RESEARCH ARTICLE

The second wave of COVID-19 disease in haemodialysis patients: An experience of a dialysis center from Pakistan

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Abstract

Objective: To evaluate the characteristics and outcomes of second wave of coronavirus disease-2019 in haemodialysis patients.

Method: The retrospective, observational cohort study was conducted at The Kidney Center Post-Graduate-Training-Institute, Karachi, Pakistan and comprised data of patients regardless of gender who contracted coronavirus disease-2019 during the second wave from November 3, 2020, till February 12, 2021. Epidemiological, clinical, laboratory, and radiological characteristics and outcomes of the patients were reviewed. Data was analysed using SPSS 21.

Results: Of 437 patients on haemodialysis, 46(10.5%) contracted coronavirus disease-2019; 29(63%) males and 17(37%) females. The overall median age was 61.5±13.02 years. Most patients developed mild disease 27(%). The most common symptom was fever 29(63%), and 6(13.1%) patients had patchy bilateral opacity on chest radiograph. Major complications were lymphocytopenia 29(63%), pneumonia 15(32.6%), thrombocytopenia 8(17.4%), and septic shock 5(10.9%). Overall, 15(32.6%) patients required hospitalisation, and 8(17.4%) required mechanical ventilation. There were 13(28.3%) deaths. Patients aged >60 years had 6.8 times more severe disease (p=0.023) and chances of death among them were 5.8 times higher (p=0.036) than in those aged <60 years.

Conclusion: There was a high susceptibility of haemodialysis patients during the second wave of coronavirus disease compared to the general population. The most important determinants of death were advanced age, lower oxygen saturation and thrombocytopenia at presentation.

Keywords: Second wave COVID-19, Clinical characteristics, Outcome, Haemodialysis. (JPMA 72: 1797; 2022)

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Introduction

The sudden emergence of the coronavirus disease-2019 (COVID-19) pandemic raised unforeseen challenges for the health community and devastating outcomes. Many countries saw a second wave of COVID-19 during 2020. Non-availability of vaccines or a specific antiviral necessitated non-pharmaceutical interventions, such as physical distancing, hand-washing and mask-wearing which have become the standard in restricting COVID-19 spread. Non-compliance with these precautions appears to be the apparent cause of the second wave of COVID-19.[1,2] In Pakistan, the government announced the second wave of COVID-19 on October 28, 2020.[3] The data released by the National Command and Operation Centre (NCOC) indicated that the positivity rate and death rate of the second wave was higher than that of the first wave.[1,4]

Considering the large population size of haemodialysis (HD) patients,[5] the compromised immune function of uraemic patients[6] along with increased frequency of co-morbidities, such as diabetes mellitus (DM), hypertension (HTN) and cardiovascular disease (CAD), it was anticipated even during the first COVID-19 wave that HD patients were more susceptible to COVID-19 infection and also to severe illness. The mortality risk for HD patients was higher than for the general population.[7-9] Apart for a higher mortality rate, clinical characteristics and outcome of COVID-19 were diverse, ranging from asymptomatic to deadly,[7-10] making the trend of the illness in individual cases unpredictable. Also, the second wave not only got linked to new variants of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but also differed in factors as age range and severity of the disease.[11,12]

The demographic, clinical characteristics and outcomes of the second wave of COVID-19 in HD patients have largely remained unknown. The current study was planned to fill the gap by evaluating the characteristics and outcomes of COVID-19 second wave in HD patients.

Materials and Methods

The retrospective, observational cohort study was conducted at The Kidney Center Post-Graduate-Training-Institute, Karachi, Pakistan and comprised data of patients regardless of gender who contracted coronavirus disease-2019 during the second wave from November 3, 2020, till February 12, 2021. Epidemiological, clinical, laboratory and radiological characteristics and outcomes the patients were

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reviewed from charts after approval from the The Kidney Centre ethical review committee. Information collected included demographics, exposure history, dialysis vintage, co-morbidities, symptoms, signs, radiological and laboratory findings, complications, treatment received during the COVID-19 infection, and outcome. For information that were either not complete or ineligible, we contacted patients or family members of expired patients, therefore informed consent was taken.

