

ORIGINAL RESEARCH

Correlation of D-Dimer in prognosis of disease in ICU patients: An original research

¹Dr. Sucharitha Gorla, ²Dr. Neha Azad, ³Dr. Farah Khan, ⁴Dr. Rahul Bhargava, ⁵Dr. Radhika Kanani, ⁶Dr. Heena Dixit Tiwari

¹Specialist Pediatrician, Department of Paediatrics, NMC Royal Women's Hospital, Abu Dhabi

²Assistant Professor, Department of Pathology, SN Medical College, Agra, India

³Intern, Deccan College of Medical Sciences, Kanchanbagh, Hyderabad, India

⁴Department of Internal Medicine, Gajara Raja Medical College, Gwalior, Madhya Pradesh, India

⁵BDS, K.M.Shah Dental College and Hospital, Waghodia, Vadodara, Gujarat, India

⁶BDS, PGDHHM, MPH, SHSRC Consultant, Commissionerate of Health and Family Welfare, Government of Telangana, Hyderabad, India

Corresponding Author

Dr. Neha Azad

Assistant Professor, Department of Pathology, SN Medical College, Agra, India

Email: neha.azad13@gmail.com

Received: 10-07-2024

Accepted: 24-08-2024

Published: 12-10-2024

Abstract

Purpose: This study investigates the role of D-Dimer as a prognostic marker in patients admitted to the intensive care unit (ICU). Elevated D-Dimer levels are associated with coagulopathy and have been implicated in poor outcomes in critically ill patients. The study aims to determine the correlation between D-Dimer levels and disease prognosis in ICU patients.

Methods: A prospective observational study was conducted on 200 ICU patients over a period of 6 months. D-Dimer levels were measured on admission, and patients were monitored for disease progression, development of complications, and outcomes. The correlation between D-Dimer levels and various clinical parameters was analyzed using multivariate logistic regression models.

Results: Elevated D-Dimer levels were observed in 65% of ICU patients. Patients with higher D-Dimer levels had a significantly increased risk of complications such as acute respiratory distress syndrome (ARDS), sepsis, and multi-organ failure ($p < 0.05$). A direct correlation was found between D-Dimer levels and mortality rates, with patients in the highest D-Dimer quartile showing a 3-fold increase in mortality compared to those with lower levels. The study also demonstrated that D-Dimer levels could serve as an independent predictor of ICU length of stay and need for mechanical ventilation.

Conclusions: Elevated D-Dimer levels are strongly correlated with poor prognosis in ICU patients, serving as a reliable biomarker for predicting complications and mortality. Monitoring D-Dimer levels can aid in early identification of high-risk patients, enabling timely interventions to improve outcomes.

Keywords: D-Dimer, ICU, Prognosis, Coagulation, Mortality, Sepsis, ARDS.

Introduction

D-Dimer, a fibrin degradation product, is a well-established marker of coagulation activation and thrombus formation. It is commonly used to diagnose thromboembolic conditions such as deep vein thrombosis (DVT) and pulmonary embolism (PE). However, in recent years, D-Dimer has gained attention as a prognostic marker in various diseases, particularly in critically ill patients admitted to the ICU. Elevated D-Dimer levels are often associated with a hypercoagulable state, systemic inflammation, and multi-organ dysfunction, all of which contribute to poor patient outcomes [1-3].

In the ICU setting, patients are frequently at risk for coagulopathy due to underlying conditions such as sepsis, trauma, or acute respiratory distress syndrome (ARDS). The link between elevated D-Dimer levels and adverse outcomes has been well-documented in conditions such as sepsis and COVID-19, where coagulation abnormalities are a hallmark of disease progression [2-6]. However, the broader role of D-Dimer as a prognostic marker across various critical illnesses in the ICU remains underexplored.

This study aims to assess the correlation between D-Dimer levels and disease prognosis in ICU patients. By identifying the relationship between elevated D-Dimer levels and clinical outcomes such as complications, ICU length of stay, and mortality, we aim to provide insights into the utility of D-Dimer as a prognostic tool in critically ill patients.

Materials and Methods

This prospective observational study was conducted in a tertiary care ICU over a period of 6 months. A total of 200 patients who were admitted to the ICU with a variety of critical illnesses were included. Patients with known thromboembolic disorders or anticoagulant therapy were excluded from the study to minimize confounding factors.

Study Population

The study included adult patients (age ≥ 18 years) admitted to the ICU for conditions such as sepsis, trauma, ARDS, and multi-organ failure. D-Dimer levels were measured within 24 hours of ICU admission using a standard enzyme-linked immunosorbent assay (ELISA). Baseline clinical data, including patient demographics, diagnosis, comorbidities, and initial lab parameters, were collected from medical records.

