Biomedical Journal of Indonesia
Journal Homepage: https://bji-fk.ejournal.unsri.ac.id

Relationship between C-Reactive Protein Levels and D-Dimer in Patients with Sepsis in the ICU of RSUD (Regional General Hospital) Prof. Dr. H. Aloei Saboe

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ARTICLE INFO

Keywords:
Coagulation
CRP
D-dimer
Inflammation
Sepsis

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.32539/BJI.v12i1.313

Received 2 January 2026;
Accepted 27 March 2026

ABSTRACT

Introduction. Sepsis remains a major global health problem with high incidence and mortality, including in Indonesia. One of the key factors contributing to sepsis-related mortality is the uncontrolled activation of inflammatory and coagulation pathways. C-reactive protein (CRP) serves as a marker of inflammation, while D-dimer reflects coagulation activation. Both biomarkers are commonly elevated in sepsis and are thought to be closely associated. This study aimed to evaluate the relationship between CRP and D-dimer levels in sepsis patients treated in the Intensive Care Unit (ICU) of RSUD Prof. Dr. H. Aloei Saboe. **Methods.** This analytic observational study employed a cross-sectional design and was conducted in the ICU of RSUD Prof. Dr. H. Aloei Saboe from July to November 2025. A total of 48 sepsis patients were included using total sampling based on medical record data from January to December 2024. The relationship between CRP and D-dimer levels was analyzed using the Pearson correlation test. **Results.** All patients showed elevated CRP levels (100%), and most had increased D-dimer levels (97.9%). Bivariate analysis demonstrated a statistically significant positive correlation between CRP and D-dimer levels, with a correlation coefficient of +0.333, indicating a weak to moderate association. **Conclusion.** There is a significant positive correlation between CRP and D-dimer levels in sepsis patients in the ICU of RSUD Prof. Dr. H. Aloei Saboe. Higher CRP levels tend to be accompanied by increased D-dimer levels, reflecting the interplay between inflammation and coagulation activation in sepsis.

1. Introduction

Sepsis continues to represent a serious global health concern because of its considerable impact on morbidity and mortality. Recent epidemiological estimates indicate that around 48.9 million individuals develop sepsis each year, resulting in approximately 11 million deaths worldwide, which corresponds to nearly one-fifth of total global mortality.[1] Although age-standardized rates of both incidence and mortality have gradually declined over recent decades, the disease still poses a significant burden on healthcare systems, particularly in low- and middle-income countries, including many regions across Asia.[2]

In the Indonesian healthcare setting, sepsis remains a significant contributor to in-hospital mortality. Current reports suggest that the prevalence of sepsis is around 30.29%, with mortality rates reported to reach nearly 49%.[3] However, regional data describing sepsis cases, particularly among patients treated in intensive care units, are still limited. In Gorontalo, published data on sepsis patients remain scarce, highlighting the need for hospital-based studies using recent clinical data.[4]

The poor clinical outcomes of sepsis are strongly linked to abnormalities in inflammatory and coagulation mechanisms. Sepsis triggers an exaggerated inflammatory response characterized by the increased release of mediators such as interleukin-6 and tumor necrosis factor-α, which may result in endothelial dysfunction and widespread damage to body tissues.[5] Concurrent activation of the coagulation cascade results in microthrombus formation, which further contributes to multiple organ dysfunction.[6]

CRP has long been utilized as a marker reflecting systemic inflammatory responses. In contrast, elevated D-dimer levels are generally interpreted as

evidence of ongoing coagulation and fibrinolytic activity.[7]. Previous studies have shown that both biomarkers are often increased in septic patients and may correlate with the severity of the condition among critically ill populations.[8]

Due to the continuing impact of sepsis and the limited availability of regional data, this research aims to investigate the correlation between C-reactive protein concentrations and D-dimer levels among patients with sepsis treated in the intensive care unit at RSUD Prof. Dr. H. Aloei Saboe.

2. Methods

This research employed an analytic observational study with a cross-sectional correlational design, which was conducted in the Intensive Care Unit (ICU) of RSUD Prof. Dr. H. Aloei Saboe in Gorontalo City from July to November 2025. The population of this study comprised all patients with a diagnosis of sepsis who were admitted to the ICU during that period.

