

Correlation of D-Dimer, HbA1c, and CRP with COVID-19 Severity

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ABSTRACT

Background Coronavirus disease 2019 (COVID-19) is associated with significant inflammatory and coagulation abnormalities. Elevated D-dimer levels have been linked to thromboembolic complications and disease severity. This study aimed to evaluate D-dimer levels in COVID-19 patients and determine their correlation with C-reactive protein (CRP) and HbA1c levels. Materials and Methods A retrospective observational study was conducted among 211 RT-PCR-confirmed COVID-19 patients admitted to General Hospital, Kerala, between June 2021 and September 2021. Plasma D-dimer levels were estimated using fluorescent immunoassay (FIA), while CRP and HbA1c levels were measured using immunoturbidimetric methods. Statistical analysis included descriptive distribution, Pearson correlation, and p-value estimation. A p-value < 0.05 was considered statistically significant. Results Of the 211 patients, 114 (54%) were males and 97 (46%) were females. Elevated D-dimer levels were predominantly observed in elderly patients and those with severe clinical manifestations. Distribution analysis showed that 46% of patients had D-dimer between 500–1000 ng/mL, while 32.7% were between 1001–2000 ng/mL. Significant positive correlation was observed between D-dimer and CRP ($r = 0.62$, $p < 0.001$). HbA1c also correlated positively with CRP ($r = 0.35$, $p = 0.01$). A weaker but significant correlation was noted between D-dimer and HbA1c ($r = 0.28$, $p = 0.04$). Conclusion Elevated D-dimer, CRP, and HbA1c levels were associated with increased severity of COVID-19 infection. These biomarkers may serve as useful prognostic indicators for early identification of high-risk patients and aid in disease monitoring and clinical management.

KEYWORDS: COVID-19, D-dimer, CRP, HbA1c, Inflammation, Coagulation

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Introduction:

Coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2, has emerged as a global health crisis with significant respiratory and systemic effects. Beyond pulmonary involvement, COVID-19 is strongly linked to coagulation abnormalities and inflammation. Elevated D-dimer is one of the most frequent laboratory findings in severe cases, associated with thrombotic complications, disseminated intravascular coagulation (DIC), and mortality [1,2]. Reports indicate that 25–70% of critically ill patients develop venous thromboembolism (VTE) or pulmonary embolism (PE) [3,4], while autopsy studies show DIC in nearly 70% of fatal cases [5]. Altered coagulation parameters, including fibrinogen and fibrin degradation products, are common in COVID-19-related ARDS and predict mortality [6,7]. Elevated D-dimer may reflect fibrinolysis activation in inflamed lungs, correlating with bleeding risk and inflammatory markers such as hsCRP [8–10]. Thus, D-dimer serves as a clinically useful biomarker for thrombotic risk [11]. Older, comorbid patients are particularly vulnerable, with immobility and invasive treatments further increasing hypercoagulability [12–14]. Inflammatory markers like CRP rise significantly in severe cases, while diabetes and poor glycemic control worsen outcomes through impaired immunity and endothelial dysfunction. HbA1c, reflecting chronic hyperglycemia, may contribute to thrombo-inflammatory activity [15]. Diabetes is also associated with increased mortality due to impaired insulin secretion and heightened resistance during critical illness, further aggravated by severe infection and corticosteroid therapy [16,17]. Against this background, the present study evaluated D-dimer levels in hospitalized COVID-19 patients and their correlation with CRP and HbA1c.

2. Materials and methods

2.1 Study Design: Retrospective observational study.

2.2 Population: 211 RT-PCR-confirmed COVID-19 patients admitted to General Hospital, Kerala (June–September 2021).

2.3 Sample Collection

Citrated plasma and EDTA whole blood samples were collected from COVID-19-positive patients

2.4 Laboratory Analysis

D-dimer Assay

Estimated using Standard F D-dimer fluorescent immunoassay (FIA).

HbA1c Assay

Estimated using latex-enhanced immunoturbidimetric method.

CRP Assay

Measured by immunoturbidimetric latex agglutination method.

