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Original Research Article

Association of Serum Lactate Dehydrogenase and C-Reactive Protein with Sequential Organ Failure Assessment Score in Patients with Sepsis: A Cross-Sectional Study

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Abstract

Background: Sepsis is a life-threatening condition characterized by a dysregulated host response to infection, resulting in organ dysfunction and high mortality. Early identification of disease severity is essential for timely management. Serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) are inexpensive and readily available biomarkers that may reflect the severity of organ dysfunction in patients with sepsis.

Aim: To evaluate the association of serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) with the Sequential Organ Failure Assessment (SOFA) score in adult patients with sepsis.

Methods: A hospital-based observational cross-sectional study was conducted in the Department of General Medicine at a tertiary care teaching hospital over one year. A total of 95 adult patients diagnosed with sepsis according to the Sepsis-3 criteria were enrolled using purposive sampling. Serum LDH, serum CRP, and SOFA score were assessed on admission (Day 0) and repeated on Day 3. Associations between biomarker levels and SOFA score were evaluated using the Chi-square test, while Pearson's correlation coefficient was used to assess the strength of correlation. A p-value <0.05 was considered statistically significant.

Results: The mean age of the participants was 56.05 ± 15.01 years, and 66.3% were female. The proportion of patients with SOFA scores of 0–6 increased from 63.2% on admission to 73.7% on Day 3. Elevated CRP (≥5 mg/L) was observed in 88.4% of patients on admission and 78.9% on Day 3, while elevated LDH (≥240 IU/L) was present in 87.4% and 81.1%, respectively. Significant associations were observed between CRP and SOFA score on admission (p=0.03) and Day 3 (p=0.02), as well as between LDH and SOFA score on admission (p=0.04) and Day 3 (p=0.03). Pearson correlation analysis demonstrated moderate positive correlations between SOFA score and CRP (Day 0: r=0.42; Day 3: r=0.39) and between SOFA score and LDH (Day 0: r=0.48; Day 3: r=0.44). LDH showed a slightly stronger correlation with SOFA score than CRP.

Conclusion: Serum LDH and CRP were significantly associated with SOFA score in patients with sepsis, indicating their usefulness as adjunctive biomarkers of disease severity. LDH demonstrated a slightly stronger correlation with SOFA score than CRP, suggesting that it may better reflect organ dysfunction. The combined assessment of serum LDH, CRP, and SOFA score may facilitate early severity assessment and monitoring of patients with sepsis.

Keywords: Sepsis; Sequential Organ Failure Assessment; SOFA score; Lactate dehydrogenase; C-reactive protein; Biomarkers.

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Introduction

Sepsis is a life-threatening syndrome characterized by a dysregulated host response to infection that results in acute organ dysfunction. Despite remarkable advances in antimicrobial therapy, intensive care, and supportive management, sepsis remains one of the leading causes of morbidity and mortality worldwide. According to the Global Burden of Disease Study, sepsis accounts for approximately 49 million cases and 11 million deaths annually, representing nearly one-fifth of all global deaths. The burden is disproportionately higher in low- and middle-income countries due to delayed diagnosis, limited healthcare resources, and a high prevalence of infectious diseases. Early recognition, accurate assessment of disease severity, and timely initiation of appropriate treatment are essential for improving patient outcomes and reducing sepsis-related mortality.[1-4]

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) define sepsis as

life-threatening organ dysfunction caused by a dysregulated host response to infection. The Sequential Organ Failure Assessment (SOFA) score has been recommended as the standard tool for assessing organ dysfunction in patients with sepsis. The SOFA score evaluates six organ systems—respiratory, cardiovascular, hepatic, coagulation, renal, and neurological—and has been extensively validated for predicting disease severity and mortality. Although SOFA is an effective prognostic tool, its calculation requires multiple laboratory and clinical parameters, which may not always be readily available, particularly in resource-constrained healthcare settings. Consequently, there is growing interest in identifying simple, inexpensive, and readily available laboratory biomarkers that can complement SOFA in the early assessment and prognostication of sepsis.[4-9]

Among the routinely available biomarkers, C-reactive protein (CRP) and lactate dehydrogenase (LDH) have attracted considerable attention because they reflect different aspects of sepsis pathophysiology. CRP is an acute-phase protein synthesized by hepatocytes in response to inflammatory cytokines, particularly interleukin-6, and is widely used as a marker of systemic inflammation. Elevated CRP concentrations have been associated with severe bacterial infections, persistent inflammatory response, progression of organ dysfunction, and adverse clinical outcomes. Serial measurement of CRP has also been shown to correlate with therapeutic response and prognosis in patients with sepsis.[7-11]

