



The Impact of Dialysis Sessions on Blood Levels of D-dimer among Chronic Kidney Disease Patients Infected with COVID-19

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SUMMARY. Coronavirus disease-19 (COVID-19) pandemic is a real challenge to our communities worldwide, exerting a high socioeconomic impact. The disease is associated with a great deal of coagulation cascade disorder, with a considerable increase in D-dimer concentration in blood. Objectives: To assess the impact of dialysis session frequency on blood levels of D-dimer among CKD patients infected with COVID-19. Patients and Methods: The study included 40 CKD patients (22 males and 18 females) infected with COVID-19, who attended the Artificial Kidney Unit at Al Hussein Teaching Hospital, Thi-Qar, Iraq for regular dialysis. They were divided into two groups; Group I: 20 CKD patients who had COVID-19. They underwent one hemodialysis session per week. The second group, which included 20 CKD patients infected with COVID-19 underwent three dialysis sessions per week. Plasma levels of D-dimer were measured one day before the start of the study and one day after three weeks in both groups. Results: The results of the present study revealed that CKD patients infected with COVID-19 who underwent three dialysis session per week (Group II) had a significant drop in blood D-dimer level at the end of three weeks in comparison to the initial values. Furthermore, the decrease in blood D-dimer level was significantly higher among CKD patients with COVID-19 who underwent three dialysis sessions per week (Group II) in comparison to COVID-19 infected CKD patients who underwent single dialysis sessions per week (Group I). Conclusions: CKD patients with COVID-19 have an elevated blood level of D-dimer. Increasing the frequency of hemodialysis plays an essential role in lowering the serum D-dimer level among these patients.

RESUMEN. La pandemia de la enfermedad por coronavirus-19 (COVID-19) es un verdadero desafío para nuestras comunidades en todo el mundo, ejerciendo un alto impacto socioeconómico. La enfermedad se asocia con una gran cantidad de trastornos de la cascada de la coagulación, con un aumento considerable de la concentración de dímero D en la sangre. Objetivos: Evaluar el impacto de la frecuencia de la sesión de diálisis en los niveles sanguíneos de dímero D entre pacientes con ERC infectados con COVID-19. Pacientes y métodos: el estudio incluyó a 40 pacientes con ERC (22 hombres y 18 mujeres) infectados con COVID-19, que asistieron a la Unidad de Riñón Artificial en el Hospital Universitario Al Hussein, Thi-Qar, Irak para diálisis regular. Fueron divididos en dos grupos; Grupo I: 20 pacientes con ERC que tenían COVID-19. Se sometieron a una sesión de hemodiálisis por semana. El segundo grupo, que incluía a 20 pacientes con ERC infectados con COVID-19, se sometió a tres sesiones de diálisis por semana. Los niveles plasmáticos de dímero D se midieron un día antes del comienzo del estudio y un día después de tres semanas en ambos grupos. Resultados: Los resultados del presente estudio revelaron que los pacientes con ERC infectados con COVID-19 que se sometieron a tres sesiones de diálisis por semana (Grupo II) tuvieron una caída significativa en el nivel de dímero D en sangre al final de las tres semanas en comparación con los valores iniciales. Además, la disminución en el nivel de dímero D en sangre fue significativamente mayor entre los pacientes con ERC con COVID-19 que se sometieron a tres sesiones de diálisis por semana (Grupo II) en comparación con los pacientes con ERC infectados por COVID-19 que se sometieron a una sola sesión de diálisis por semana (Grupo I). Conclusiones: Los pacientes con ERC con COVID-19 tienen un nivel elevado de dímero D en sangre. El aumento de la frecuencia de la hemodiálisis juega un papel esencial en la reducción del nivel de dímero D en suero entre estos pacientes.

KEY WORDS: chronic kidney disease, dialysis sessions, D-dimer.

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INTRODUCTION

The pandemic of COVID-19 represents a major health disaster affecting millions of people worldwide with catastrophic effects on life style, families, business and economy ¹. Coronavirus disease-19 is caused by β coronavirus ², the manifestation of the disease varies from asymptomatic cases to severe critical cases with multiple system involvement and sudden death ³. The disease tends to be more serious among elderly people and those individuals with underlying health disorders, such as respiratory disease, cardiovascular disease, diabetes mellitus and obesity ⁴. People with CKD seem to be more vulnerable to contract the COVID-19 infection since they are usually older and already have a variety of systemic organ dysfunction, impaired physical activity, cognitive disorder and immune system derangement ⁵. D-dimers are byproducts of fibrin degradation, normally it is present in the blood in very small amounts (100-200 ng/mL). High blood levels of D-dimer indicates coagulation disorder with increased fibrinolysis ⁶. Assessment of the blood level of D-dimers is usually used in the diagnosis of venous thromboembolism disorder like pulmonary embolism, or deep vein thrombosis ⁷. Furthermore, several recent studies revealed that the blood concentration of D-dimer is positively correlated with the degree of fibrinolysis in various coagulator disorders and it has been utilized as a biomarker for severity of these disorders ⁸. It is well-known that COVID-19 infection is associated with various degrees of coagulation abnormalities and increased D-dimer levels in the blood ⁹. Furthermore, most recent researches showed a significant correlation between severity of the disease and D-dimer level ¹⁰⁻¹². The present study is an attempt to assess blood levels of D-dimer, among CKD patients on regular hemodialysis and its relation to the dialysis session frequencies.