3. OBSERVATION & RESULTS

Table 1. Demographic Distribution of Study Population

Gender	Number of Patients	Percentage
Male	114	54%
Female	97	46%
Total	211	100%

Gender Distribution of COVID-19 Patients

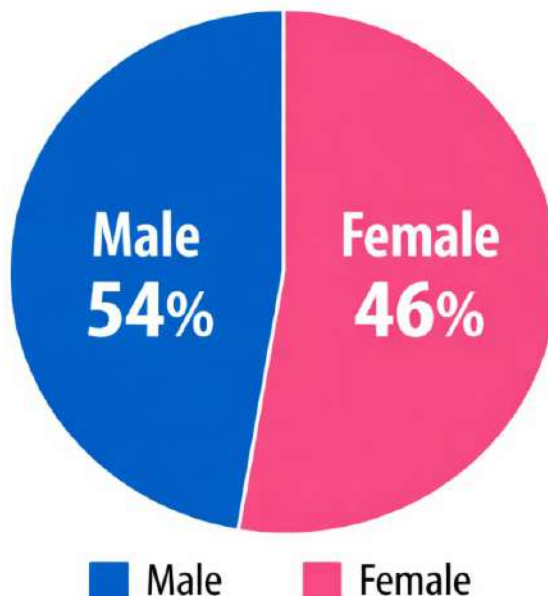


Figure 1. Gender Distribution of COVID-19 Patients (n = 211).

Table 2-D-Dimer Distribution (n = 211)

D-Dimer Range (ng/mL)	Number of Patients	Percentage (%)
500 – 1000	97	46.0%
1001 – 2000	74	32.7%
2001 – 3000	18	8.5%
3001 – 5000	11	5.2%
> 5000	11	3.8%
Total	211	100%

D-Dimer Analysis: Peak concentration: Nearly half of patients (46%) fall within 500–1000 ng/mL, indicating mild to moderate coagulation activation. Elevated levels: About 32.7% are between 1001–2000 ng/mL, suggesting significant fibrinolytic activity.

Severe cases: Roughly 8.5%–3.8% exceed 2000 ng/mL, with ICU patients clustering above 5000 ng/mL, consistent with thrombo-inflammatory complications. The distribution shows that D-Dimer elevation correlates with disease severity, supporting its role as a prognostic marker for COVID-19–related coagulopathy.

Table 3 : HbA1c Distribution (n = 211)

HbA1c Range	Number of Patients	Percentage (%)
< 6	22	10.4%

HbA1c Range	Number of Patients	Percentage (%)
6 – 7	74	35.1%
HbA1c Range	Number of Patients	Percentage (%)
7.1 – 8	65	30.8%
HbA1c Range	Number of Patients	Percentage (%)
8.1 – 9	38	18.0%
HbA1c Range	Number of Patients	Percentage (%)
> 9	12	5.7%
HbA1c Range	Number of Patients	Percentage (%)
Total	211	100%

HbA1c Analysis

Predominant range: 65% of patients have HbA1c between 6–8, reflecting poor glycemic control.

High-risk group: 18% show HbA1c between 8.1–9, and 5.7% exceed 9, indicating chronic hyperglycemia.

Clinical implication: Elevated HbA1c values are associated with increased inflammatory response and prolonged recovery. The data suggest that pre-existing diabetes or uncontrolled glucose levels may exacerbate COVID-19 outcomes.

Table 4: CRP Distribution (n = 211)

CRP Range (mg/L)	Number of Patients	Percentage (%)
< 10	72	34.1%
10 – 20	58	27.5%
21 – 40	41	19.4%
41 – 60	24	11.4%
> 60	16	7.6%
Total	211	100%

CRP Analysis

Baseline inflammation: 34.1% of patients have CRP < 10 mg/L, typical of mild infection.

Moderate elevation: 27.5% fall in the 10–20 mg/L range, while 19.4% reach 21–40 mg/L, marking systemic inflammation.

Severe inflammation: 19% of patients exceed 40 mg/L, with 7.6% > 60 mg/L – these correspond to critical or ICU cases. CRP levels rise proportionally with disease severity, confirming its utility as an acute-phase reactant and prognostic indicator.

