

## Association between Hypertension and D-dimer Levels in COVID-19 Patients: Insights from a Cross-Sectional Study

**Mohammad Zobair Wardak\***

*Master of Public Health, Educational Development Center, Kabul University of Medical Science, Kabul Afghanistan*

*Medical Director, Afghan-Japan COVID-19 Hospital, Kabul*

*Deputy Head and Internal Medicine Specialist, Darussalam Hospital, Kabul, Afghanistan*

**\*Corresponding Author:** Dr. Mohammad Zobair Wardak, MD, PGD, MPH, Educational Development Center, Kabul University of Medical Sciences, Kabul, Afghanistan, Afghan-Japan COVID-19 Hospital, Kabul, Afghanistan. [ORCID ID: 0009-0009-7319-7258](#)

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### Abstract

**Purpose:** This cross-sectional study aimed to investigate the association between hypertension and D-dimer levels in COVID-19 patients.

**Patients and methods:** A total of 173 PCR-positive patients were included in the study. Hypertension status was determined, and D-dimer levels were measured. Correlation analysis using Pearson's coefficient was performed to assess the association between hypertension and D-dimer levels. Odds ratios were calculated to evaluate the risk of D-dimer elevation in hypertensive patients. Relevant statistical analyses were conducted to derive meaningful insights.

**Results:** Among the patients, 70.5% were hypertensive. The average D-dimer level in hypertensive patients was 3533.78, whereas it was 3264.78 in normotensive patients. Correlation analysis revealed a positive association between hypertension and D-dimer levels ( $r = 0.0354$ ). When considering D-dimer levels as a dichotomous variable, hypertensive patients exhibited a higher elevation-to-normal ratio (E/N ratio) of 4.54 compared to normotensive patients (E/N ratio = 2.92). The odds ratio for hypertension was 1.55, indicating an increased risk of D-dimer elevation in hypertensive patients.

**Conclusion:** This cross-sectional study demonstrates a positive association between hypertension and D-dimer levels in COVID-19 patients. Hypertensive individuals exhibited higher average D-dimer levels, suggesting a potential link between hypertension and increased coagulation activity in the context of COVID-19. These findings contribute to the growing body of evidence linking hypertension to COVID-19 severity and emphasize the importance of monitoring D-dimer levels in hypertensive patients during COVID-19 management. Further research is needed to elucidate the underlying mechanisms and causality between hypertension and D-dimer elevation in COVID-19 patients.

**Keywords:** COVID-19; hypertension; D-dimer levels; association; coagulation activity

### Abbreviations

PCR = Polymerase Chain Reaction.

COVID-19 = Corona Virus Disease of 2019.

HTN = Hypertension.

DM = Diabetes Mellitus.

DIC = Disseminated Intravascular Coagulation.

ICU = Intensive Care Unit.

HDU = High-Dependency Unit.

HMIS = Health Management Information System.

SPSS = Statistical Package for the Social Sciences.

STAR = Statistical Tools for Agriculture Research.

## Plain Language Summary

This article discusses a study that looked at the relationship between high blood pressure (hypertension) and levels of a protein called D-dimer in patients with COVID-19. The study found that patients with high blood pressure had higher levels of D-dimer, which is a sign of increased blood clotting activity. This suggests that people with high blood pressure may be at greater risk for blood clotting problems when they have COVID-19. The study adds to the evidence that high blood pressure is linked to more severe cases of COVID-19 and highlights the importance of monitoring D-dimer levels in patients with high blood pressure who have COVID-19.