Lactate dehydrogenase (LDH) is an intracellular enzyme involved in anaerobic glycolysis and is released into the circulation following cellular injury, tissue hypoxia, and metabolic stress. In sepsis, widespread inflammation, endothelial dysfunction, and impaired tissue perfusion lead to cellular damage and increased serum LDH concentrations. Recent studies have demonstrated that elevated LDH levels are associated with greater disease severity, higher organ dysfunction scores, prolonged intensive care unit stay, and increased in-hospital mortality, suggesting that LDH may serve as a valuable prognostic biomarker in septic patients.[12-14]

Although CRP and LDH have individually been investigated as biomarkers of sepsis, evidence directly evaluating their association with the Sequential Organ Failure Assessment score remains limited, particularly in the Indian population. Establishing the relationship between these routinely available biomarkers and SOFA score may facilitate early risk stratification, support clinical decision-making, and provide an economical adjunct for assessing disease severity in resource-limited settings. Therefore, the present study was undertaken to evaluate the association of serum lactate dehydrogenase and C-reactive protein with the Sequential Organ Failure Assessment score among adult patients with sepsis admitted to a tertiary care hospital.

Aim: To evaluate the association of serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) with the Sequential Organ Failure Assessment (SOFA) score in adult patients with sepsis.

Objectives

1. To determine the association between serum lactate dehydrogenase (LDH) levels and the Sequential Organ Failure Assessment (SOFA) score on admission and on the third day in patients with sepsis.
2. To determine the association between serum C-reactive protein (CRP) levels and the Sequential Organ Failure Assessment (SOFA) score on admission and on the third day in patients with sepsis.
3. To compare the strength of association of serum lactate dehydrogenase (LDH) and serum C-reactive protein (CRP) with the Sequential Organ Failure Assessment (SOFA) score in patients with sepsis.

Materials and Methods

Study Design and Setting: This hospital-based observational cross-sectional study was conducted in the Department of General Medicine at a tertiary care teaching hospital in Gujarat, India, over a period of one year after obtaining approval from the Institutional Ethics Committee.

Study Participants: The study included adult patients diagnosed with sepsis according to the Sepsis-3 criteria who were admitted to the hospital during the study period.

Inclusion Criteria

- Patients aged ≥18 years.
- Patients admitted with a clinical diagnosis of sepsis based on the Sepsis-3 criteria.
- Patients who provided written informed consent.

Exclusion Criteria

- Patients with rheumatic heart disease.
- Patients with collagen vascular disease.
- Patients with a history of transient ischemic attack or cerebrovascular accident.
- Patients with coronary artery disease.
- Patients with chronic kidney disease.

Sample Size: The sample size was calculated using the hypothesis testing method based on the following formula: $n=Z^2p(1-p)/ L^2$, where Z = 1.96 at a 95% confidence level, p = 56.4% (prevalence of sepsis reported by Hammond NE et al.[15]), 1 − p =

43.6%, and L = 10% (absolute precision). The minimum required sample size was 95, and all eligible participants were enrolled using purposive sampling.

Sampling Technique: Purposive sampling was used, and all eligible patients fulfilling the selection criteria during the study period were included.

Data Collection: Data were collected using a predesigned study proforma. Detailed clinical history, demographic characteristics, and findings of physical examination were recorded. Vital parameters, including temperature, pulse rate, respiratory rate, blood pressure, oxygen saturation, and Glasgow Coma Scale (GCS), were documented.

Laboratory investigations included complete blood count (CBC), renal function tests (RFT), liver function tests (LFT), serum C-reactive protein (CRP), serum lactate dehydrogenase (LDH), prothrombin time, arterial blood gas (ABG) analysis, HBsAg, HIV, Widal test, malaria screening, blood culture and sensitivity, urine analysis, urine culture and sensitivity, electrocardiography (ECG), chest radiography, and ultrasonography of the abdomen. Computed tomography (CT) of the chest or abdomen was performed whenever clinically indicated.