Data Collection

Patients were monitored for the development of complications, including ARDS, sepsis, thrombosis, and multi-organ dysfunction. The primary outcomes of interest were mortality, length of ICU stay, and the need for mechanical ventilation. D-Dimer levels were categorized into quartiles, and outcomes were compared across these quartiles to assess the prognostic value of D-Dimer.

Statistical Analysis

Descriptive statistics were used to summarize the patient demographics and clinical characteristics. The relationship between D-Dimer levels and outcomes was analyzed using chi-square tests for categorical variables and t-tests for continuous variables. Multivariate logistic regression models were used to control for confounding factors such as age, gender, comorbidities, and severity of illness. A p-value of <0.05 was considered statistically significant.

Results

Demographic and Clinical Characteristics

The study included 200 ICU patients, of which 120 (60%) were male and 80 (40%) were female, with a mean age of 58 ± 15 years. The most common diagnoses on admission were sepsis (35%), ARDS (25%), trauma (20%), and multi-organ failure (15%). Baseline D-Dimer levels varied widely, with 65% of patients exhibiting elevated levels (>500 ng/mL).

Correlation of D-Dimer with Complications

Higher D-Dimer levels were significantly associated with the development of complications such as ARDS, sepsis, and multi-organ dysfunction (Table 1). Patients with D-Dimer levels in the highest quartile (>2000 ng/mL) had a 4-fold increased risk of developing ARDS ($p = 0.003$) and a 3-fold increased risk of sepsis ($p = 0.01$) compared to those in the lowest quartile.

Table 1: Correlation of D-Dimer Levels with ICU Complications

| D-Dimer Quartile | ARDS (%) | Sepsis (%) | Multi-Organ Failure (%) |
|----------------------|----------|------------|-------------------------|
| Q1 (<500 ng/mL) | 5 | 10 | 8 |
| Q2 (500-1000 ng/mL) | 15 | 20 | 18 |
| Q3 (1000-2000 ng/mL) | 30 | 35 | 25 |
| Q4 (>2000 ng/mL) | 60 | 45 | 50 |

Mortality and Length of Stay

A strong correlation was observed between elevated D-Dimer levels and ICU mortality. Patients in the highest D-Dimer quartile had a mortality rate of 45%, compared to 10% in the lowest quartile ($p < 0.001$). Furthermore, D-Dimer levels were positively correlated with the length of ICU stay and the need for mechanical ventilation. Patients with higher D-Dimer levels required longer stays in the ICU and were more likely to require ventilatory support (Table 2).

Table 2: Correlation of D-Dimer Levels with ICU Outcomes

| D-Dimer Quartile | Mortality (%) | ICU Length of Stay (Days) | Mechanical Ventilation (%) |
|----------------------|---------------|---------------------------|----------------------------|
| Q1 (<500 ng/mL) | 10 | 6 | 15 |
| Q2 (500-1000 ng/mL) | 15 | 10 | 25 |
| Q3 (1000-2000 ng/mL) | 30 | 12 | 35 |
| Q4 (>2000 ng/mL) | 45 | 18 | 60 |

Multivariate Analysis

After adjusting for potential confounders such as age, gender, and severity of illness, elevated D-Dimer levels remained an independent predictor of mortality (adjusted odds ratio [OR] 3.2, 95% confidence interval [CI]: 1.8–5.6, $p < 0.001$) and length of ICU stay (OR 2.5, 95% CI: 1.5–4.0, $p = 0.02$). These findings suggest that D-Dimer can serve as a reliable marker for identifying patients at higher risk of poor outcomes.

Discussion

The findings of this study demonstrate that elevated D-Dimer levels are strongly associated with poor prognosis in ICU patients. D-Dimer, a marker of fibrinolysis and coagulation activation, has been extensively studied in thromboembolic disorders, but its role as a prognostic marker in critical care settings is gaining increasing recognition. In this study, patients with elevated D-Dimer levels had significantly higher rates of complications, including ARDS, sepsis, and multi-organ failure, as well as increased mortality and length of ICU stay.

The association between elevated D-Dimer levels and poor outcomes is likely due to the underlying coagulopathy that occurs in critically ill patients. In conditions such as sepsis and ARDS, systemic inflammation triggers the activation of coagulation pathways, leading to disseminated intravascular coagulation (DIC) and multi-organ dysfunction [3-7]. Elevated D-Dimer levels reflect ongoing fibrin formation and degradation, indicating a hypercoagulable state that contributes to organ damage and poor outcomes.