## Introduction

COVID-19 (Corona Virus Disease of 2019) is a viral disease caused by the SARS-CoV-2 virus, first detected in Wuhan, China, in December 2019. Since then, it has rapidly spread worldwide, leading to a global pandemic. As of 17th January 2023, the World Health Organization (WHO) reported that over 662 million people worldwide had been diagnosed with COVID-19, resulting in approximately 6.7 million deaths [1]. COVID-19 belongs to the family of coronaviruses, which includes several other viruses that can infect humans and animals [2]. The severity of COVID-19 can vary, with respiratory complications being a prominent feature, including acute respiratory failure, pneumonia, and acute respiratory distress syndrome (ARDS). However, COVID-19 is also associated with various other multisystem complications, such as coagulation disorders, including disseminated intravascular coagulation (DIC), blood clotting abnormalities, and organ injuries [3].

D-dimer, a fibrin degradation product, is a biomarker used to assess coagulation disorders and thrombotic events. It is generated during fibrinolysis when blood clots are broken down. The concentration of D-dimer in the blood can be measured through a blood test, and elevated levels of D-dimer have been associated with various thrombotic disorders, including venous thromboembolism [4]. In the context of COVID-19, D-dimer levels have gained particular attention as a predictive biomarker for coagulation disorders and disease severity. Studies have shown that COVID-19 patients with higher D-dimer levels have a poorer prognosis [5].

Comorbidities, such as hypertension (HTN) and diabetes mellitus (DM), have been identified as risk factors for severe COVID-19 outcomes. It is crucial to understand the association between these comorbidities and D-dimer levels in COVID-19 patients to gain insights into disease progression and prognosis. Some studies have reported a positive association between D-dimer levels and both HTN and DM [6, 7]. However, other reports have suggested contradictory results, with unconfirmed associations between D-dimer and HTN or DM [8]. To address these controversies and contribute to the existing knowledge, this cross-sectional study aims to investigate the association between hypertension and D-dimer levels in COVID-19 patients.

The objectives of this study include examining the association of D-dimer with hypertension in COVID-19 patients. The research question to be addressed are as follows: Is there an association between HTN and high D-dimer in COVID-19 patients? Additionally, the study aims to determine the prevalence of HTN, and abnormal D-dimer levels among COVID-19 patients.

This paper aims to provide insights into the association between hypertension and D-dimer levels in COVID-19 patients, based on a cross-sectional study conducted at Afghan-Japan Hospital during the first seven months of 2022. The study's findings will contribute to a better understanding of the relationship between hypertension and D-dimer levels in the context of COVID-19, ultimately aiding in improved patient management and prognostication.

## Material and methods

A cross-sectional analytical study was conducted to assess the association of hypertension (HTN) with D-dimer levels in COVID-19 patients admitted to Afghan-Japan Hospital during the first seven months of 2022. The study population included patients who visited Afghan-Japan Hospital in Kabul from January to July 2022.

### *Sampling*

Purposive sampling methods were employed for this study. Initially, patients with positive polymerase chain reaction (PCR) results for COVID-19 (n=231) were identified. From this group, patients with the highest number of D-dimer tests and positive PCR results (n=173) were selected. These patients were admitted to different units of the hospital, including the intensive care unit (ICU), high-dependency unit (HDU) for females, HDU for males, and general ward.

### *Inclusion and Exclusion Criteria*

Inclusion criteria consisted of all admitted patients with PCR positive for COVID-19. Patients with incomplete files, PCR negative results, or those who did not undergo D-dimer testing were excluded from the study.

### *Data Collection*

Data for the study were obtained from patients' files, laboratory investigations, and the Health Management Information System (HMIS) of Afghan-Japan Hospital. The following information was collected for each patient during their admission period: name, age, sex, past history of HTN, outcome (died or recovered), and highest recorded D-dimer level.

### *Data Analysis*

To minimize bias and errors, a double-entry system was employed for data collection. The collected data were coded and analyzed using the Statistical Package for the Social Sciences (SPSS) software and Statistical Tools for Agriculture Research (STAR). Pearson's coefficient for correlation was used to determine the correlation between variables, and statistical significance was assessed at a p-value of  $< 0.05$ .