A total sampling technique was applied. All sepsis patients who met the inclusion criteria and had complete laboratory data for C-reactive protein (CRP) and D-dimer examinations were included in the study. During the study period, 48 patients fulfilled the criteria and were included as study subjects.

The inclusion criteria were patients diagnosed with sepsis and treated in the ICU, aged ≥18 years, and having documented CRP and D-dimer laboratory results recorded during the early phase of ICU admission. The exclusion criteria were patients with incomplete medical records, missing CRP or D-dimer results, or laboratory measurements performed outside the initial ICU evaluation period. CRP and D-dimer levels were obtained from routine laboratory examinations recorded in the medical records. Both parameters were measured as part of the initial laboratory assessment during ICU treatment. Data collection was conducted using a structured documentation checklist to extract demographic and laboratory information from medical records.

This study focused on analyzing the correlation between two continuous variables, namely CRP levels and D-dimer levels, without assigning independent or dependent variable status. Statistical processing of the data was carried out using SPSS software. The normality of the variables was first evaluated using the Shapiro–Wilk test prior to conducting correlation analysis. Since the data followed a normal distribution, the relationship between CRP and D-dimer levels was analyzed using Pearson's correlation test. A p-value below 0.05 was considered indicative of statistical significance.

Ethical approval for this study was granted by the Health Research Ethics Committee of Universitas Negeri Gorontalo (Approval No. 060/UN47.B7/KE/2025, dated June 26, 2025). The confidentiality of patient-related data was strictly protected in line with ethical standards for medical research.

3. Results

3.1. Characteristics of Participants by Sex

Table 1 shows the distribution of participants by sex. Female patients constituted more than half of the study population, accounting for 26 participants (54.2%), while male patients comprised 22 participants (45.8%).

3.2. Characteristics of Participants by Age

Table 2 presents the age distribution of participants. The majority of patients were aged 45–64 years, totaling 27 participants (56.3%). This was followed by patients aged 65–74 years (22.9%), 25–44 years (12.5%), and 15–24 years (6.3%). Only one participant (2.1%) was aged 75 years or older.

3.3. Characteristics of Participants by Comorbid Diseases

Figure 3 shows that pneumonia and pulmonary tuberculosis were the most common comorbidities (each 20.8%), indicating respiratory tract infections as the primary source of sepsis. Type II diabetes mellitus (12.5%) and chronic kidney disease (10.4%) were also identified as metabolic and immunological risk factors. In addition, encephalopathy (8.3%), acute kidney failure (6.3%), and intracranial injury (6.3%) further worsened the critical condition of the participants. Other comorbidities such as cancer, hypertension, stroke, and gastric perforation also contributed to the severity of the clinical condition, although in smaller proportions.

3.4. Distribution of Data Based on C-Reactive Protein

Figure 4 shows the distribution of CRP levels among 48 participants with sepsis: all participants exhibited elevated CRP levels (48/48, 100%), whereas no participants had normal CRP levels (0%).

3.5. Distribution of Data Based on D-dimer

Figure 5 shows the distribution of D-dimer levels among 48 participants with sepsis, indicating that almost all participants had elevated D-dimer levels, totaling 47 participants (97.9%), while only 1 participant (2.1%) had normal D-dimer levels. These findings indicate an increase in D-dimer levels among patients with sepsis, reflecting coagulation system disorders and increased fibrinolytic activity in the majority of participants.

Table 1. Distribution of participants by sex (n = 48)

Sex	n	%
Female	26	54.2
Male	22	45.8

Table 2. Distribution of participants by age group (n = 48)

Age Group (years)	n	%
15–24	3	6.3
25–44	6	12.5
45–64	27	56.3
65–74	11	22.9
≥75	1	2.1

Table 3. Descriptive statistics of D-dimer levels and correlation with CRP among sepsis patients (n = 48)

Analysis Component	Value
D-dimer (µg/mL FEU)	
Mean ± SD	3029.29 ± 1791.38
Median (Min–Max)	2895.5 (338–7466)
Correlation Analysis (CRP vs D-dimer)	
Pearson correlation coefficient (r)	0.333
Coefficient of determination (R^2)	0.111
p-value	0.021

