



# EVALUATION OF D-DIMER VALUES IN COVID-19 IRAQI PATIENTS AND ITS CORRELATION WITH THE UNDERLYING CO-MORBID DISEASES

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<p><b>Received:</b> February 20<sup>th</sup> 2023 <b>Accepted:</b> March 26<sup>th</sup> 2023 <b>Published:</b> April 28<sup>th</sup> 2023</p>	<p><b>Background :</b> COVID-19, a communicable ailment that originated in China, caused by a new <math>\beta</math> coronavirus of group 2B, has varying symptoms among people. These symptoms range from no symptoms or a mild infection to severe respiratory tract infections, which could lead to death. D-dimer, the end product of fibrin degradation, is commonly utilized to evaluate thrombosis. Individuals with underlying diseases such as cancer, diabetes, stroke, or pregnancy may experience increased D-dimer levels after contracting COVID-19. <b>Aim :</b> The primary aim of this study is to determine the correlation between high D-dimer levels and underlying chronic illnesses among COVID-19 positive Iraqi patients. This study also investigates the relationship between age, gender, and D-dimer values in COVID-19 infected Iraqi patients. <b>Materials &amp; Methods:</b> This study also investigates the relationship between age, gender, and D-dimer values in COVID-19 infected Iraqi patients. For this case control study, a total of 143 COVID-19 patients were included during the period of June 2020 to June 2021. Cases were collected from private hospitals and labs in Karbala and Babil in a prospective manner. Patient data, including age, gender, and history of chronic diseases, such as diabetes, hypertension, chronic heart disease, and renal disease, were collected during D-Dimer test requests. Subsequently, SPSS software (SPSS 24.0 for Windows, IBM, Chicago, IL, USA) was utilized for statistical analysis. A statistically significant p-value of less than 0.05 was determined. <b>Results:</b> The study suggests that there is no significant correlation between D-Dimer values and gender in COVID-19 patients. Nevertheless, a meaningful difference in D-dimer level was seen between patients with and without chronic illnesses (p-value 0.004). The results also indicated that there is a significant difference between the D-dimer level of patients with diabetes and hypertension than those without these underlying diseases (p-values of 0.026 and 0.000, respectively). Furthermore, age correlated significantly (p-value 0.000) with D-dimer values. <b>Conclusion:</b> COVID-19 viral contagion has significant effects on chronically ill patients. D-dimer estimation proves useful in following the severity of COVID-19 infection in patients with chronic diseases. However, the investigation found no significant correlation between D-Dimer values and gender in patients with COVID-19.</p>

**Keywords:** . D-dimer

## INTRODUCTION

In the past three years, occurrences of CoVs in East Asia and the Middle East have resulted in catastrophic outbreaks. Such incidents generated a pandemic affecting various countries and territories worldwide which then gave rise to a global health threat (1). It is a member of the Coronaviridae family, the CoVs can manifest in different ways with symptoms varying from mild like the common cold, to severe and life-threatening conditions such as SARS, MERS, and

COVID-19. (SARS-CoV-2) is among the seven members of the CoV that can infiltrate human beings (2). The genetic makeup of coronaviruses contains a non-segmented, single-stranded RNA genome with a positive sense that stretches about 30 kb. The virus has a protective outer layer with a 5' cap and 3' poly(A) tail. It is believed that SARS-CoV-2 might have originated from bats. However, it is also likely that other animal hosts could have contributed to its spread to human populations.(4)The primary structural proteins of



coronaviruses feature four prominent elements, including spike (S), nucleus (N), envelope (E), and membrane (M) (5). D-dimer is a fundamental degradation fragment of fibrin and acts as an indicator of the syntheses and breakdowns of fibrin (10). The critical role played by D-dimer in signifying the stimulates of coagulation and fibrinolysis has been firmly established in abundant research. In the typical healthy individuals, there is moderately low titer of D-dimer compared to higher levels featured in individuals with thrombotic events. D-dimer has proved instrumental in diagnosing, monitoring, and addressing the impacts of venous thrombosis and embolism (VTE) and has now become a part of routine healthcare precautions. Chronic inflammatory conditions like asthma, malignancies, sickle cell disease, and rheumatoid arthritis have an inclination of raising D-dimer titer amongst individuals (6,7). Though research is vague on the extent of worrying about varying D-dimer levels in patients diagnosed with COVID-19; that aside, multiple micro-thrombi have been observed in many parts of the body of individuals with COVID-19, and the effects of the D-dimer have yet to be elucidated (8,9). D-dimer is a substance that is created when crosslinked fibrin is broken down with the aid of factor XIII. Its presence in the bloodstream is an indication that the hemostatic system is still being activated. The cutoff value for D-dimer is a reading below 500 ng/mL or 0.4  $\mu$ / mL. When D-dimer is first formed, thrombin causes a polymerization site on fibrinogen to come to light, which then enables the linking of another fibrinogen molecule or monomeric fibrin molecule. Recent studies revealed that having high D-dimer values in patients with COVID-19 is associated with an increased risk of death and critical illness. Pathological reports have clearly shown that there are numerous

macro and micro-thrombi present in multiple microcapillaries in COVID-19 patients(15,16). Our research posits a correlation between chronic health conditions and elevated D-dimer levels. Studies have demonstrated that elevated D-dimer levels are tied to an increased mortality rate in COVID-19 patients. Our investigation aims to illuminate the connection between high D-dimer levels and the presence of preexisting health conditions.