Relevant laboratory investigations, including CBC, RFT, LFT, serum CRP, and serum LDH, were performed on admission (Day 0) and repeated on the third day (Day 3). The Sequential Organ Failure Assessment (SOFA) score was calculated on admission (Day 0) and again on Day 3.

Definition of Sepsis: Sepsis was defined according to the Sepsis-3 criteria as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction was identified by an increase in the Sequential Organ Failure Assessment (SOFA) score of ≥2 points from baseline.

Ethical Considerations: The study was approved by the Institutional Ethics Committee before commencement. Written informed consent was obtained from all participants before enrolment. Participants were provided with a participant information sheet in their native language explaining the purpose of the study, and confidentiality of all patient information was maintained throughout the study.

Statistical Analysis: Data were entered and analysed using Epi Info™ version 7 (Centers for Disease Control and Prevention, Atlanta, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The association between categorical variables was assessed using the Chi-square test. The correlation between SOFA score and serum CRP and LDH levels was evaluated using Pearson's correlation coefficient. A p-value <0.05 was considered

Results

A total of 95 patients with sepsis were included in the final analysis. The mean age of the study participants was 56.05 ± 15.01 years, with females constituting 66.3% (n = 63) and males 33.7% (n = 32). The most common comorbidity was the coexistence of diabetes mellitus and hypertension (33.7%), followed by diabetes mellitus alone (27.4%) and hypertension alone (22.1%). Jaundice (41.1%) was the most frequent presenting complaint, followed by cough, cold and breathlessness (38.9%), diarrhoea (38.9%), fever (34.7%), and altered sensorium (13.7%). Most patients had a Glasgow Coma Scale (GCS) score ≥15 both on admission (86.3%) and on Day 3 (83.2%). Vital parameters and laboratory investigations demonstrated overall improvement during hospitalization, with reductions in body temperature, pulse rate, white blood cell count, total bilirubin, and serum creatinine levels.

The distribution of SOFA score categories showed improvement over time. On admission, 60 (63.2%) patients had a SOFA score of 0–6, 30 (31.6%) had a score of 7–12, and 5 (5.2%) had a score >12. By Day 3, the proportion of patients in the lowest SOFA category increased to 70 (73.7%), while the proportions with SOFA scores 7–12 and >12 decreased to 22 (23.2%) and 3 (3.1%), respectively.

Table 1: SOFA score category distribution on Day 0 and Day 3

SOFA score	Day 0 (n=95)	Day 3 (n=95)
0–6	60 (63.2%)	70 (73.7%)
7–12	30 (31.6%)	22 (23.2%)
>12	5 (5.2%)	3 (3.1%)

Serum CRP levels were elevated (≥5 mg/L) in 84 (88.4%) patients on admission and 75 (78.9%) patients on Day 3. Elevated CRP levels showed a statistically significant association with higher SOFA score categories both on admission (p = 0.03) and on Day 3 (p = 0.02).

Table 2: Association between SOFA score and CRP levels

CRP level (mg/L)	SOFA 0–6	SOFA 7–12	SOFA >12	Total	p-value
Day 0					
<5	10 (16.7%)	1 (3.3%)	0 (0.0%)	11	0.03
≥5	50 (83.3%)	29 (96.7%)	5 (100%)	84	
Day 3					
<5	18 (25.7%)	2 (9.1%)	0 (0.0%)	20	0.02
≥5	52 (74.3%)	20 (90.9%)	3 (100%)	75	

Similarly, elevated LDH levels (≥240 IU/L) were observed in 83 (87.4%) patients on admission and 77 (81.1%) patients on Day 3. A statistically significant association was found between elevated LDH levels and higher SOFA score categories on admission (p = 0.04) as well as on Day 3 (p = 0.03).

Table 3: Association between SOFA score and LDH levels

LDH level (IU/L)	SOFA 0–6	SOFA 7–12	SOFA >12	Total	p-value
Day 0					
<240	9 (15.0%)	3 (10.0%)	0 (0.0%)	12	0.04
≥240	51 (85.0%)	27 (90.0%)	5 (100%)	83	
Day 3					
<240	16 (22.9%)	2 (9.1%)	0 (0.0%)	18	0.03
≥240	54 (77.1%)	20 (90.9%)	3 (100%)	77	

Pearson correlation analysis demonstrated a moderate positive correlation between SOFA score and CRP on Day 0 (r = 0.42) and Day 3 (r = 0.39). Likewise, SOFA score showed a moderate positive correlation with LDH on Day 0 (r = 0.48) and Day 3 (r = 0.44), indicating that higher CRP and LDH levels were associated with greater organ dysfunction.