A confirmed case of COVID-19 was defined as a positive result on at least one of two tests done 24-hours apart on real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assay of nasal swab specimens.[13] The incubation period was defined as the interval between the earliest date of likely contact of the transmission source (person with suspected or confirmed case) and the earliest date of symptom onset. Lymphocytopenia was defined as a lymphocyte count <1500 cells per cubic millimetre (mm^3). Thrombocytopenia was defined as a platelet count >150,000mm^3. Pneumonia was diagnosed using the American Thoracic Society (ATS) guidelines for community-acquired pneumonia[14] septic shock, using the third international consensus definition,[15] isseminated intravascular complication (DIC), according to the International Society on Thrombosis and Haemostasis (ISTH) criteria,[16] acute respiratory distress syndrome (ARDS) as per the Berlin definition,[17] acute hepatic injury (AHI) was defined as an elevation in alanine aminotransferase (ALT) of >10 times the upper limit of normal.[18]

The severity of COVID-19 was categorised as mild, moderate-severe, and critical. Mild referred to patients who had mild symptoms without manifestation of viral pneumonia on chest X-ray (CXR). Moderate-severe referred to patients who had symptoms, such as fever and respiratory tract symptoms, etc., with features of viral pneumonia on CXR with or without respiratory rate >30 breaths/min; oxygen saturation (SPO2) <93% at rest state, and pulmonary lesion progression of >50% within 24-48 hours on radiological imaging. Critical referred to patients with respiratory failure requiring mechanical ventilation, and/or with the presence of shock, and/or another organ failure that required monitoring and treatment in the high dependency unit (HDU) or the intensive care unit (ICU).

Data was analysed using SPSS 21. Mean with standard deviation (SD) and median with Interquartile range (IQR) were calculated for continuous variables, while for categorical variables, frequencies and percentages were calculated. To observe the effect of different variables on disease severity and outcome, logistic regression was run and odds ratio (OR) with 95% confidence interval were worked out. For binary logistic regression, the three categories of disease severity were merged into twom as severe and non-severe. P<0.05 was considered significant.

Results

Of the 437 maintenance HD patients registered at the study site, 101(23.1%) were suspected and 46(10.5%) were confirmed as COVID-19 cases. There were 29(63%) males and 17(37%) females. The overall mean age was 61.5±13.02 years. Mean HD vintage was 4.36±3.47 years. The most common co-morbidity was HTN 42(91.3%), while 9(17.4%) and 2(4.3%) patients had a history of former or current smoking, respectively. Exposure history was positive in 8(17.4%) patients, and 1(2.2%) patient had a travel history to high-prevalence COVID-19 areas within the country.

Overall, 4(8.7%) patients after their initial symptoms remained asymptomatic throughout the course. The median incubation period was 4.5(3.5 IQR) days. Most patients developed mild disease 27(58.7%), followed by 15(32.6%) critical and 4(8.7%) moderate-severe (Table 1).

The most common symptoms were fever in 29(63%), followed by cough 27(58.7%), shortness of breath 18(39.1%) and diarrhoea 15(32.6%), while 6(13.1%) patients had patchy bilateral opacity on CXR. Mean haemoglobin (Hb) level was 10.1±1.66g/dl, leucocytes 8.0±3.08/mm^3, and platelets 248.1±100.7/ mm^3 (Table 2).

The most common complication was lymphocytopenia 29(63%), followed by pneumonia 15(32.6%). Oxygen and intravenous (IV) antibiotics were given in 14(30.4%) patients, and 14(30.4%) received systemic steroids. Overall, 15(32.6%) patients needed hospitalisation, with 3(6.5%) in HDU and 6(13%) in ICU. Mechanical ventilation was needed in 8(17.4%) patients who all fell in the critical category. Overall, there were 13(28.3%) deaths (Table 3). Survival at week 1 from the date of a positive SARS-CoV-2 test was 43(93.5%) and survival at week 2 was 37(80.4%). The mean time of death from the date of positive SARS-CoV-2 PCR test was 9.76±7.4 days and from the date of onset of symptoms it was 12.3±7.31 days. The mean time of recovery was 11.39±4.85 days from the date of positive test, whereas 12.3±7.31 days from the date of onset of symptoms.

