |
| RR D1      | 25.74   | 4.735  |
| TEMP20     | 101.632 | 1.8691 |
| GCS day 1  | 11.87   | 2.859  |
| qSOFA D1   | 2.58    | 0.516  |

**Table 5: Pearson Correlation – SOFA Day 1 & 5**

| SOFA DAY 1          | AEC DAY 1 | BAND FORMS DAY 1 | MPV DAY 1 |
|---------------------|-----------|------------------|-----------|
| Pearson Correlation | -0.079    | -0.027           | 0.13      |
| Sig. (2-tailed)     | 0.432     | 0.793            | 0.198     |
| SOFA DAY 5          | AEC DAY 5 | BAND FORMS DAY 5 | MPV DAY 5 |
| Pearson Correlation | -0.815    | 0.888            | 0.802     |
| Sig. (2-tailed)     | 0.001*    | 0.001*           | 0.001*    |

Moving on to complication, on day 1 there was no significant difference, whereas on day 5 there was a drastic fall in mean AEC level among patients who

developed complications. Similarly on day 1 there was no significant difference whereas on day 5 there was a significant increase in mean band forms among

patients who developed complications. Similarly, on day 1 there was no significant difference and on day 5 there was a increase in mean MPV level among patients who developed complications.

Coming to patients who required mechanical ventilation and their relationship with blood indices, on day 1 there was no significant difference between groups on day 5 there was a drastic fall in mean AEC level among patients who required mechanical ventilation. In band forms on day 1 there was no significant difference between groups on day 5, there was a increase in mean band forms among patients who required mechanical ventilation. Coming to

mean platelet volume, on day 1 there was no significant difference between groups on day 5, there was a increase in mean MPV level among patients who required mechanical ventilation.

Coming on to prognosis, on day 1 there was no significant difference between groups on day 5 there was drastic fall in mean AEC among patients who died. In band forms both on day 1 and on day 5 there was increase in mean band forms. On day 5 there was stark increase among patients who died. Coming to mean platelet volume, both on day 1 and on day 5 there was a increase in mean MPV level among patients who died.

**Table 6: Mean Band Forms VS Mortality**

| BAND FORMS | PROGNOSIS |       | P VALUE |
|------------|-----------|-------|---------|
|            | DEATH     | ALIVE |         |
| DAY1       | 9.78%     | 8.45% | 0.005   |
| DAY 5      | 11.28%    | 7.75% | 0.001   |

## DISCUSSION

In this study 100 critically ill patients who were diagnosed with sepsis/septic shock according to surviving sepsis campaign guidelines 2021.

Only 40 of the 100 patients in our study were under 40; the other patients were all over 40, with the most prevalent age range being 51 to 60. According to Angus et al. older people had a greater incidence of severe sepsis<sup>[4]</sup>. Patients with severe sepsis were 63.8 years old on average. There were 55 females and 45 males in our study population. According to studies, women seem to be less likely than men to acquire sepsis.<sup>[4,5]</sup>

Next, we analyzed qSOFA score in 40 patients it was two, in 59 patients it was three. Rodriguez et al. (2018) showed that qSOFA is equal or better than SIRS (systemic inflammatory response syndrome) in predicting the critical illness in patients with sepsis admitted from ED.<sup>[6,7]</sup>

we calculated PAO<sub>2</sub>/FIO<sub>2</sub> ratio to asses ARDS severity, around 33 patients had value less than 300 among which mild was 16, moderate was 11 and severe ARDS was 6. PaO<sub>2</sub>/FiO<sub>2</sub> is important for the diagnosis of sepsis as one of the variables in sequential organ failure assessment (SOFA) score.<sup>[8,9]</sup> A retrospective study of 135 elderly patients with sepsis showed that PaO<sub>2</sub>/FiO<sub>2</sub> was a promising tool and biomarker for predicting 28-day mortality.<sup>[10]</sup> Vasoactive agents were used in 52 patients in our study.

Urine output was reduced in 39 patients in our study. Sepsis-associated acute kidney injury increases the risk of developing chronic comorbidities and is associated with extremely high mortality.

Although sepsis is the most common contributing factor for developing AKI, AKI of any origin is associated with higher risk of developing sepsis. The diagnosis of AKI is currently based on an increase serum creatinine concentration and/or a decrease in urine output.<sup>[11,5]</sup>

Coming to comorbidities in our study population Type 2 DM was present in 87 patients, 69 patients had SHT, 16 had CAD, 9 patients had CKD and 4 patients had COPD. Esper et al,<sup>[12]</sup> made a similar finding, noting that individuals with diabetes had a higher chance of getting sepsis but that their condition has little bearing on how well they do.<sup>[13]</sup>

Culture was done and was positive for organisms in 98 patients. Contrary to this, Multicenter studies published in the last decade found that culture-negative patients accounted for 28%, 35%, 38%, and 48% of all cases of severe sepsis in North American, Spanish, French, and Canadian ICUs, respectively,<sup>[14]</sup> The corresponding figure was 40% in the pan-European Sepsis Occurrence in Acutely Ill Patients (SOAP) study.<sup>[15]</sup> In the United States, 49% of hospitalized patients with sepsis were culture-negative.

Among our study population, 27 patients required ICU stay for less than 5 days, 63 patients required ICU stay for 6-10 days and rest 10 required stay for more than 10 days.

Therefore, the Surviving Sepsis Campaign Guidelines (SSCG) 2021 suggested that patients with sepsis who require intensive care should be admitted to the ICU within 6 hours of their ED visits.

