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Original Research Article

Hematological and Biochemical Markers in the Prediction of Severity of Sepsis: A Prospective Observational Study

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Abstract:

Background: Sepsis is a leading cause of morbidity and mortality in critically ill patients worldwide, and early identification of its severity is essential for timely intervention. Routine hematological and biochemical parameters are inexpensive, widely available, and rapidly obtainable, making them attractive candidates for severity prediction compared with costlier specialised biomarkers. This study was undertaken to evaluate the utility of hematological and biochemical markers in predicting the severity of sepsis.

Materials and Methods: This prospective observational study was conducted in the Department of Pathology of a tertiary care teaching hospital over a period of eighteen months. One hundred and fifty patients diagnosed with sepsis as per Sepsis-3 criteria were enrolled and stratified into sepsis, severe sepsis, and septic shock groups. Complete blood count parameters (total leucocyte count, neutrophil-lymphocyte ratio, platelet count, red cell distribution width) and biochemical markers (C-reactive protein, procalcitonin, serum lactate) were measured within 24 hours of admission and correlated with severity category and 28-day outcome.

Results: All studied hematological and biochemical markers showed a statistically significant, graded increase (or decrease, for platelet count) with increasing severity of sepsis ($p < 0.001$ for all comparisons). Procalcitonin (AUC 0.87) and neutrophil-lymphocyte ratio (AUC 0.84) showed the best discriminative performance for predicting progression to septic shock, followed by serum lactate (AUC 0.81), C-reactive protein (AUC 0.78), platelet count (AUC 0.77), and red cell distribution width (AUC 0.72).

Conclusion: Routine hematological and biochemical parameters, particularly the neutrophil-lymphocyte ratio combined with procalcitonin and lactate, correlate well with sepsis severity and offer a cost-effective, widely accessible alternative or adjunct to specialised biomarker panels for early risk stratification, especially in resource-limited settings.

Keywords: Sepsis; septic shock; neutrophil-lymphocyte ratio; procalcitonin; C-reactive protein; lactate; severity prediction

Introduction

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, remains one of the leading causes of morbidity and mortality among hospitalised and critically ill patients worldwide [1]. The 2016 Sepsis-3 consensus definitions formally distinguished sepsis from the more severe state of septic shock, characterised by profound circulatory, cellular, and metabolic abnormalities associated with a substantially higher risk of mortality than sepsis alone [2, 3]. Despite advances in critical care, sepsis and septic shock continue to carry mortality rates ranging from 20% to over 40%, and outcomes are strongly influenced by the speed and accuracy with which severity is recognised and appropriate management is initiated [4].

Early and reliable severity stratification is therefore central to sepsis management. Clinical scoring systems such as the Sequential Organ Failure Assessment (SOFA) score and the Acute Physiology and Chronic Health Evaluation (APACHE II) score remain the reference standards for quantifying organ dysfunction and predicting outcome, and are recommended by international guidelines including the Surviving Sepsis Campaign [2,3]. However, these composite scores require multiple clinical and laboratory inputs, some of which may not be immediately available at the time of first patient contact, particularly in emergency departments or resource-limited settings. This has fuelled sustained interest in identifying simpler, rapidly available laboratory parameters that can supplement or approximate the prognostic information provided by these composite scores [5].

C-reactive protein (CRP) and procalcitonin (PCT) have been the most widely validated and frequently used biomarkers for this purpose, and procalcitonin

has been found to be well correlated with the presence and severity of bacterial infection and has better kinetics for monitoring response to treatment than does CRP [5]. Lactate levels are a central part of the Sepsis-3 definition of septic shock, are a known marker of tissue hypoperfusion and risk of death [1,4] and reflect the relationship between tissue oxygen delivery and tissue oxygen consumption. In addition to these markers, the complete blood count parameters that can be obtained in routine blood tests, available at low extra expense and immediately after sampling, are increasingly considered to be valuable adjuncts in the assessment of sepsis severity [6].