MATERIALS AND METHODS

Study design

The study included 40 CKD patients (22 males and 18 females) infected with COVID-19, who were attending the Artificial Kidney Unit for regular hemodialysis at Al-Hussein Teaching Hospital, Thi-Qar Province, Iraq during the period from July to November 2020. They were divided into two groups according to the dialysis frequency per week.

1. Group I included 20 CKD patients (11 males and 9 females) infected with COVID-19. They underwent one hemodialysis session per week for three successive weeks.

2. Group II included 20 CKD patients (11 males and 9 females) infected with COVID-19. They underwent three hemodialysis session /week for three successive weeks.

The diagnosis of COVID-19 was conducted according to the most usual guidelines adopted depending on epidemiologic history, clinical signs, and symptoms, finding of the virus by a reverse transcription polymerase chain reaction (RT-PCR), chest X-ray and CT scan of the lung. All patients included in this study were treated according to the standard treatment protocol including daily injection of anticoagulant (Enox-heparin 4000 IU/day).

Biochemical analysis

For every patient who participated in this study the blood level of D-dimer was determined one day before dialysis at the start of the study (initial values) and one day after dialysis at the end of third week for both groups (final values). The blood level of D-dimer was determined on the whole blood by obtaining 5 mL of venous blood by venipuncture from a suitable vein into an EDTA tube. The blood level of D-dimer was measured by fluorescence immunoassay ¹³.

Statistical analysis

Statistical analysis was performed using the SPSS version 25 software. Frequency, percentage, correlation, and paired tests were used to analyze variables. Data are represented as mean \pm SD, since p value < 0.05 was defined as significant.

RESULTS

Forty CKD patients (18 females and 22 males) enrolled in this study to evaluate the effect of the frequency of dialysis on the blood level of D-dimer, even-though males showed higher levels of D-dimer. However, there was no significant statistical difference in the distribution of the levels of D-dimer in both groups regarding the gender difference (p > 0.05; Table 1).

	Gender	D-dimer1	D-dimer 2	ANOVA, p-value, Eta
	Mean	906.8182	713.4545	1.425
Male	N	22	22	0.24
	S.D	167.93951	237.019	0.19
Female	Mean	846.3889	710	0.002
	N	18	18	0.964
	S.D	147.85093	239.68	0.007
Total	Mean	879.625	711.9	
	N	40	40	
	S.D	160.13195	235.14	

Table 1. Differences of D-dimer (ng/mL) means according to gender on two occasions of measurements

	Age (year)	N	Mean Square	Sig.	
D1	Between groups	24	21970.752	0.791	
	Within groups	16	31516.622		
D2	Between groups	24	44005.622	0.872	
	Within groups	16	73355.244		
	Gender		Mean	S. D	Std. Error Mean
Age (year)	Male	22	38.4545	10.29899	2.19575
	Female	18	45.8333	9.88314	2.32948

Table 2. Group statistics of age and D-dimer. Whole sample age differences regarding the D-dimer value and gender distribution also show no significant statistical differences ($p > 0.05$).

		Mean	N	SD	t	P-value	correlation	Sig
Pair 1	D- before -1st group	864.75	20	142.58	-0.854-	0.404	0.647	0.002
	D- after -1st group	887	20	134.21				
Pair 2	D- before -1st group	864.75	20	142.58	-0.565-	0.578	-0.063-	0.792
	D- before -2nd group	894.5	20	178.42				
Pair 3	D- before -1st group	864.75	20	142.58	6.996	0.0001	0.146	0.539
	D- after -2nd group	536.8	20	175.89				
Pair 4	D- before -2nd group	894.5	20	178.43	6.267	0.0001	-0.038-	0.873
	D- after -2nd group	536.8	20	175.89				
Pair 5	D- after -1st group	887	20	134.21	6.206	0.0001	-0.312-	0.18
	D- after -2nd t group	536.8	20	175.89				

Table 3. Paired samples statistics.