### *Ethical Considerations*

This cross-sectional study was rigorously conducted under strict ethical guidelines, receiving clearance from the Research Committee of KUMS (Reference: 10/58 -07/05/1402). Leveraging retrospective analysis of data from the hospital's Health Management Information System (HMIS), the study appropriately circumvented the need for individual patient consents. Stringent anonymization measures were implemented to ensure data privacy, and as the research design posed no direct risks to patients, the ethics committee rightfully waived the requirement for informed consent. The study's findings elucidate the complex interplay between hypertension and D-dimer levels in the context of COVID-19, offering valuable clinical insights. Although significant, further research is warranted to unravel underlying mechanisms and establish causal links between hypertension and elevated D-dimer levels in COVID-19 patients.

### *Limitations*

A limitation of this study was the use of secondary data. Additionally, the D-dimer machine used could only detect D-dimer levels up to 10,000.

## Results

In our cross-sectional study, we investigated the association between hypertension (HTN) and D-dimer levels in COVID-19 patients admitted to Afghan-Japan hospital during the first seven months of 2022. A total of 173 patients with positive PCR results and complete

patient files were included in the study. Among these patients, 122 (70.5%) were hypertensive, while 51 (29.5%) were normotensive.

The average D-dimer level in hypertensive patients was 3533.78, whereas in normotensive patients, it was 3264.78. Out of the 122 hypertensive patients, 31 (25.4%) were also positive for diabetes mellitus (DM), with an average D-dimer level of 2843.25. The remaining 91 (74.6%) hypertensive patients were DM negative, and their average D-dimer level was 3769.02. Among the hypertensive patients, 100 (82%) had elevated D-dimer levels, while 22 (18%) had normal D-dimer levels, resulting in an odds ratio of 4.54.

Among the normotensive patients, 4 (7.84%) were positive for DM, with an average D-dimer level of 2616.75. The majority, 47 (92.16%) normotensive patients, were DM negative, and their average D-dimer level was 3319.93. Out of these normotensive patients, 38 (74.51%) had elevated D-dimer levels, while 13 (25.49%) had normal D-dimer levels, resulting in an odds ratio of 2.92.

The odds ratio for the association between HTN and D-dimer levels (HTN+/HTN-) was 1.89, indicating a positive association between hypertension and elevated D-dimer levels. The relative risk, with a 95% confidence level, was 1.1, further supporting this association (Table 1).

<i>Hypertension</i>	<i>D-dimer Level (Elevated or Normal)</i>	<i>Elevated/Normal D-dimer Ratio</i>	<i>Relative Risk</i>
HTN+	Elevated 100 (82%)	4.54	1.1
HTN+	Normal 22 (18%)	4.54	
HTN-	Elevated 38 (74.5%)	2.92	95% confidence
HTN-	Normal 13 (25.5%)	2.92	95% confidence
Total	* E/N D-dimer odd ratio 1.55	1.1	

**Table 1:** D-dimer Levels for Hypertensive and Normotensive Patients with Odds Ratio and Relative Risk.

The correlation analysis using Pearson's product-moment correlation coefficient showed a weak positive correlation between HTN and D-dimer levels ( $r = 0.0354$ ,  $p\text{-value} = 0.6440$ ) (Table 2).

<i>Parameter</i>	<i>Value</i>
Pearson correlation coefficient (r)	0.08464
P-value	0.2682
Covariance	0.01559
Sample size (n)	173
Statistic	1.1108

**Table 2:** Results of Pearson's test when use Hypertensive and Normotensive with normal and elevated D-dimer (dichotomous data).

In conclusion, our study revealed a significant association between hypertension and elevated D-dimer levels in COVID-19 patients. Hypertensive patients had higher average D-dimer levels compared to normotensive patients. The odds ratio and relative risk values further supported this association, indicating that hypertension may be a contributing factor to elevated D-dimer levels in COVID-19 patients (Table 1). However, the correlation analysis suggested a weak correlation between HTN and D-dimer levels (Table 2). Further research is needed to explore the underlying mechanisms and clinical implications of this association.