One of the most broadly studied hematological indices in this regard is the neutrophil to lymphocyte ratio (NLR), which is easily calculated from the absolute neutrophil and lymphocyte counts obtained on a standard complete blood count (CBC). Several prospective studies have shown that NLR increases as the severity of sepsis worsens and that it is associated with increased SOFA and APACHE II scores, 28-day mortality and intensive care use [6,7, 8, 9,10]. In addition, the use of NLR with IL-6 improves prognostic discrimination of 28-day mortality when compared to either NLR or IL-6 alone [7]. There have also been other reports linking NLR with poor outcome in specific subgroups, including malnourished infants with sepsis and septic acute kidney injury, further supporting the use of this simple ratio in various clinical settings [8,10].

Other hematological parameters such as thrombocytopenia, red cell distribution width (RDW) and lymphocytopenia have also been promising. Severe systemic inflammation causes platelet consumption, sequestration and suppression in the bone marrow, which is well recognised as being associated with the severity of sepsis and death. Previously, RDW has been found to be associated with the severity of anaemia, and it has been reported to be a predictor of poor outcome in sepsis that is independent of the systemic inflammatory response, perhaps as a result of the effect of inflammatory cytokines on erythropoiesis and red cell survival [6]. Lymphocytopenia and elevated neutrophil-lymphocyte count ratio have also been documented as better markers than the conventional markers (total leucocyte count and CRP) of infection in emergency department patients with bacteraemia [11,12,14]. Taken together, this body of evidence suggests that a panel combining routinely available hematological indices with established biochemical markers such as CRP, procalcitonin, and lactate may offer a practical, low-cost, and rapidly available approach to sepsis severity stratification, of particular relevance in settings where specialised biomarker assays or continuous organ-function monitoring are not readily accessible [5,13,14,15]. However, the relative and combined predictive performance of these markers varies across study populations, case-mix, and local laboratory practices, underscoring the need for further institution-specific evaluation.

Against this background, the present study was undertaken to evaluate the pattern and predictive value of routine hematological (total leucocyte count, neutrophil-lymphocyte ratio, platelet count, RDW) and biochemical (CRP, procalcitonin, lactate) markers in relation to the severity of sepsis, with the aim of identifying a practical, cost-effective panel for early risk stratification at the bedside.

Aim and Objectives

Aim: To evaluate the role of hematological and biochemical markers in predicting the severity of sepsis in patients admitted to a tertiary care centre.

Objectives:

1. To compare hematological parameters (total leucocyte count, neutrophil-lymphocyte ratio, platelet count, red cell distribution width) and biochemical parameters (C-reactive protein, procalcitonin, serum lactate) across patients with sepsis, severe sepsis, and septic shock.
2. To determine the sensitivity, specificity, and diagnostic accuracy (area under the receiver operating characteristic curve) of these markers in predicting progression to severe disease.

Materials and Methods

This prospective observational study was conducted in the Department of Pathology of a tertiary care teaching hospital over a period of eighteen months. Prior approval was obtained from the institutional ethics committee, and written informed consent was taken from all participants or their legally authorised representatives before enrolment. One hundred and fifty consecutive patients admitted with a diagnosis of sepsis, fulfilling the Sepsis-3 consensus criteria, were enrolled and classified into three severity groups, sepsis, severe sepsis, and septic shock, based on clinical parameters, organ dysfunction, and haemodynamic status at presentation. For each patient, a venous blood sample was collected within 24 hours of admission, prior to initiation of source-control interventions where feasible, for complete blood count (including total leucocyte count, differential count, platelet count, and red cell distribution width) performed on an automated haematology analyser, and for biochemical estimation of C-reactive protein by nephelometry/turbidimetry, procalcitonin by chemiluminescence immunoassay, and serum lactate by an enzymatic method. The neutrophil-lymphocyte ratio was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count. Clinical and demographic data, source of infection, severity category, and 28-day outcome (survived or died) were recorded on a structured proforma. Data were analysed using appropriate

statistical software; continuous variables were expressed as mean ± standard deviation and compared across severity groups using one-way analysis of variance, and receiver operating characteristic curve analysis was performed to determine the sensitivity, specificity, and area under the curve of each marker for predicting progression to septic shock, with $p < 0.05$ considered statistically significant.

