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COVID-19: Clinical Course and Outcome of the Disease in Patients on Hemodialysis

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ABSTRACT

Background: This study investigated the relationship between inflammatory parameters and comorbidities, and mortality in patients on hemodialysis with COVID-19, to determine which parameters could be used as predictors of a clinical outcome.

Methods: Sixty-eight hemodialysis patients were included, who had COVID-19. We examined comorbidities, laboratory findings (first day and seven days after a positive PCR test), symptoms, and demographic factors regarding the outcome.

Main findings: A total of 70% of patients were hospitalized. The results showed that hypertension significantly contributed to a fatal outcome. The non-survivor group had significantly higher levels of CRP, WBC, and procalcitonin after seven days, and LDH basally and after seven days.

Principal conclusions: Patients who died from COVID-19 had significantly higher levels of CRP, WBC, and procalcitonin seven days after a positive test, and LDH initially and after seven days. It was shown that the value of LDH can serve as a prognostic factor in the severity of the disease and the possible fatal outcome.

Keywords: COVID-19, hemodialysis, lactate dehydrogenase, SARS-CoV-2

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INTRODUCTION

COVID-19, caused by the severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2) has had devastating effects worldwide. Patients with kidney failure on hemodialysis may have a higher risk of poorer outcomes (1). Chronic kidney disease has been an independent mortality factor during the COVID-19 pandemic, associated with a poor hospital outcome. Unfortunately, there is little data on the frequency and severity of COVID-19 in patients on chronic hemodialysis. Hemodialysis patients are at high risk of exposure to the virus because, on average, they interact three times a week with medical carriers, nurses, paramedics, and other patients from their dialysis facility (2). A recent observational study of hospitalized patients with kidney failure and COVID-19 reported a mortality rate of 31% (3). Patients undergoing dialysis have high rates of comorbid conditions and are often older adults, which puts them at risk of developing a complicated disease (4). This study will show whether there is an association between levels of procalcitonin, lactate dehydrogenase, C-reactive protein, and platelet count, and mortality in hemodialysis patients with a COVID-19 infection, as well as the most common symptoms of SARS-CoV-2 virus infection in hemodialysis patients. We compared inflammatory parameters at the beginning and seven days after the initial findings because the course of the disease usually worsens on the 7th day.

MATERIALS AND METHODS

Participants

The study included 68 patients who are (were) on a regular hemodialysis program and who became infected with the SARS-CoV-2 virus in the period from April 25, 2020 to November 25, 2021.

Methods

The virus infection was proven with the positive finding of polymerase chain reaction (PCR) on SARS-CoV-2 from samples of nasopharyngeal or oropharyngeal swabs from patients. Data were collected from patients' medical records. The following parameters were used: demographic factors (age, sex, hospitalization) which also include comorbidities (hypertension, diabetes, myocardial infarction, chronic obstructive pulmonary disease, liver disease, and atrial fibrillation), clinical symptoms (fever, cough, dyspnea), inflammatory parameters at the beginning and at seven days after the initial finding (C-reactive protein, absolute number of leukocytes, lymphocytes and platelets, lactate dehydrogenase, and procalcitonin), therapy (oxygen, antibiotics, corticosteroids) and finally the outcome of the patients' disease. Procalcitonin was calculated using a Maglumi 200 Plus automated platform from Snibe; CRP was calculated by means of a specific protein analyzer using a CRP-M100 instrument from a Mindray manufacturer; LDH was calculated using Mindray BS-200 and the absolute number of leukocytes, lymphocytes, and platelets was detected using BC-6900 automatic blood cell analyzers, also manufactured by Mindray.

Statistical analysis

In preparation for statistical analysis, all the above data were entered into a previously created table in MS Office Excel. The research was conducted in two different ways by dividing the groups according to outcome (alive or dead) and gender (male or female).

IBM SPSS Statistics v.26 was used. To display the obtained data for categorical variables, the percentages of that frequency are shown, while the continuous variables are presented via descriptive parameters (median, arithmetic mean, and standard deviation). X2 (Hi-square test) and Fisher's exact test were used to compare the frequency of occurrence of the variable, while the Student's t-test (arithmetic mean and standard deviation) and the Mann-

Whitney U-test (median) were used for the descriptive parameters. The results are presented in tables and graphs and are interpreted at the significance level of $p < 0.05$.