Patients aged >60 years had 6.8 times more severe disease than patients aged <60 years (p=0.023) in univariate regression analysis (Table 4) which remained statistically significant with multivariate analysis (p=0.05) (Table 5). SPO_2 and thrombocytopenia at presentation had significant association with severe disease (p<0.001 and p=0.008, respectively) in univariate analysis. The same association was maintained on multivariate analysis.

Gender, co-morbidities, such as DM, HTN, CAD, obesity, HD vintage, dialyser use, vaccination with flu and Bacille Calmette-Guerin (BCG) vaccine and other laboratory parameters, such as lymphocytopenia, C-reactive protein (CRP) and albumin did not significantly relate with disease severity (p>0.05)

Deaths among patients aged >60 years were 5.8 times more compared to patients aged <60 years (p=0.036) in

Table-1: Baseline characteristics of haemodialysis patients with coronavirus disease-2019 (COVID-19) in second wave according to disease severity.

Variables	All patients	Disease Severity		
	(n=46)	Mild (n= 27)	Moderate-Severe (n= 04)	Critical (n=15)
	Mean±SD, Median, IQR / n(%)			
Gender				
Male	29 (63)	17 (58.6)	3(10.3)	9(31)
Female	17 (37)	10(58.8)	1(5.9)	6(35.3)
Mean Age (years)	60.3±13.02,61.5,15.25	56.7±14.75,60,16	61.75±8.84,60,16.25	66.4±7.74,68,10
< 60 years [n (%)]	18 (39.1)	13(72.2)	2(11.1)	3(16.7)
>& = 60 years [n (%)]	28 (60.9)	14(50)	2(7.1)	12(42.9)
Smoking history [n (%)]				
Never smoked	36 (78.3)	22(61.1)	2(5.6)	12(33.3)
Former smoker	8 (17.4)	4(50%)	1(12.5)	3(37.5)
Current smoker	2 (4.3)	1(50)	1(50)	0(0)
Exposure to source of transmission within past 14days	8 (17.4)	5(62.5)	1(12.5)	2(25)
Living in same house of covid-19	7 (15.2)	4(57.1)	1(14.3)	2(28.6)
Having face to face contact	1 (2.2)	1(100)	0(0)	0(0)
Contact with health care worker	0(0)	0(0)	0(0)	0(0)
H/o past 14days travel in COVID-19 infected area	1 (2.2)	1(100)	0(0)	0(0)
Median incubation period	4.5	4	-	4
Cause of ESRD				
Unknown	18 (39.1)	7(38.9)	2(11.1)	9(50)
Diabetes	8 (17.4)	5(62.5)	1(12.5)	2(25)
Hypertension	7 (15.2)	4(57.1)	0(0)	3(42.9)
Glomerulonephritis	4 (8.7)	3(75)	0(0)	1(25)
ADPKD	1 (2.2)	1(100)	0(0)	0(0)
Other	8 (17.4)	7(87.5)	1(12.5)	0(0)
Comorbidities				
Diabetes	24 (52.2)	9(37.5)	4(16.7)	11(45.8)
Hypertension	42 (91.3)	23(54.8)	4(9.5)	15(35.7)
Coronary artery disease	11 (23.9)	4(36.4)	1(9.1)	6(54.5)
Congestive heart failure	5 (10.9)	3(60)	0(0)	2(40)
Pulmonary disease	4 (8.7)	0(0)	1(25)	3(75)
Hepatitis B or C	3(100)	3(100)	0(0)	0(0)
Obesity(BMI > 30)	10(21.7)	6(60)	0(0)	4(40)
History of renal transplantation in past	0(0)	0(0)	0(0)	0(0)
Haemodialysis vintage	4.36±3.47,4.0,4.0	4.7±4.07,4.0,5.0	2.0±1.4,1.5,2.5	4.2±2.37,5.0,4.0
< 5 years (n + %)	28(60.9)	17(60.7)	4(14.3)	7(25)
>& = 5 years (n + %)	18(39.1)	10(55.6)	0(0)	8(44.4)
Access for haemodialysis				
AVF	44 (95.7)	27(61.4)	3(6.8)	14(31.8)
AV graft	0(0)	0(0)	0(0)	0(0)
Permacather	2 (4.3)	0(0)	1(50)	1(50)
Dialyzer type				
Single-use	22(47.8)	10(45.5)	4(18.2)	8(36.4)
Re-use	24 (52.2%)	17(70.8)	0(0)	7(29.2)
Vaccination				
Flu vaccine	31(67.4)	18(58.1)	1(3.2)	12(38.7)
BCG vaccine	39 (84.8)	23(59)	4(10.3)	12(30.8)