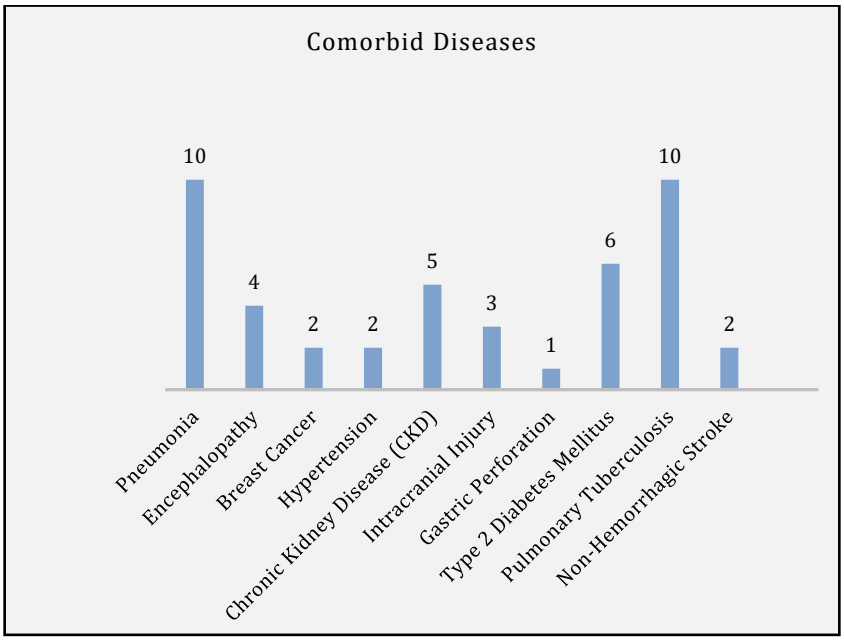

Figure 3. Comorbid diseases present in study participants

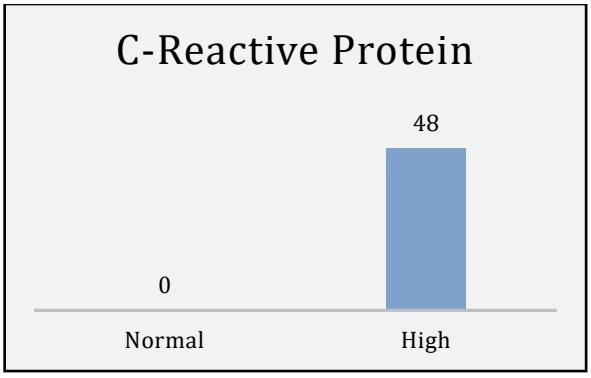

Figure 4. Distribution of C-reactive protein data in study participants

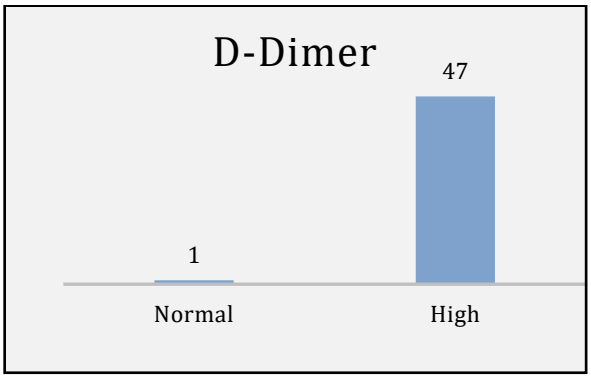

Figure 5. Distribution of D-dimer in study participants

3.6. Bivariate Analysis

Bivariate analysis revealed a significant correlation between CRP and D-dimer levels, as indicated by a p-value of 0.021 ($p < 0.05$). The obtained correlation coefficient (+0.333) reflects a positive association with weak to moderate magnitude, suggesting that elevated CRP levels are generally associated with higher D-dimer values. An R^2 value of 0.111 indicates that CRP contributes 11.1% to the variation in D-dimer levels, while the remaining variation is influenced by other factors.

Elevated D-dimer levels were observed among sepsis patients receiving treatment in the ICU, with a mean value of 3029.29 ± 1791.38 µg/mL FEU and a median of 2895.5 µg/mL FEU, with values ranging from 338 to 7466 µg/mL FEU. This elevation reflects increased activity of coagulation and fibrinolytic mechanisms in these patients. Subsequent analysis demonstrated a statistically significant positive relationship between CRP and D-dimer levels, with Pearson correlation revealing a weak to moderate positive association ($r = 0.333$; $p = 0.021$), with the coefficient of determination ($R^2 = 0.111$) indicating that approximately 11.1% of the variation in D-dimer levels could be explained by variations in CRP levels.