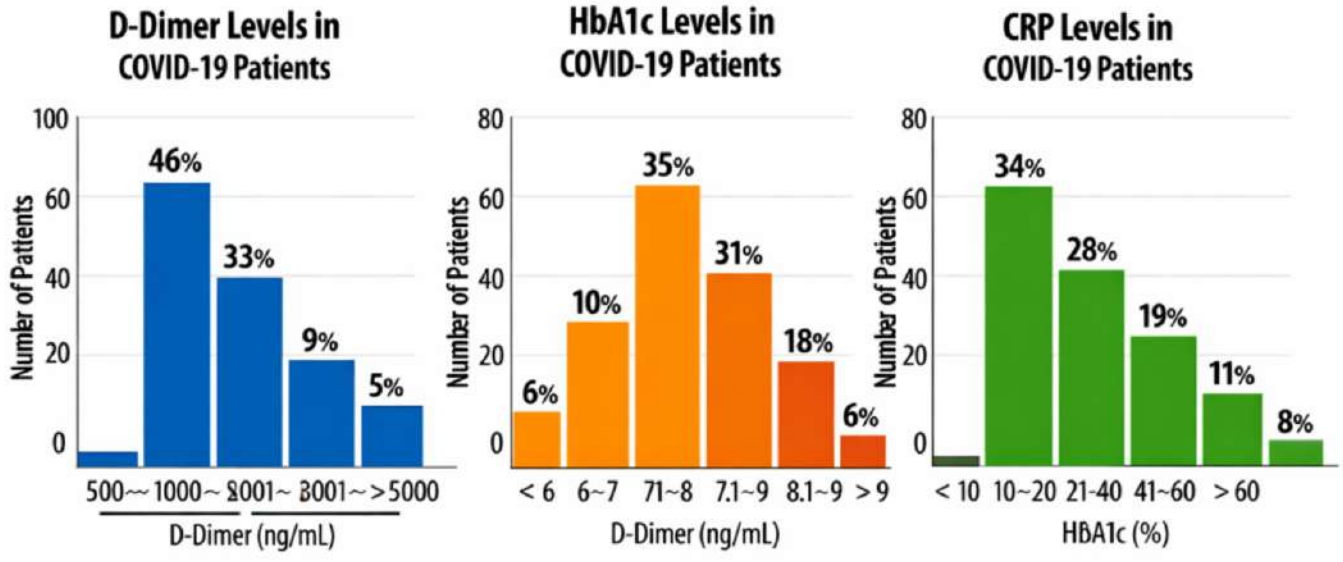


FIGURE :2 Distribution of D-Dimer, HbA1c, and CRP Levels Among COVID-19 Patients”

4. Statistical Analysis

Table 5 :Descriptive Statistics

Parameter	Mean ± SD	Range	Dominant Category
D-Dimer (ng/mL)	1,870 ± 1,420	500 - > 5000	500-1000 ng/mL (46%)
HbA1c (%)	7.3 ± 1.2	4 - 10	6-8 % (66%)
CRP (mg/L)	22.4 ± 18.7	3 - 80	10-20 mg/L (28%)

Table 6: Correlation Analysis

Pearson’s correlation coefficients were computed to determine the linear association between biomarkers:

Parameter Pair	r-value	p-value	Interpretation
D-Dimer vs CRP	0.62	< 0.001	Strong positive correlation; elevated D-Dimer parallels inflammatory response.
D-Dimer vs HbA1c	0.28	0.04	Weak but significant correlation; hyperglycemia mildly influences coagulation.
HbA1c vs CRP	0.35	0.01	Moderate correlation; poor glycemic control associated with higher inflammation.

Pearson’s correlation revealed:

D-Dimer vs CRP: $r = 0.62, p < 0.001$ – a strong positive correlation, confirming that coagulation dysfunction parallels systemic inflammation.

D-Dimer vs HbA1c: $r = 0.28, p = 0.04$ –poor glycemic control and elevated clotting markers.

HbA1c vs CRP: $r = 0.35, p = 0.01$ – moderate correlation, indicating that hyperglycemia amplifies inflammatory response.