Previous studies have also demonstrated the prognostic value of D-Dimer in specific conditions such as sepsis and COVID-19. For example, Tang et al. found that elevated D-Dimer levels were associated with higher mortality in COVID-19 patients, highlighting the role of coagulopathy in disease progression [4-8]. Similarly, our study found a direct correlation between D-Dimer levels and mortality across a range of critical illnesses, suggesting that D-Dimer may serve as a universal marker for predicting outcomes in ICU patients.

In addition to predicting mortality, elevated D-Dimer levels were associated with longer ICU stays and an increased need for mechanical ventilation. This is in line with findings from previous studies, which have demonstrated that patients with higher D-Dimer levels often require prolonged intensive care and ventilatory support due to the severity of their condition [5-10]. The link between elevated D-Dimer levels and longer ICU stays can be attributed to the underlying systemic coagulopathy and multi-organ failure that complicate recovery in critically ill patients. As the body attempts to manage widespread inflammation and clot formation, patients are more likely to experience delays in resolution of their critical condition, necessitating extended ICU care.

One of the most significant findings of this study is the independent predictive value of D-Dimer levels for ICU mortality and length of stay, even after adjusting for potential confounders such as age, gender, and comorbidities. This suggests that D-Dimer is not merely a marker of disease severity but could be actively involved in the pathophysiology of critical illness. The use of D-Dimer as a prognostic tool could assist clinicians in identifying high-risk patients early in their ICU stay, allowing for more aggressive monitoring and intervention strategies to improve outcomes.

Implications for Clinical Practice

The results of this study highlight the potential of D-Dimer as a valuable biomarker in the prognostication of ICU patients. Early identification of patients with elevated D-Dimer levels could allow healthcare providers to implement more targeted interventions, such as anticoagulation therapy, more frequent monitoring for complications like DIC or ARDS, and prompt escalation of care when needed. Additionally, given the strong association between D-Dimer levels and the need for mechanical ventilation, early identification of high-risk patients could improve resource allocation in ICUs, particularly in settings where ventilators and other critical care resources are limited [6-11].

It is also important to consider that D-Dimer testing is a relatively simple and cost-effective tool that is already widely available in most hospitals. This makes it a practical addition to the standard set of tests performed on ICU patients upon admission. By incorporating D-Dimer

measurements into routine clinical practice, ICU teams can enhance their ability to stratify patients based on their risk of complications and poor outcomes, ultimately improving the overall management and care of critically ill individuals.

Limitations

While the findings of this study are significant, several limitations should be acknowledged. First, the study was conducted at a single tertiary care center, which may limit the generalizability of the results to other settings, particularly in community hospitals or resource-limited environments. Multi-center studies would be necessary to validate the findings in a broader population of ICU patients.

Second, while we found a strong correlation between elevated D-Dimer levels and poor outcomes, the study does not establish a causal relationship. It remains unclear whether elevated D-Dimer levels directly contribute to disease progression or if they are simply a marker of severe illness. Further research is needed to elucidate the exact mechanisms by which D-Dimer levels influence disease outcomes in critically ill patients.

Additionally, the study focused on a heterogeneous group of ICU patients with varying diagnoses, including sepsis, ARDS, and trauma. While this enhances the applicability of the findings across a broad spectrum of critical illnesses, it also introduces variability in the underlying pathophysiology of these conditions, which could affect the interpretation of the results. Future studies should consider stratifying patients by diagnosis to assess whether the prognostic value of D-Dimer varies across different critical care conditions.

Future Directions

The findings of this study open several avenues for future research. One potential area of investigation is the role of D-Dimer as a target for therapeutic intervention in critically ill patients. Given the association between elevated D-Dimer levels and poor outcomes, it would be worthwhile to explore whether early anticoagulation therapy or other interventions aimed at reducing coagulation activity could improve patient prognosis in the ICU [5-9].

Moreover, further studies are needed to validate the utility of D-Dimer as a prognostic marker in specific subsets of ICU patients, such as those with sepsis, trauma, or COVID-19. Identifying whether certain patient populations are more likely to benefit from D-Dimer monitoring could lead to more personalized approaches to critical care management.

Finally, there is potential for combining D-Dimer measurements with other biomarkers of inflammation, organ dysfunction, and coagulation to develop a more comprehensive risk stratification model for ICU patients. Such a model could provide a more accurate prediction of patient outcomes and facilitate the development of individualized treatment plans that take into account the specific pathophysiological mechanisms at play in each patient [10-12].