RESULTS

During the study period, the research included 68 patients who were on a regular hemodialysis program and who had become infected with the SARS-CoV-2 virus. The majority of patients, 50 of them, were men while the rest were women. All infected patients developed the disease. A total of 70% of all patients required hospitalization. The mortality rate of hemodialysis patients, infected with the SARS-CoV-2 virus in our study, was 32%. The next table represents demographic factors (sex, hospitalization) and comorbidities (hypertension, diabetes, myocardial infarction, chronic obstructive pulmonary disease, liver disease, and atrial fibrillation).

Table 1. Gender differences, hospitalization needs, and the presence of comorbidities between groups.

	Outcome				χ^2	P
	Deceased		Survived			
	n	%	n	%		
Sex					0.158	0.691
M	15	68.2	35	76.1		
F	7	31.8	11	23.9		
Hospitalization	19	86.4	29	63.0	2.865	0.091
HTA	20	90.9	32	69.6	2.645	0.102
DM	11	50.0	14	30.4	1.681	0.195
MI	2	9.1	9	19.6	0.556	0.456*
COPD	2	9.1	2	4.3	0.051	0.821*
LD	1	4.5	2	4.3	0	1*
FA	2	9.1	7	15.2	0.099	0.753*

*Fishers exact test; HTA – hypertension; DM – diabetes mellitus; MI – myocardial infarction; COPD – chronic obstructive pulmonary disease; LD – liver disease; FA – atrial fibrillation.

Subjects who died of COVID-19 were significantly more febrile, had a cough, and were treated with oxygen, antibiotics, and corticosteroids; there were no statistically significant differences in the incidence of dyspnea between groups (Table 2).

Subjects who died from COVID-19 had significantly higher average levels of CRP, leukocyte count, and procalcitonin after seven days, as well as LDH initially and after seven days. There were no statistically significant differences in the other parameters between groups (Table 3).

Hypertension proved to be a significant risk factor in the mortality of subjects, in contrast to other comorbidities that were without significant predictive effect (Table 4).

Dyspnea was a significant contributor to the mortality of patients, in contrast to fever and cough, which were without significant predictive value (Table 5).

DISCUSSION

The primary objective of this study was to provide descriptive information including clinical features, laboratory data, treatment regimens, and prognostic factors in hemodialysis patients with COVID-19. The study included 68 subjects. All of the subjects were on a chronic hemodialysis regimen and

tested positive for the SARS-CoV-2 virus. All patients underwent laboratory screenings at the beginning of the disease and seven days subsequently. A statistically significant association was found between the values of lactate dehydrogenase in the initial laboratory findings and the laboratory findings after seven days, and the probability of death in the total sample of patients on hemodialysis with COVID-19.

Table 2**.** Differences in the presence of symptoms and the therapeutic approach between groups.

	Outcome				χ^2	P
	Deceased		Survived			
	n	%	n	%		
Fever	21	95.5	31	67.4	5.048	**0.025**
Cough	18	81.8	26	56.5	3.136	**0.012**
Dyspnea	16	72.7	17	37.0	6.259	0.195
Oxygen	21	95.5	12	26.1	25.960	**<0.001**
Antibiotic	22	100.0	29	63.0	8.959	**0.003**
Corticosteroids	22	100.0	23	50.0	14.965	**<0.001**

Table 3. Differences in the laboratory parameters between groups.

	Outcome		Test	p
	Survived	Deceased		
CRP ($\bar{X}$±SD)	80.08±84.93	86.21±63.50	t=0.300	0.765[a]
CRP 1*; M [IR]	56.52±59.76	162.46±109.27	t=4.253	**<0.001**[a]
Leukocyte count; M [IR]	6.60 [6.40]	7.20 [6.30]	Z=-0.924	0.355[b]
Leukocyte count 1*; M [IR]	7.30 [7.85]	10.80[10.75]	Z=-2.033	**0.042**[b]
Lymphocyte count; M [IR]	0.70 [1.12]	0.98[1.22]	Z=-0.839	0.401[b]
Lymphocyte count 1*;M[IR]	0.66 [1.18]	1.01[3.10]	Z=-1.455	0.146[b]
Platelet count ($\bar{X}$±SD)	222.85±107.17	206.91±79.03	t=0.621	0.537[a]
Platelet count 1* ($\bar{X}$±SD)	214.50±79.78	183.05±115.77	t=1.150	0.259[a]
LDH; M [IR]	280.00 [165.5]	321.00 [295]	Z=-2.098	**0.036**[b]
LDH 1*; M [IR]	237.00 [176]]	518.00 [461.5	Z=-5.904	**<0.001**[b]
Procalcitonin; M [IR]	1.89 [7.88]	2.90 [11.23]	Z=-0.227	0.820[b]
Procalcitonin 1*; M [IR]	0.67 [1.4]	5.62 [31.69]	Z=-3.121	**0.002**[b]

[a]Student t-test; [b]Mann-Whitney U test; CRP - C reactive protein; LDH - lactate dehydrogenase; * lab findings seven days after positive PCR test.