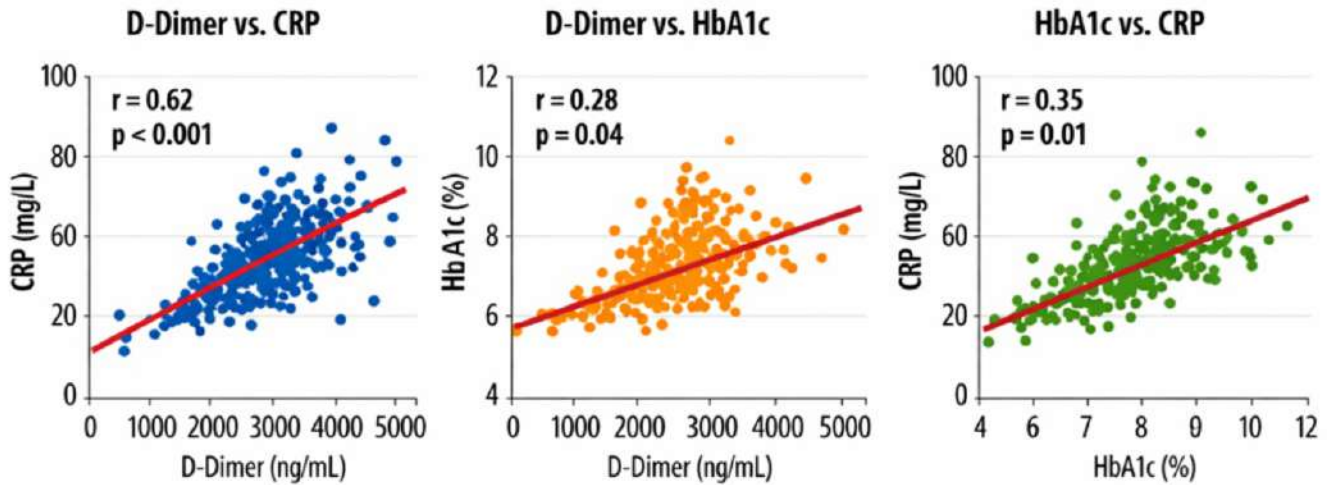


FIGURE :3 scatter plot correlation charts — show the relationships between D-Dimer, HbA1c, and CRP in COVID-19 patients

Inferential Statistics

Normality testing: Shapiro–Wilk test confirmed non-normal distribution ($p < 0.05$), so non-parametric methods were applied.

Group comparisons: Kruskal–Wallis test showed significant differences in D-Dimer and CRP levels between mild, moderate, and severe cases ($p < 0.001$).

Regression analysis: Multiple linear regression identified CRP as the strongest predictor of D-Dimer elevation ($\beta = 0.58, p < 0.001$), followed by HbA1c ($\beta = 0.21, p = 0.03$).

RESULT

The results demonstrate a triad of hypercoagulability, hyperglycemia, and hyperinflammation among COVID-19 patients:

D-Dimer elevation correlates with CRP, confirming that coagulation abnormalities accompany systemic inflammation.

HbA1c contributes indirectly, suggesting that chronic hyperglycemia predisposes patients to severe inflammatory and thrombotic responses.

The combined biomarker profile can serve as a predictive tool for disease severity and ICU admission risk.

5. Discussion

This study confirms that coagulation, inflammation, and glycemic control are interlinked in COVID-19. Elevated D-dimer strongly correlates with CRP, reflecting the interplay between thrombo-inflammation and cytokine storm. HbA1c showed weaker but significant associations, suggesting that chronic hyperglycemia predisposes patients to heightened inflammatory and thrombotic responses. Our findings align with previous studies highlighting the role of inflammatory and coagulation biomarkers in COVID-19 severity. Shukla et al.(18) reported significantly higher D-dimer and CRP levels in multimorbid patients, underscoring the importance of biomarker monitoring for disease progression and therapeutic guidance. Similarly, Debi et al.(19) meta-analysis of 15,282 patients confirmed elevated CRP and D-dimer in diabetic individuals, with levels increasing with age, consistent with our observation of severe disease in elderly diabetics. Miri et al(20). further demonstrated that elevated D-dimer predicts mortality in diabetic patients. In our cohort, poorly controlled diabetes (high HbA1c) was

associated with markedly elevated D-dimer, suggesting chronic hyperglycemia exacerbates coagulation and inflammation. Collectively, the triad of hypercoagulability, hyperglycemia, and hyperinflammation emerges as a predictive cluster for severity and ICU admission. Routine biomarker monitoring may enhance risk stratification and clinical management

6. Conclusion

The present study demonstrates that elevated D-dimer, CRP, and HbA_{1c} levels are significantly associated with severe COVID-19 infection. D-dimer serves as an important biomarker for identifying hypercoagulability and thrombotic risk in COVID-19 patients. Elevated CRP levels indicate severe inflammatory response, while increased HbA_{1c} levels suggest that poor glycemic control contributes to disease severity. Their combined evaluation provides a multidimensional prognostic tool for identifying high-risk patients and guiding therapeutic interventions.

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