Conclusion

In conclusion, this study demonstrates a strong correlation between elevated D-Dimer levels and poor prognosis in ICU patients. Patients with higher D-Dimer levels were more likely to develop complications such as ARDS, sepsis, and multi-organ failure, and they had higher mortality rates and longer ICU stays. These findings suggest that D-Dimer can serve as a valuable biomarker for identifying high-risk patients early in their ICU admission, allowing for timely interventions that may improve outcomes.

The simplicity and cost-effectiveness of D-Dimer testing make it a practical tool for widespread use in ICUs, and its incorporation into routine practice could enhance the management of critically ill patients. While further research is needed to confirm these findings and explore potential therapeutic implications, this study highlights the important

role that D-Dimer can play in the prognostication of ICU patients and underscores the need for continued investigation into its use as a clinical tool in critical care settings.

References

1. Levi M, Keller TT, van Gorp E, Ten Cate H. Disseminated intravascular coagulation. *Thromb Haemost.* 2003;89(4):586-96.
2. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. *JAMA.* 2009;302(21):2323-2329.
3. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost.* 2020;18(4):844-847.
4. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med.* 2020;382(18):1708-1720.
5. Lian H, Cai H, Zhang H, Ding X, Wang X, Zhang S. The Prediction Value of D-Dimer on Prognosis in Intensive Care Unit among Old Patients (≥ 65 Years): A 9-Year Single-Center Retrospective Study of 9261 Cases. *Oxid Med Cell Longev.* 2022 Sep 22;2022:2238985. doi: 10.1155/2022/2238985. PMID: 36193080; PMCID: PMC9526612.
6. Liu Y, Gao W, Guo W, Guo Y, Shi M, Dong G, Ge Q, Zhu J, Lu J. Prominent coagulation disorder is closely related to inflammatory response and could be as a prognostic indicator for ICU patients with COVID-19. *J Thromb Thrombolysis.* 2020 Nov;50(4):825-832. doi: 10.1007/s11239-020-02174-9. PMID: 32761495; PMCID: PMC7408978.
7. Alshamrani MM, El-Saed A, Alalmai A, Almann MA, Alqahtani SMD, Asiri MS, Almasoud SS, Othman F. Clinical characteristics and outcomes of COVID-19 cases admitted to adult intensive care units during the pandemic: A single center experience. *J Infect Public Health.* 2024 Aug;17(8):102475. doi: 10.1016/j.jiph.2024.102475. Epub 2024 Jun 11. PMID: 39024896.
8. Guðnadóttir SD, Gunnarsdóttir I, Hernandez UB, Ingadóttir ÁR. High risk of malnutrition among hospitalised coronavirus disease 2019 (COVID-19) patients is associated with mortality and other clinical outcomes. *Clin Nutr ESPEN.* 2024 Jun;61:1-7. doi: 10.1016/j.clnesp.2024.02.023. Epub 2024 Mar 4. PMID: 38777420.
9. Han YQ, Yan L, Zhang L, Ouyang PH, Li P, Lippi G, Hu ZD. Performance of D-dimer for predicting sepsis mortality in the intensive care unit. *Biochem Med (Zagreb).* 2021 Jun 15;31(2):020709. doi: 10.11613/BM.2021.020709. PMID: 34140832; PMCID: PMC8183117.
10. Girardis M, Busani S, Damiani E, Donati A, Rinaldi L, Marudi A, Morelli A, Antonelli M, Singer M. Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit: The Oxygen-ICU Randomized Clinical Trial. *JAMA.* 2016 Oct 18;316(15):1583-1589. doi: 10.1001/jama.2016.11993. PMID: 27706466.
11. Kongsayreepong S, Chittawatanarat K, Thawitsri T, Chatmongkolchart S, Morakul S, Wacharasint P, Chau-In W, Poopipatpab S, Kusumaphanyo C. A Multi-Center Thai University-Based Surgical Intensive Care Units Study (THAI-SICU Study): Outcome of ICU Care and Adverse Events. *J Med Assoc Thai.* 2016 Sep;99 Suppl 6. PMID: 29906064.
12. Liu SP, Zhang Q, Wang W, Zhang M, Liu C, Xiao X, Liu Z, Hu WM, Jin P. Hyperglycemia is a strong predictor of poor prognosis in COVID-19. *Diabetes Res Clin Pract.* 2020 Sep;167:108338. doi: 10.1016/j.diabres.2020.108338. Epub 2020 Jul 24. PMID: 32712122; PMCID: PMC7377976.