4. Discussion

Overall, patients with sepsis in the ICU of RSUD Prof. Dr. H. Aloei Saboe showed high CRP levels, with a mean value of 133.21 mg/L. This value indicates a massive acute-phase response due to severe infection and failure of the immune system to limit local inflammation, making CRP a crucial parameter for evaluating clinical status. All sepsis patients in this study (100%) demonstrated elevated CRP levels, indicating the presence of a strong inflammatory response. This response is triggered by the release of pro-inflammatory cytokines such as IL-6, IL-1β, and TNF-α, which promote substantial CRP synthesis in the liver. A pronounced rise in CRP may therefore have prognostic value, as it reflects uncontrolled infection that can increase the likelihood of death and complications related to coagulation abnormalities, such as Disseminated Intravascular Coagulation. [9,10]

From a pathophysiological perspective, intense inflammatory responses during sepsis promote endothelial injury and stimulate coagulation through tissue factor expression, leading to increased fibrin formation and D-dimer levels. This confirms that the participants were in the phase of severe sepsis or septic shock.[11,12]

The present study found that 97.9% of sepsis patients treated in the ICU of RSUD Prof. Dr. H. Aloei Saboe had increased D-dimer levels, indicating a high prevalence of hypercoagulability and immunothrombotic processes in these patients. Comparable observations have been reported in earlier studies involving critically ill patients with sepsis. According to K. M. Rudd, abnormalities in the coagulation system are commonly encountered in severe sepsis and are closely associated with organ failure and mortality.[13] In addition, Toshiaki Iba and Jerrold H. Levy described that excessive coagulation activation during sepsis contributes to the development of immunothrombosis and microvascular clot formation, which is reflected by increased circulating D-dimer levels.[14] Supporting this observation, Francesco Valerio and colleagues reported that persistently elevated D-dimer levels were more commonly detected in non-surviving sepsis patients, highlighting their potential prognostic value in critical illness.[15]

Pathophysiologically, excessive release of pro-inflammatory cytokines during sepsis induces tissue factor expression on endothelial cells and monocytes, initiating widespread fibrin formation and microthrombus development.[16] Subsequent fibrin degradation results in increased circulating D-dimer levels, which serve as indicators of diffuse coagulation activation and an increased risk of disseminated intravascular coagulation (DIC). Therefore, elevated D-dimer levels provide clinically relevant information regarding coagulation disturbances commonly observed in patients with sepsis.

The analysis using Pearson correlation revealed a statistically significant positive relationship between CRP and D-dimer levels ($r = 0.333$; $p < 0.05$). This result reflects a weak to moderate association between inflammatory and coagulation biomarkers among sepsis patients.[17] Although an increase in CRP levels tends to occur alongside elevated D-dimer levels, the strength of this relationship is relatively modest. In addition, the coefficient of determination ($R^2 = 0.111$) indicates that CRP explains only 11.1%

of the variation in D-dimer concentrations, suggesting that most of the variability may be attributed to other clinical or biological factors that were not examined in this research.[18]

Consequently, the correlation identified in this study should be interpreted as a descriptive association rather than as evidence of a causal or predictive link between CRP and D-dimer. Although both biomarkers represent interconnected inflammatory and coagulation responses in sepsis, the weak to moderate correlation observed indicates that coagulation activation in critically ill patients is influenced by multiple factors. These results are in line with previous studies that have reported statistically significant yet relatively modest relationships between inflammatory and coagulation markers in sepsis and other severe infections. Such findings highlight that the complex pathophysiology of sepsis cannot be adequately explained by a single biomarker across different patient populations.[19]

Elevated CRP levels are associated with the release of pro-inflammatory cytokines, particularly IL-6, which initiate the acute-phase inflammatory response. In addition, these cytokines can induce endothelial damage and stimulate tissue factor expression, thereby activating the extrinsic coagulation cascade. This activation promotes fibrin deposition and microthrombus formation, which are later degraded by the fibrinolytic pathway, producing increased levels of D-dimer. The positive relationship between CRP and D-dimer thus reflects the dynamic interplay between inflammation and coagulation mechanisms in sepsis. Such interactions contribute to disease progression and are linked to the development of coagulopathy, organ failure, and higher mortality risk. Therefore, evaluating both biomarkers simultaneously may have important implications for clinical assessment.[20]