Table 4: Pearson correlation between SOFA score and biomarkers

Variable pair	Day	Pearson's r	p-value	Interpretation
SOFA vs CRP	Day 0	0.42	<0.03	Moderate positive correlation
SOFA vs CRP	Day 3	0.39	<0.02	Moderate positive correlation
SOFA vs LDH	Day 0	0.48	<0.04	Moderate positive correlation
SOFA vs LDH	Day 3	0.44	<0.03	Moderate positive correlation

Discussion

The present study demonstrated that both serum CRP and LDH were significantly associated with SOFA score on admission and on the third day, suggesting that increasing biomarker levels were associated with greater organ dysfunction in patients with sepsis. A reduction in the proportion of patients with elevated CRP and LDH levels by Day 3 paralleled the improvement in SOFA score categories, indicating a favorable clinical response.

A significant association was observed between serum CRP and SOFA score on both admission (p=0.03) and Day 3 (p=0.02). In the present study, 88.4% of patients had CRP ≥5 mg/L on admission, decreasing to 78.9% on Day 3. Similar findings were reported by Anush MM et al.[16], who observed a 52.5% reduction in CRP among survivors with parallel improvement in SOFA score. Likewise, Kumar C et al.[17] reported a 57.5% reduction in CRP by Day 5 among survivors, whereas non-survivors showed progressively increasing CRP levels. Jiang X et al.[18] also demonstrated that persistently elevated CRP trajectories were associated with the highest in-hospital mortality, supporting the role of CRP as an indicator of disease severity.

Serum LDH also showed a significant association with SOFA score on admission (p=0.04) and Day 3 (p=0.03). In the present study, 87.4% of patients had LDH ≥240 IU/L on admission, decreasing to 81.1% by Day 3. Lu J et al.[19] reported that elevated LDH was independently associated with 28-day mortality (HR 1.005; p=0.001), while Yu H et al.[20] found significantly higher in-hospital mortality among patients with elevated LDH in two large sepsis cohorts. Similarly, Prasad A et al.[21] demonstrated progressively increasing LDH levels with worsening disease severity, further supporting LDH as a useful marker of organ dysfunction in sepsis.

Pearson correlation analysis showed that both biomarkers were moderately correlated with SOFA score; however, LDH demonstrated a slightly stronger correlation than CRP on admission (r=0.48 vs. 0.42) and on Day 3 (r=0.44 vs. 0.39). These findings are consistent with those of Lu J et al.[19] and Prasad A et al.[21], who reported superior prognostic performance of LDH compared with conventional inflammatory markers. The present findings suggest

that although both biomarkers are valuable, LDH may better reflect the extent of organ dysfunction, whereas CRP primarily reflects systemic inflammation.

Overall, the present study indicates that serum LDH and CRP are simple, inexpensive, and readily available biomarkers that are significantly associated with SOFA score. Their combined assessment alongside SOFA scoring may improve early severity assessment and monitoring of patients with sepsis.

CONCLUSION

The present study demonstrated that both serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) were significantly associated with the Sequential Organ Failure Assessment (SOFA) score in patients with sepsis on admission and on the third day of hospitalization. Elevated levels of both biomarkers were associated with greater severity of organ dysfunction. Pearson correlation analysis showed that LDH had a slightly stronger correlation with SOFA score than CRP, suggesting that LDH may better reflect the extent of organ dysfunction. As both biomarkers are inexpensive, readily available, and routinely performed laboratory investigations, their combined assessment with SOFA score may be useful for early severity assessment and monitoring of patients with sepsis.

Limitations

1. The study was conducted at a single tertiary care centre with a relatively small sample size, which may limit the generalizability of the findings.
2. Biomarker assessment was limited to admission and the third day; longer follow-up could have provided additional information regarding disease progression and clinical outcomes.
3. Clinical outcomes such as long-term mortality and post-discharge prognosis were not evaluated.

Recommendations

1. Larger multicentre prospective studies should be conducted to validate the association of serum LDH and CRP with SOFA score across diverse patient populations.
2. Serial monitoring of serum LDH and CRP should be evaluated over longer follow-up periods to determine their role in predicting treatment response and prognosis.

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