**MATERIALS & METHODS**

this cross sectional study, a 143 case of COVID-19 patients had been included during the period ( June 2020- June 2021). Cases was collected randomly from private hospitals and labs in Karbala and Babil in a prospective manner. When patients ask for D-Dimer test ,data collected including age, gender, and presence or absence of chronic disease and type of chronic disease if present with ensuring the positivity for COVID 19 by previous PCR or rapid Ag-Ab test

Exclusion criteria: pregnant women

From each patient about 2 cc of blood was withdrawn in sodium citrate tube , centrifuged and tested for D dimer value using mini-VIDAS instrument and biomerit d-dimer kit. Normal range for D dimer was 200-500 ng/ml. A value of 500 or more is considered positive (elevated)

Data as age ,sex , D dimer value, presence or absence of chronic disease and type of chronic disease were arranged in Exel sheet and analysed by IBM SPSS 24.0 for Windows.

Analysis plan : SPSS software (USA, Chicago, IL,) was used for quantitative variables and statistical analysis was stated as the mean plus standard deviation (SD). P-value < 0.05 to considered statistically important.

**RESULTS:**

When D-dimer value was classified into normal and high no significant difference was seen between males and females

Table 1: correlation between high D-dimer value and gender .

		gender		Total
		male	female	
d-dimer level	normal	28	27	55
	high	44	44	88
Total		72	71	143

Significant difference seen regarding D-dimer level between patients with and without chronic disease as in figure 1.

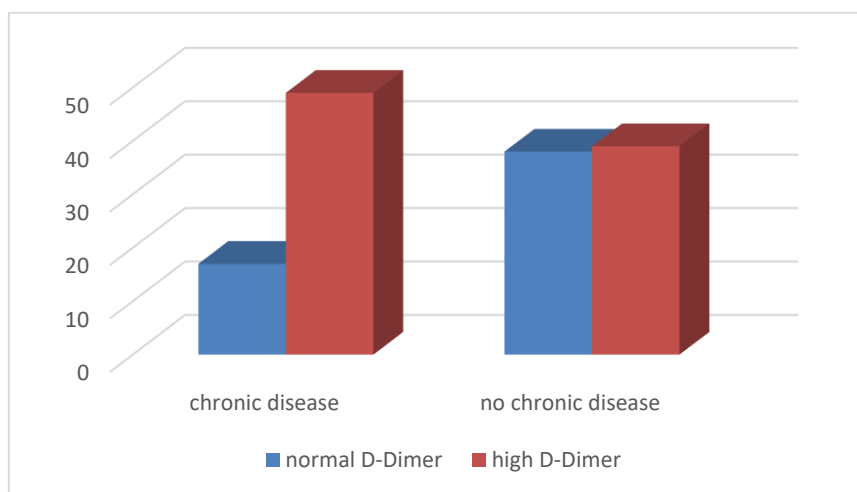


Figure 1: correlation between high d-dimer value and chronic disease.

Table (2) show Significant difference regarding D-dimer values between patients with and without diabetes mellitus (DM) with p- value of 0.019.

**d-dimer level \* DM Crosstabulation**

Count

		DM		Total
		no DM	DM	
d-dimer level	normal	46	9	55
	high	60	28	88
Total		106	37	143

**Chi-Square Tests<sup>c</sup>**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.215 <sup>a</sup>	1	.040	.050	.030	
Continuity Correction <sup>b</sup>	3.448	1	.063			
Likelihood Ratio	4.408	1	.036	.050	.030	
Fisher's Exact Test				.050	.030	
Linear-by-Linear Association	4.185 <sup>d</sup>	1	.041	.050	.030	.019
N of Valid Cases	143					

Table (3) A significant correlation was seen between age and D-dimer level (using Spearman rho non-parametric correlation)

**Correlations.**

		age	d-dimer
age	Correlation Coefficient	1.000	.310**
	Sig. (2-tailed)	.	.000
	N	143	143
d-dimer	Correlation Coefficient	.310**	1.000
	Sig. (2-tailed)	.000	.
	N	143	143



\*\* . Correlation is significant at the 0.01 level (2-tailed).