CRP synthesis in hepatocytes is primarily mediated through the STAT3 signaling pathway in response to interleukin-6, representing a key mechanism of CRP production in both acute and chronic inflammatory states.[21] In addition to infection, various host-related factors such as obesity and elevated body mass index may contribute to higher CRP levels, as adipose tissue functions as a source of pro-inflammatory cytokines.[22] Other factors, including advanced age through the process of inflammaging, female sex related to hormonal influences, smoking habits, and chronic conditions such as diabetes mellitus and chronic kidney disease, have also been reported to influence baseline CRP concentrations. Conversely, regular physical activity has been associated with lower CRP and IL-6 levels, reflecting reduced systemic inflammation. [23]

However, it is important to acknowledge that these factors were not analyzed using multivariate statistical methods in the present study. As a result, the individual contribution of age, metabolic conditions, renal disease, cardiovascular comorbidities, and lifestyle factors to CRP levels could not be independently assessed. Therefore, the observed CRP levels should be interpreted as reflecting overall inflammatory status rather than the effect of specific contributing factors. Future studies employing multivariate analysis are needed to better elucidate the relative influence of these variables on inflammatory markers in patients with sepsis.

Elevated D-dimer levels occur in acute thromboembolic conditions as a marker of fibrin breakdown, in cancer as an independent procoagulant state due to tissue factor expression by tumor cells. Postoperative conditions also lead to increased D-dimer levels as a response to tissue trauma, while in inflammatory conditions such as sepsis, this increase reflects the phenomenon of immunothrombosis.[24] Physiological conditions such as advanced age and pregnancy, as well as chronic liver and kidney diseases, may also impair D-dimer clearance. External factors, including the use of anticoagulants, thrombolytic agents, and strenuous physical activity, can transiently affect D-dimer levels; therefore, clinical interpretation must be performed with caution.[25] Given the numerous confounding factors influencing CRP and D-dimer levels, this study has limitations related to its cross-sectional design. Single-time measurements in patients with sepsis without inclusion of SOFA scores limit the ability to assess therapeutic response dynamics and the comprehensive relationship between clinical biomarkers.

5. Conclusion

The present study demonstrates that most sepsis patients treated in the ICU of RSUD Prof. Dr. H. Aloei Saboe exhibited elevated CRP levels, along with increased D-dimer values in many cases. Statistical analysis showed a significant positive relationship between CRP and D-dimer levels; however, the correlation strength was considered weak to moderate. These findings indicate that markers of inflammation and coagulation often increase concurrently in sepsis, although this association does not imply a causal or predictive linkage. The results further underline the presence of both inflammatory responses and coagulation disturbances in septic patients. From a clinical standpoint, the combined evaluation of CRP and D-dimer may assist in providing additional insight into the inflammatory and coagulation status of critically ill patients when considered alongside clinical assessment and other laboratory parameters. Future research is recommended to employ longitudinal study designs with serial measurements of CRP and D-dimer at multiple time points during ICU treatment, such as at admission, 24–48 hours, and during the course of clinical improvement or deterioration. Incorporating larger sample sizes, multivariate analytical approaches, and clinical severity scores (e.g., SOFA) would allow for better adjustment of confounding

factors and a more comprehensive understanding of the dynamic relationship between inflammation and coagulation in sepsis.

6. Author Contribution

The primary author (P.N.Y) carried out the research process, conducted statistical analysis, and prepared the manuscript draft. Supervision and conceptual input were provided by R.P. and Z.K.Y., who also performed critical revisions of the manuscript. S.R. and A.D.I.K. assisted in methodological considerations, interpretation of the data, and evaluation of the manuscript. The final version of the manuscript was reviewed and approved by all authors.

7. Acknowledgements

The authors would like to acknowledge RSUD Prof. Dr. H. Aloei Saboe, Gorontalo, for facilitating access to the medical record data required for this research. Appreciation is also extended to all individuals and institutions who offered assistance and support throughout the conduct of this study.

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