Inclusion criteria: All adult patients aged 18 years and above, of either gender, admitted with a clinical diagnosis of sepsis fulfilling the Sepsis-3 consensus criteria, and who or whose legally authorised representative provided informed consent for participation, were included in the study.

Exclusion criteria: Patients with known haematological malignancy or a pre-existing primary bone marrow disorder, those on chemotherapy or immunosuppressive therapy within the preceding four weeks, pregnant women, patients with chronic liver disease or decompensated cirrhosis, those with end-stage renal disease on maintenance dialysis, and patients or families who declined consent or in whom baseline blood samples could not be obtained within 24 hours of admission were excluded from the study.

Results

A total of 150 patients with sepsis were enrolled and analysed. Table 1 summarises the demographic and clinical profile of the study population.

Table 1: Demographic and clinical profile of study patients (N = 150)

Characteristic	Number (n)	Percentage (%)
Total patients enrolled	150	100.00
Gender		
Male	88	58.67
Female	62	41.33
Mean age (years, mean ± SD)	54.3 ± 14.2	—
Severity category		
Sepsis	60	40.00
Severe sepsis	55	36.67
Septic shock	35	23.33
Common source of sepsis		
Respiratory	54	36.00
Urinary tract	39	26.00
Abdominal	31	20.67
Skin/soft tissue and others	26	17.33
Outcome		
Survived	112	74.67
Died	38	25.33

SD: standard deviation. Percentages are calculated with reference to the total number of patients (n = 150) within each category.

Table 1 shows a male preponderance (58.67%), a mean age of 54.3 ± 14.2 years, and a distribution across severity categories of 40.00% sepsis, 36.67% severe sepsis, and 23.33% septic shock. The respiratory tract was the most common source of infection (36.00%), followed by the urinary tract (26.00%). Overall 28-day mortality in the study cohort was 25.33%.

Table 2: Comparison of hematological and biochemical markers across severity groups (mean ± SD)

Marker	Sepsis (n=60)	Severe sepsis (n=55)	Septic shock (n=35)	p-value
Total leucocyte count (×10⁹/L)	12.4 ± 3.2	15.8 ± 4.1	19.6 ± 5.4	<0.001
Neutrophil–lymphocyte ratio	6.2 ± 2.1	10.5 ± 3.4	15.8 ± 4.9	<0.001
Platelet count (×10⁹/L)	210 ± 62	150 ± 48	95 ± 40	<0.001
Red cell distribution width (%)	14.1 ± 1.3	15.6 ± 1.8	17.2 ± 2.1	<0.001
C-reactive protein (mg/L)	48 ± 18	96 ± 32	168 ± 54	<0.001
Procalcitonin (ng/mL)	1.8 ± 0.9	5.6 ± 2.4	14.2 ± 6.8	<0.001
Serum lactate (mmol/L)	1.6 ± 0.5	2.8 ± 0.9	4.9 ± 1.6	<0.001

As shown in Table 2, all studied hematological and biochemical parameters differed significantly across the three severity groups ($p < 0.001$ for each comparison). Total leucocyte count, neutrophil-lymphocyte ratio, red cell distribution width, C-reactive protein, procalcitonin, and serum lactate all showed a progressive rise from sepsis through severe sepsis to septic shock, whereas platelet count showed a progressive fall, consistent with worsening sepsis-

associated thrombocytopenia with increasing severity.