Table (4) When D-dimer value was classified into normal and high a significant difference was seen between patients with and without hypertension

**d-dimer level \* hypertension Crosstabulation**

Count		hypertension		Total
		no hypertension	hypertension	
d-dimer level	normal	43	12	55
	high	53	35	88
Total		96	47	143

**Chi-Square Tests<sup>c</sup>**

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)	Point Probability
Pearson Chi-Square	4.945 <sup>a</sup>	1	.026	.029	.020	
Continuity Correction <sup>b</sup>	4.165	1	.041			
Likelihood Ratio	5.113	1	.024	.029	.020	
Fisher's Exact Test				.029	.020	
Linear-by-Linear Association	4.910 <sup>d</sup>	1	.027	.029	.020	.012
N of Valid Cases	143					

**DISCUSSION**

Our study was done on 143 patients with COVID-19 infection ensuring the positivity for COVID 19 by previous PCR or rapid Ag-Ab test and tested for D-dimer value . In this study we found .According to Table (1), no considerable correlation between gender and D-Dimer values was demonstrated in COVID-19 patients. In cases where D-dimer values were categorized as normal or elevated, there didn't appear to be any significant dissimilarity between the genders, as per the data analyzed.

A research conducted by Mukhopadhyay A and his team revealed that out of 4,574 hospitalized COVID-19 patients, those who identified as male showed lower levels of early D-dimer compared to their female counterparts. In addition, a high level of D-dimer was observed to have considerable impact on aggravating COVID-19 symptoms in men, as compared to women. These findings indicate an evident gender-based variation in the correlation between D-dimer levels and COVID-19 severity. (17)

Chronic diseases were another important risk factor that should not be overlooked. In this study we found Significant difference seen regarding D-dimer level between patients with and without chronic disease . Out of the 143 individuals with the coronavirus, 66 of them

suffered from long-term illnesses. An association can be observed in Figure 1 between chronic diseases and D-dimer levels. It has been noticed that patients with chronic diseases evident higher levels of D-dimer. Further analysis reveals that there is a significant difference when comparing the normal and high classifications of D-dimer values between patients with long-term illnesses and those without. The results showed that 74.24% of those with elevated D-dimer levels and chronic diseases.

According to a study conducted by Hai-Han Yu et al, patients with severe COVID-19 infection were found to have irregular coagulation function, and a considerably elevated level of D-dimer indicating a severe condition (18).

Our study has revealed that Diabetes Mellitus (DM) is a long-lasting disease, characterized by high levels of D-dimer in patients. From our investigation, we found a noticeable variability in D-dimer levels between those suffering from the illness and those who aren't, as shown in Table (2). Additionally, when we categorized D-dimer values into normal and elevated ranges, we observed that 75.67% of individuals with DM had an elevated D-dimer level, compared to those without the disease.



According to Mishra Y et al's research, individuals with diabetes mellitus who were diagnosed with COVID-19 exhibited elevated levels of D-dimer. The study revealed a substantial rise in D-dimer titer in COVID-19 patients with diabetes mellitus. This suggests that COVID-19 patients with diabetes may be more vulnerable to developing a hypercoagulable state with a poorer prognosis.(19)

In a recent study conducted at the University Medical Center of Oujda in Morocco, it was discovered that COVID-19 patients with diabetes are at an increased risk of developing hypercoagulation, which leads to a poor prognosis. The retrospective study included 201 confirmed COVID-19 patients and the final analysis showed that diabetics with COVID-19 are more prone to hypercoagulation and generally have a worse outcome.(20)

Our research indicates that hypertension is a prevalent comorbidity with far-reaching complications for patients. Our study observed a discernible discrepancy in D-dimer levels for patients with hypertension as compared to those without, as shown in Table 4. A marked difference was evident between those with and without hypertension when D-dimer counts were categorized as normal or elevated. Interestingly, 74.46% of individuals with hypertension depicted an increase in D-dimer levels amongst COVID-19 patients. It's worth noting that COVID-19 patients with hypertension are at a higher risk of hospitalization and, sadly, death, as Peng M et al outline in their work (21). However, though this is true, hypertension doesn't necessarily have an impact on COVID-19 outcomes as confirmed by Zhong L et al's multicenter retrospective study (22).

SABPA, which stands for Sino American Biotechnology and Pharmaceutical Professional Association, has conducted research that links hypertension with elevated D-dimer levels in individuals of black ethnicity. This is due to the prevalent occurrence of hypertension, which increases the risk of developing cardiovascular ailments. (23)

Andina et al. conducted a cross-sectional investigation that studied 96 adult patients diagnosed with COVID-19. The results showed that hypertensive patients with COVID-19 had a significantly higher D-dimer titer compared to non-hypertensive patients. (24)

## **CONCLUSION**

-The impact of COVID-19 on patients with chronic illness is tremendous.

-Patients with chronic illness who have COVID-19 show heightened levels of D-dimer. This implies that D-dimer

levels may be used to monitor COVID-19 severity in chronic illness patients.

-Surprisingly, it was discovered that gender had no correlation with the D-dimer levels in COVID-19 patients.

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