SD: Standard deviation, IQR: Interquartile range, ESKD: End-stage kidney disease, ADPKD: Adult polycystic kidney disease, BMI: Body mass index, AVF: Arteriovenous fistula, AV: Arteriovenous, BCG: Bacille Calmette-Guerin.

univariate regression analysis, but it was not statistically significant in multivariate analysis (p=0.088). DM and CAD were associated with higher death rate in univariate analysis (p=0.043 and p=0.034 respectively), but their association was not significant in multivariate analysis (p-0.209 and p=0.151, respectively). Decreases SPO_2 at presentation was found to be associated with increased death both in univariate (p=0.001) and multivariate analysis (p=0.007), while thrombocytopenia was associated with higher death rate in univariate analysis (p=0.028), but not in multivariate analysis (p=0.118).

Table-2: Clinical, laboratory and radiological findings.

Variables	All patients	Disease Severity		
	(n=46)	Mild (n= 27)	Moderate-Severe (n= 04)	Critical (n=15)
		Mean±SD, Median, IQR / n(%)		
Symptoms				
Fever	29 (63)	16 (55.2)	4(13.8)	9 (31)
Chills	6 (13)	3 (50)	0(0)	3 (50)
Fatigue	13 (28.3)	9(69.2)	1(7.7)	3 23.1)
Myalgia/arthralgia	7 (15.2)	7(100)	0(0)	0(0)
Cough	27 (58.7)	13(48.1)	4 (14.8)	10 (37)
Sore throat	1 (2.2)	1(100)	0(0)	0(0)
Shortness of breath	18 (39.1)	4 (22.2)	1(5.6)	13 (72.2)
Sputum production	0(0)	0(0)	0(0)	0(0)
Haemoptysis	1 (2.2)	0(0)	1(100)	0(0)
Conjuctival congestion	0(0)	0(0)	0(0)	0(0)
Nasal congestion	1(2.2)	1(100)	0(0)	0(0)
Headache	4 (8.7)	3(75)	0(0)	1 (25)
Nausea/vomiting	6 (13)	1(16.7)	1 (16.7)	4(66.7)
Diarrhoea	15 (32.6)	8(53.3)	1 (6.7)	6 (40)
Signs				
Throat congestion	1(2.2)	1 (100)	0(0)	0(0)
Tonsil swelling	1 (2.2)	1 (100)	0(0)	0(0)
Rash	0(0)	0(0)	0(0)	0(0)
Enlargement of LN	0(0)	0(0)	0(0)	0(0)
Respiratory rate/min	21.1±3.77,20,6.0	20.8±3.58,20,4	18.7±1.50,19,2.75	22.1±4.3,22,6
Heart rate/min	84.3±15.6,85,19	84.1±12.9,86,18	73.7±12.1,71,22.75	87.3±20.2,83,33
B.P systolic(mmHg)	142.5±24.7,141,37	140.4±24.8,142,37	144.2±6.75,145,12.25	145.8±28.1,140,55
B.P diastolic(mmHg)	74.0±14.5,70.0,20.75	73.4±13.2,70,20	72.5±6.45,72.5,12.5	75.6±18.4,77,26
Laboratory tests (mean±SD ,median , IQR)				
SPO_2	95.03±7.15,97,2	97.5±1.3,97.5,2.25	94.25±4.92,96,8.25	82.46±13,81.1,21
HB (g/dl)	10.1±1.66,10.1,2.32	10.16±1.58,10.0,2.4	10.55±2.47,10.3,4.6	10.32±1.63,10.3,2.5
WBC per mm3	8.0±3.08,7.85,2.8	7.82±3.0,7.85,2.53	7.89±3.27,8.39,6.24	7.90±3.56,6.88,5.04
Lymphocyte count per mm3	1316±563.1,1367,718.5	1368.23±695.5,1367,804.5	1429±530,1316,992	1054.66±439.4,1076,804