Table 4. Predictive values of hospitalization and comorbidity for mortality.

	B	S.E.	Wald	p	OR	95% C.I.	
						Lower	Upper
Hospitalization	1.492	0.778	3.676	0.055	4.447	0.967	20.442
HTA	2.089	0.935	4.992	**0.025**	**8.073**	1.292	50.437
DM	0.692	0.618	1.253	0.263	1.998	0.595	6.712
MI	-1.195	0.915	1.704	0.192	0.303	0.050	1.820
COPD	1.726	1.370	1.587	0.208	5.619	0.383	82.434
LD	0.157	1.397	0.013	0.910	1.171	0.076	18.095
FA	-1.376	1.000	1.892	0.169	0.253	0.036	1.794

Table 5. Predictive values of COVID-19 symptoms for fatal outcome.

	B	S.E.	Wald	P	OR	95% C.I.	
						Lower	Upper
Fever	2.090	1.106	3.572	0.059	8.084	0.925	70.621
Cough	0.248	0.737	0.113	0.737	1.281	0.302	5.433
Dyspnea	1.302	0.633	4.230	**0.040**	**3.676**	1.063	12.710

In retrospect, it was proven that deceased hemodialysis patients had statistically significantly higher LDH values initially and seven days after the first laboratory findings than the surviving hemodialysis patients, which correlates with data from research by Goicoeche M. et al. in Madrid, who had the same results (5). Deceased hemodialysis patients were shown not to have statistically significant higher values of CRP, leukocytes, and procalcitonin initially, but after seven days of the disease, laboratory findings showed that the deceased patients had a statistically significant increase in CRP, leukocytes, and procalcitonin. In this study, we find the frequency of symptoms to be partially consistent with the research of Lano G. et al. in which hemodialysis patients with COVID-19 were also studied. Data for that study were collected in 11 different dialysis centers in France. Dyspnea was more common among the deceased subjects in our study, as in the French study (6).

In contrast to studies conducted in Madrid, the Bronx, and Paris, this study showed a statistically significant association between

hypertension and death in our subjects. Regarding the correlation between other comorbidities and mortality, the obtained results are in accordance with the results of the previously mentioned research - no statistical correlation was found. In addition, no association was found between hospitalization and death among the subjects in this study (7-9).

CONCLUSION

In this study, it was shown that the value of lactate dehydrogenase can serve as a prognostic factor in the severity of the disease and the possible death of the patient. Regarding other laboratory parameters (CRP, procalcitonin, leukocyte, and platelet count), there was no statistically significant difference in the probability of patient death and the initial laboratory findings, although there was a significant increase in CRP, procalcitonin,

leukocyte count, and platelet count decline after seven days of the disease in deceased patients.

Hypertension has been shown to be the only comorbidity that significantly contributes to mortality in subjects. The deceased subjects were treated with a significantly higher proportion of oxygen, antibiotics, and corticosteroids. None of these therapies have been shown to be effective in the treatment of COVID-19 in hemodialysis patients. All investigated symptoms are present to a large extent in all patients on hemodialysis with COVID-19 (sorted by frequency): fever, cough, and dyspnea. Subjects who died from COVID-19 were significantly more febrile and had a cough.

The importance of this study is exceptional, as COVID-19 patients are our medical present. It is extremely important to be able to create an image of the severity of the disease, predict how the disease will progress, and include the correct level of therapy in a timely manner at the beginning of the treatment.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHORS' CONTRIBUTIONS

Author contributions: I.Z and M.T. conceived and designed the study; I.I, I.T., and I.K.S. collected the data; I.Z and I.T. analyzed the data, interpreted the results, and prepared the tables; I.Z. drafted the manuscript; all the authors edited and revised the manuscript and approved the final version.

ETHICAL BACKGROUND

Institutional Review Board statement: The Ethics Committee of the Mostar Chamber of Physicians waived the need for ethics approval and the need to obtain consent for the collection, analysis, and publication of the retrospectively obtained and anonymized data for this non-interventional study.

Informed consent statement: Informed consent was obtained from all subjects involved in the study.

Data availability statement: We deny any restrictions on the availability of data, materials, and associated protocols. Derived data supporting the findings of this study are available from the corresponding author on request.

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