Complications developed in 64 patients in our study population. Patients with sepsis are prone to many complications, which have high mortality. Thus, close monitoring and prevention of these complications are vital. The chances of developing complications of severe sepsis can depend on the type of infection and its location. Septic patients with respiratory infections are at higher risk of developing respiratory organ dysfunction, including complications such as acute respiratory distress syndrome (ARDS). In serious severe sepsis cases, the brain can be injured as a complication of sepsis.

In our study it is 58%. Invasive mechanical ventilation during sepsis maintains adequate oxygenation, reduces the work of breathing, and

could protect, if started early, diaphragmatic muscle fibers from the initial inflammatory insult.

In our study, 39 patients identified with sepsis or septic shock died. Death due to sepsis ranges from 15% in patients with sepsis to 40-50% in patients with septic shock with multi-organ dysfunction syndrome (MODS).<sup>[16]</sup> Next we moved on to correlation of various parameters with three important rheological indices of our study, Absolute eosinophil count, band forms and mean platelet volume.

To start with we analyzed SOFA score on day 1 and day 5 using Pearson correlation. In our study increase in SOFA score had a negative correlation with AEC and band form on both day 1 and day 5, on day 5 this correlation was statistically significant too which mean increase in SOFA score has a fall in AEC and Band forms, while for Mean platelet volume there was positive correlation which was statistically significant on Day 5.

Moving on to complication, on day 1 there was no noteworthy difference while on day 5 there was a dire fall in mean AEC level among patients who established complications (24.92) when compared to patients who did not develop complications (152.47). This was statistically significant with a p value of 0.001.

Similarly on day 1 there was no significant difference whereas on day 5 there was a significant increase in mean band forms among patients who developed complications (10.93%) when compared to patients who did not develop complications (5.91%). This was statistically significant with a p value of 0.001.

Similarly, on day 1 there was no significant difference and on day 5 there was an increase in mean MPV level among patients who developed complications (11.91) when compared to patients who did not develop complications (10.28). This was statistically significant with a p value of 0.001.

On day 1, there was no significant difference between groups on day 5 there was a drastic fall in mean AEC level among patients who required mechanical ventilation (41.81) when compared to patients who did not require mechanical ventilation (113.24). This was statistically significant with a p value of 0.001.

In band forms on day 1 there was no significant difference between groups on day 5 there was an increase in mean band forms among patients who required mechanical ventilation (10.32%) when compared to patients who did not require mechanical ventilation (7.41%). This was statistically significant with a p value of 0.001.

Coming to mean platelet volume, on day 1 there was no significant difference between groups on day 5 there was an increase in mean MPV level among patients who required mechanical ventilation (11.17) when compared to patients who did not require mechanical ventilation (10.64). This was statistically significant with a p value of 0.001.

Regarding the prognosis, there was no noteworthy variance between the groups on day 1; however, on day 5, the mean AEC of the dead patients plunged

intensely (20.47) associated to the alive patients (103.11), which was statistically significant with a p value of 0.001.

The mean band forms increased on both days, with the death rate among the deceased patients rising sharply (11.28%) compared to the living patients (7.75%).

Coming to mean platelet volume, both on day 1 and on day 5 there was an increase in mean MPV level among patients who died. On day 5 the mean MPV was high (11.93) when compared to patients who did not require mechanical ventilation (10.91). On both days, it was statistically significant.

Eosinopenia occurs in response to acute infection because cytokines regulating the production of eosinophils are not significantly activated in sepsis. Gil et al., demonstrated significant differences in mean values of eosinophils between patients with infectious and noninfectious episodes, and counts less than 40 cells/mm<sup>3</sup> were strongly related to bacterial etiology.

Furthermore, in a recent study, Abidi et al.,<sup>[17]</sup> reports that eosinopenia constitutes a good diagnostic marker in identifying sepsis conditions and discriminating their severity. Eosinopenia has also been reported as an important prognostic marker in the sepsis syndromes even after mechanical ventilation is made. Bandemia is a common finding in sepsis and severe bacterial infection and is also a laboratory criterion for severity in many diseases like necrotizing enterocolitis, neonatal sepsis, etc.;<sup>[18]</sup>

MPV and the MPV/P ratio are prognosticators of clinical severity and death in sepsis. The MPV and its measurement are pointers of the biological actions of platelets in sepsis. For critical patients, platelet indices may be a valuable tool for diagnosis and monitoring, as they are simple, inexpensive, and regularly performed in the hospital laboratory.<sup>[19]</sup>

Similar to our study, in a study done by Chan Ho Kim et al., the main findings of this study are as follows First, they confirmed that MPV increased within the first 72 hours following hospitalization, and discovered that non-survivors saw a steeper MPV increase than survivors.

MPV increased in patients with shock-related thrombocytopenia, according to Dastugue et al.<sup>[20]</sup> Patients with sepsis have a greater MPV, according to Van der Lelie and Von dem Borne.<sup>[21]</sup>

## CONCLUSION

Absolute eosinophil count (AEC) is a simple and cost-effective marker that may be helpful in diagnosis as well as in predicting the prognosis of sepsis as evidenced by its correlation with the outcomes.

In sepsis, an increased percentage of immature white blood cells, called bands, can help predict the prognosis and clinical trajectory of a patient. The presence of elevated bands has already demonstrated utility in the initial diagnosis of sepsis, as absolute bandemia has been shown to correlate with the

presence of serious infection in both the ICU and ED settings

We discovered a larger increase of MPV in died patients with severe sepsis in comparison in alive patients during hospital stay and also identified that a rise in MPV from baseline is a self-regulating risk factor for mortality. So based on our study outcome above Rheological indices can be used as prognostic marker in sepsis.

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