There were significant statistical differences in the D -dimer levels when compared to the

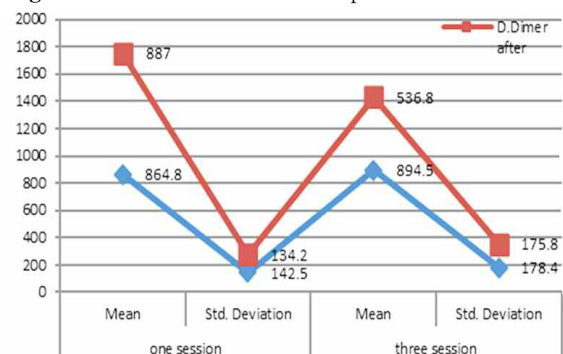
second reading of the second group (three sessions of dialysis).

	Group	Age (year)	D1	D2
group	Pearson's correlation	1	0.094	-0.754.**
	Sig. (1-tailed)		0.282	0
	N	40	40	40
age	Pearson's correlation	-0.036-	0.158	0.041
	Sig. (1-tailed)	0.414	0.165	0.402
	N	40	40	40
D1	Pearson's correlation	0.094	1	0.074
	Sig. (1-tailed)	0.282	0.165	0.325
	N	40	40	40
D2	Pearson's correlation	-0.754.**	0.041	1
	Sig. (1-tailed)	0	0.325	0.074
	N	40	40	40

Table 4. Correlation analysis of the independent variables for the D-dimer on two occasions. **. Correlation is significant at the 0.01 level (1-tailed).

Initial readings regarding means and SD of D-dimer values for the two groups were higher than those after two weeks as shown in Fig. 1.

Figure 1. Distribution of statistical parameters of D-dimer



of the comparative groups

The second reading of D-dimer of the three sessions' group tending to be independently affected by the frequency of dialysis.

DISCUSSION

Coronavirus disease 2019 may subsequently lead to a serious coagulation disorder, with subsequent clot formation especially in the pulmonary vessels that threatens patients recovery and survival¹⁴. The problem tends to be further complicated when COVID-19 infected patients with CKD, since CKD by itself may be associated with a conflicting hemostatic imbalance varying from a prothrombotic state to bleeding tendency¹⁵. The commonly used replacement therapy for CKD is hemodialysis: this procedure may further causes a coagulation disorder with clot formation. Due to this complication, heparin is usually administered as an anticoagulant to prevent clot formation¹⁶. D-dimer is a well-known biomarker of hemostasis mechanism¹⁷ and it has been widely used recently as an indicator of the severity of COVID-19 infection¹⁰. The results of this study showed abnormally high blood levels of D-dimer (more than 800 ng/mL) among all CKD patients infected with COVID-19 (Groups I and II). These abnormally high blood levels of D-dimer values indicate serious coagulator dysregulation among CKD patients with COVID-19¹⁸. In a recent study, the researchers reported a significant increase in the blood levels of D-dimer among CKD patients with COVID-19. They also concluded that high blood level D-dimer can be taken as predictive of a worse outcome¹⁹. In addition to clot formation in the pulmonary vessels, other patterns of coagulability disorder have been reported among patients with COVID-19. Tang *et al.* described a higher rate (71.4%) of disseminated intravascular coagulation in fatal cases of COVID-19 infected patients¹⁴. The real underlying mechanism of high blood levels of D-dimer among patients with COVID-19 is not clear. One of the possible explanations is interaction of the virus with the endothelial cells of blood vessels. This interaction will impair the normal programmed cell death (apoptosis) with subsequent endothelial cell injury which in turn contributes to clot formation²⁰. The results of the present study revealed that CKD patients infected with COVID-19 who underwent three dialysis sessions per week (Group II) had a significant drop in blood D-dimer levels when we compared the initial values with the ending values (after three weeks). Furthermore, the decrease in blood D-dimer levels was significantly higher among CKD patients with COVID-19 who underwent three dialysis sessions per week (Group II) in comparison to COVID-19 infected CKD patients who underwent

single dialysis sessions per week (Group I). The process of dialysis probably had some contribution to the reduction of D-dimer by removal of these particles together with other molecules and uremic toxins²¹. The hemodialysis process is also associated with improving immunity function of the patients. This may contribute to reducing the severity of COVID-19 and may further improve patient coagulator system²².

CONCLUSION

In conclusion, D-dimer tends to increase in CKD patients infected with COVID-19. The increased frequency of hemodialysis was found to be associated with a significant decrease in the blood level of D-dimer among these patients.

Acknowledgments

This study was conducted in the department of the artificial kidney at al hussein teaching hospital in the department of health in Thi-Qar province. Therefore, we extend our thanks and appreciation to all members of the said department, including nurses, service workers, resident doctors, and statistics employees. We also extend our thanks and appreciation to the staff of the statistics department at the college of medicine, who contributed to the process of tabulating the results.

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