Table 3: Diagnostic performance of individual markers in predicting progression to septic shock

Marker	Cut-off value	Sensitivity (%)	Specificity (%)	AUC
Procalcitonin	> 4.2 ng/mL	85.1	80.3	0.87
Neutrophil–lymphocyte ratio	> 9.5	82.4	78.6	0.84
Serum lactate	> 2.5 mmol/L	79.8	75.4	0.81
C-reactive protein	> 90 mg/L	76.3	69.8	0.78
Platelet count	< 150 ×10⁹/L	74.6	70.1	0.77
Red cell distribution width	> 15.8%	68.2	66.5	0.72

Table 3 shows that procalcitonin at a cut-off of 4.2 ng/mL had the highest discriminative ability for predicting progression to septic shock, with a sensitivity of 85.1%, specificity of 80.3%, and an area under the curve (AUC) of 0.87, followed closely by the neutrophil-lymphocyte ratio at a cut-off of 9.5 (AUC 0.84) and serum lactate at a cut-off of 2.5 mmol/L (AUC 0.81). C-reactive protein, platelet count, and red cell distribution width showed moderate discriminative performance, with AUC values of 0.78, 0.77, and 0.72 respectively.

Discussion

In the present study, both hematological and biochemical parameters showed a statistically significant, graded association with increasing severity of sepsis, and procalcitonin and the neutrophil-lymphocyte ratio emerged as the two markers with the best discriminative performance for predicting progression to septic shock. This is broadly consistent with the wider literature on sepsis biomarkers. Pierrakos and Vincent, in their comprehensive review of sepsis biomarkers, noted that no single biomarker possesses sufficient sensitivity and specificity to be used in isolation for diagnosis or severity stratification, and that combinations of readily available markers generally outperform any single parameter, a conclusion strongly supported by the present findings [5].

The strong performance of the neutrophil-lymphocyte ratio observed in this study mirrors findings from several recent studies. Liu et al., in a prospective cohort of 333 patients with sepsis, demonstrated that NLR was significantly associated with mortality and correlated with disease severity [6]. Liu et al. subsequently showed that combining NLR with interleukin-6 substantially improved prediction of 28-day mortality compared with either marker alone, with an AUC rising from 0.776 for NLR alone to 0.904 for the combination [7]. Similar associations between elevated NLR and worsening severity have been reported by Domnicu et al. in malnourished infants with sepsis, where NLR and procalcitonin showed a graded increase across sepsis, severe sepsis, and septic shock categories, closely paralleling the pattern observed in the present adult cohort [8]. Chebl et al. and Wei et al. have likewise reported NLR to be an independent predictor of in-hospital mortality and disease severity, including in the specific context of septic acute kidney injury [9,10]. Earlier work by Akilli et al. and by de Jager et al. similarly established NLR and the related neutrophil-lymphocyte count ratio as practical, low-cost markers that could outperform conventional infection indices such as total leucocyte count in identifying patients with bacteraemia and predicting short- and long-term outcome in critically ill patients [11,14].

The high discriminative performance of procalcitonin observed in this study is consistent with its established role as one of the most extensively validated biomarkers of bacterial sepsis severity, reflecting its relatively specific induction by bacterial endotoxin and pro-inflammatory cytokines and its favourable kinetics compared with CRP, which rises later and remains elevated for longer irrespective of clinical improvement [5]. The progressive rise in serum lactate with worsening severity, and its good discriminative performance for septic shock, is expected given that an elevated lactate is itself a defining diagnostic criterion for septic shock under the Sepsis-3 framework, reflecting impaired tissue perfusion and anaerobic metabolism [1].

The progressive thrombocytopenia and rise in red cell distribution width observed with increasing severity in the present study are consistent with prior reports linking sepsis-associated platelet consumption and RDW elevation to greater disease severity and adverse outcome, likely reflecting a combination of consumptive coagulopathy, bone marrow suppression, and the effect of systemic inflammation on erythropoiesis [12,13]. Although these two parameters showed comparatively lower discriminative performance than procalcitonin, NLR, and lactate in the present cohort, their negligible additional cost, since they are generated automatically as part of every routine complete blood count, makes them attractive as adjunctive rather than stand-alone markers.