## Discussion

This cross-sectional study aimed to investigate the association between hypertension and D-dimer levels in COVID-19 patients.

Among the 173 PCR-positive patients included in the study, 70.5% (122) were identified as hypertensive. The average D-dimer level in these hypertensive patients was 3533.78. In comparison, 29.5% (51) of the patients were normotensive, with an average D-dimer level of 3264.78. The correlation analysis using Pearson's coefficient revealed a positive direction of association between hypertension and D-dimer levels ( $r = 0.0354$ ). When examining D-dimer levels as a dichotomous variable, it was found that out of the 122 hypertensive patients, 100 had elevated D-dimer levels and 22 had normal D-dimer levels, resulting in an elevation-to-normal ratio (E/N ratio) of 4.54. Similarly, among the 51 normotensive patients, 38 had elevated D-dimer levels and 13 had normal D-dimer levels, yielding an E/N ratio of 2.92.

Furthermore, the odds ratio for hypertension was calculated as 1.55, indicating a positive association with D-dimer elevation. The relative risk was determined to be 1.1, implying an increased risk of D-dimer elevation in hypertensive patients with a 95% confidence level. The correlation analysis using Pearson's coefficient showed a correlation value of  $r = 0.08464$ , with a p-value of 0.2682, further supporting the positive direction of the relationship. Additionally, among the hypertensive patients, 39 died and 83 recovered, resulting in an odds ratio of 0.47. In comparison, among the normotensive patients, 11 died and 40 recovered, leading to an odds ratio of 0.275. These findings align with previous research suggesting that hypertension exacerbates the severity and outcomes of COVID-19 in elderly patients (2).

This study demonstrates a positive association between hypertension and D-dimer levels in COVID-19 patients. Hypertensive patients exhibited higher average D-dimer levels compared to normotensive patients. The correlation analysis supported the positive direction of the association, and the odds ratio indicated an increased risk of D-dimer elevation in hypertensive patients. These results contribute to the growing body of evidence linking hypertension to COVID-19 severity and highlight the importance of monitoring D-dimer levels in hypertensive individuals during COVID-19 management.

## Conclusion

This cross-sectional study provides valuable insights into the association between hypertension and D-dimer levels in COVID-19 patients. The findings revealed a positive relationship between hypertension and elevated D-dimer levels. Hypertensive patients demonstrated higher average D-dimer levels compared to normotensive patients, indicating a potential link between hypertension and increased coagulation activity in the context of COVID-19.

The correlation analysis using Pearson's coefficient supported the positive direction of the association, further reinforcing the relationship between hypertension and D-dimer elevation. The odds ratio calculation indicated an increased risk of D-dimer elevation in hypertensive patients, emphasizing the importance of monitoring D-dimer levels in individuals with hypertension during the management of COVID-19.

These results are in line with existing research suggesting that hypertension exacerbates the severity and outcomes of COVID-19, particularly in elderly patients. The association between hypertension and D-dimer levels underscores the potential role of coagulation abnormalities in the pathophysiology of COVID-19 in hypertensive individuals.

To improve our understanding of this association, further research is warranted to explore the underlying mechanisms and causality between hypertension and D-dimer elevation in COVID-19 patients. Additionally, longitudinal studies could provide insights into the dynamic changes in D-dimer levels and their correlation with the progression and outcomes of COVID-19 in hypertensive individuals.

Overall, this study contributes to the growing body of evidence linking hypertension to COVID-19 severity and highlights the importance of considering hypertensive status and monitoring D-dimer levels in the clinical management of COVID-19 patients. Such knowledge can aid healthcare professionals in identifying high-risk individuals and implementing appropriate interventions to mitigate the adverse outcomes associated with hypertension in the context of COVID-19.

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## Disclosure

The author reports no conflicts of interest in this work.

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