Neutrophil count per mm3	5895.7±3085.3,5197,2639.8	5667±2944,5143,2634.25	5616±2970,5607,.4,5731.6	5488±3182,4875,5278.4
Neutrophil to lymphocyte ratio (NLR)	6.4±8.26,3.43,3.4	5.82±6.4,3.36,2.54	4.4±3.62,3.11,6.07	7.96±11.59,5.06,4.78
Platelet count per mm3	248.1±100.7,228.5,103.7	255.7±91.7,247.5,120.75	186.75±31.22,183.5,59.75	193±105.54,193,74
C-reactive protein (mg/l)	74±179.1,24,85.5	70.9±192.47,24,54	64.3±61.07,45.5,106	20.4±25.6,6,18
D-dimer	31.78±163.9,1.5,1.75	1.59±1.21,1.3,1.2	226.3±449.1,1.85673.9	3.05±2.86,2.25,5.25
Transferrin saturatio[n (%)]	34.5±13.97,32.24,17.61	30.5±13.1,28.9,20.5	43.65±20.56,37.2,37.16	33.87±7.40,34,14
Ferritin	1472.9±1618,1315.8,1426.7	958.6±835.8,634.6,1209	1714.1±436.1,1587,795.1	1416.3±2146.6,648.1279
Serum albumin (mg/dl)	3.54±0.52,3.64,0.79	3.53±0.49,3.69,0.71	3.57±0.46,3.64,0.87	3.68±0.59,3.6,0.99
Alanine aminotransferase (SGPT)	28.3±67,12,11	17.96±21.96,12,13.5	101.25±176.5,13.5,265.7	9.86±3.88,9,7
Intact PTH (pg/ml)	469.7±575.1,286.1,487.3	458.3±613.5,263.9,408.4	395.6±326.6,294.8,573.8	248.4±168.8,177.1,197.3
Radiological findings (Chest X-ray)				
Normal	31(67.4)	27(87.1)	1(3.2)	3(9.7)
Local patchy opacity	0(0)	0(0)	0(0)	0(0)
Bilateral patchy opacity	6(13.1)	0(0)	3(50)	3(50)
Interstitial Opacity	0(0)	0(0)	0(0)	0(0)

SD: Standard deviation, IQR: Interquartile range, LN: Lymph node, BP: Blood pressure, SPO_2: Oxygen saturation, HB: Haemoglobin, WBC: Shite cell count, PTH: Parathyroid hormone.

Overall death rate during the COVID-19 second wave in HD patients was 1.54 time higher than the same period before the COVID-19 pandemic; 22 from November 2019 to February 2020 versus 34 from November 2020 to February 2021, of which deaths due to COVID-19 were 13(38.2%).

Discussion

The first wave of COVID-19 was particularly dramatic for HD patients worldwide, with mortality ranging from 21% to 32.8% in different studies,[8,9,19,20] which as much higher than that for the general population.[9,19] Many countries have gone through the second wave that is linked to new SARS-CoV-2 variants, and empirical data suggests that it also differs in factors, such as age range and disease severity.[11,12] In Pakistan, the second wave of Covid-19 was announced on October 28, 2020[3] which had a higher positivity percentage and death rate than the first wave, according to the NCOC.[1,4] The present study aimed at assessing the impact of second COVID-19 wave on an HD patient cohort.