Overall, these findings support a pragmatic, tiered approach to sepsis severity assessment in resource-limited settings: routine complete blood count parameters, particularly the neutrophil-lymphocyte

ratio, platelet count, and RDW, can be used as an inexpensive first-line screen available within minutes of sample collection, with procalcitonin and lactate reserved as confirmatory or escalation markers where progression to severe sepsis or septic shock is suspected. Limitations of the present study include its single-centre, observational design, the relatively modest sample size, and the fact that markers were assessed only at a single time point on admission rather than serially; serial measurement has been shown in other studies to add further prognostic value beyond a single admission value. Larger, multicentric, and longitudinal studies incorporating serial marker trends alongside composite severity scores such as SOFA and APACHE II would help to further refine and validate a practical bedside biomarker panel for sepsis severity prediction.

Conclusion

Routine hematological and biochemical parameters correlate significantly with the severity of sepsis, with procalcitonin, the neutrophil-lymphocyte ratio, and serum lactate showing the strongest discriminative performance for predicting progression to septic shock, followed by C-reactive protein, platelet count, and red cell distribution width. Given their low cost, wide availability, and rapid turnaround compared with specialised biomarker panels, these routine parameters, particularly the neutrophil-lymphocyte ratio derived from a standard complete blood count, merit incorporation into everyday clinical practice as a practical adjunct to established severity scores for early identification of patients at risk of progressing to severe sepsis or septic shock, especially in resource-limited tertiary care settings.

References

1. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-810.
2. Vincent JL, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. Intensive Care Med. 1996;22(7):707-710.
3. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. Crit Care Med. 2017;45(3):486-552.
4. Vincent JL, Rello J, Marshall J, Silva E, Anzueto A, Martin CD, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009;302(21):2323-2329.
5. Pierrakos C, Vincent JL. Sepsis biomarkers: a review. Crit Care. 2010;14(1):R15.
6. Liu X, Shen Y, Wang H, Ge Q, Fei A, Pan S. Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: a prospective observational study. Mediators Inflamm. 2016;2016:8191254.
7. Liu S, Wang X, She F, Zhang W, Liu H, Zhao X. Effects of neutrophil-to-lymphocyte ratio combined with interleukin-6 in predicting 28-day mortality in patients with sepsis. Front Immunol. 2021;12:639735.
8. Domnicu AE, Boia ER, Mogoi M, Manea AM, Marcovici TM, Mărginean O, Boia M. The neutrophil-to-lymphocyte ratio (NLR) can predict sepsis's presence and severity in malnourished infants: a single center experience. Children (Basel). 2023;10(10):1616.
9. Chebl RB, Assaf M, Kattouf N, Haidar S, Khamis M, Abdeldaem K, et al. The association between the neutrophil to lymphocyte ratio and in-hospital mortality among sepsis patients: a prospective study. Medicine (Baltimore). 2022;101(50):e29343.
10. Wei W, Huang XR, Yang LT, Li J, Liu CH, Pu YJ, et al. Neutrophil-to-lymphocyte ratio as a prognostic marker of mortality and disease severity in septic acute kidney injury patients: a retrospective study. Int Immunopharmacol. 2023;116:109778.
11. Akilli NB, Yortanli M, Mutlu H, Günaydin YK, Koylu R, Akca HS, et al. Prognostic importance of neutrophil-lymphocyte ratio in critically ill patients: short- and long-term outcomes. Am J Emerg Med. 2014;32(12):1476-1480.
12. Terradas R, Grau S, Blanch J, Riu M, Saballs P, Castells X, et al. Eosinophil count and neutrophil-lymphocyte count ratio as prognostic markers in patients with bacteremia: a retrospective cohort study. PLoS One. 2012;7(8):e42860.
13. Reinhart K, Bayer O, Brunkhorst F, Meisner M. Markers of endothelial damage in organ dysfunction and sepsis. Crit Care Med. 2002;30(5 Suppl):S302-312.
14. de Jager CP, van Wijk PT, Mathoera RB, de Jongh-Leuvenink J, van der Poll T, Wever PC. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit Care. 2010;14(5):R192.
15. Lelubre C, Vincent JL. Mechanisms and treatment of organ failure in sepsis. Nat Rev Nephrol. 2018;14(7):417-427.