The study found high susceptibility (10.5%) of HD patients to COVID-19 during the second wave compared to the general population in Pakistan where the positivity rate was 3.5% to 8% during the study period.[21] High susceptibility of HD patients was also found during the first wave in several reports[7-9] and this was attributed to the compromised immune function of uraemic patients[6] along with the increased frequency of co-morbidities in HD patients.

Among the study patients, only 8(17.4%) had a positive history of exposure, while 4(8.7%) patients remained asymptomatic after their initial symptoms had gone. This may suggest that the primary source of COVID-19 spread may be asymptomatic patients or patients in the

Table-3: Complications, treatments used and outcomes.

Variables	All patients	Disease Severity		
	(n=46)	Mild (n= 27)	Moderate-Severe (n= 04)	Critical (n=15)
		Mean±SD, Median, IQR / n(%)		
Complications				
Lymphocytopenia	29(63)	14(48.3)	3(10.3)	12(41.4)
Thrombocytopenia	8(17.4)	2(25)	0(0)	6(75)
Pneumonia	15(32.6)	0(0)	3(20)	12(80)
Acute hepatic injury	1(2.2)	0(0%)	1(100)	0(0)
Septic shock	5(10.9)	0(0)	0(0)	5(100)
DIC	0(0)	0(0)	0(0)	0(0)
Acute respiratory distress syndrome	2(4.3)	0(0)	0(0)	2(100)
Treatment used				
Oxygen therapy	14(30.4)	0(0)	2(14.3)	12(85.7)
IV antibiotics	14(30.4)	0(0)	2(14.3)	12(85.7)
HCQ	1(2.2)	0(0)	0(0)	1(100)
Remdisivir	6(13)	0(0)	2(33.3)	4(66.7)
Tocilimab	1(%)	0(0)	0(0)	1(100)
Systemic glucocorticoids	14(30.4)	1(7.1)	2(14.3)	11(78.6)
IV immunoglobulin	0(0)	0(0)	0(0)	0(0)
Convalescent plasma	0(0)	0(0)	0(0)	0(0)
Outcome				
Hospitalization	15(32.6)	0(0)	2(13.3)	13(86.7)
Isolation Ward	6(13)	0(0)	2(33.3)	4(66.7)
ICU	6(13)	0(0)	0(0)	6(100)
HDU	3(6.5)	0(0)	0(0)	3(100)
Mechanical Ventilation	8(17.4)	0(0)	0(0)	8(100)
Invasive	3(6.5)	0(0)	0(0)	3(100)
Non-invasive	5(10.9)	0(0)	0(0)	5(100)
Recovery	33(71.7)	27(81.8)	4(12.1)	2(6.1)
Time from the date of positive test (days)	11.39±4.85,13,7	10.88±4.79,10,7	11.25±3.5,11.5,6.75	18.5±3.53,18.5,0
Time from the date of onset of symptoms (days)	14.03±5.2,14,6	13.14±4.94,14,6	15.75±2.36,15,4.25	22.5±6.36,22.5,0
Death	13(28.3)	0(0)	0(0)	13(100)
Time from the date of positive test (days)	9.76±7.4,6,10.5	-	-	9.76±7.4,6,10.5
Time from the date of onset of symptoms (days)	12.3±7.31,10,10.5	-	-	12.3±7.31,10,10.5

SD: Standard deviation, IQR: Interquartile range, DIC: Disseminated intravascular complication, IV: Intravenous, HCQ: Hydroxychloroquine, ICU: Intensive care unit, HDU: High dependency unit.

incubation period,[22] or those having close contact with other individuals in the HD centre. In the dialysis centre where the current study was conducted, all patients were checked for temperature twice, and before starting their sessions, the patients were asked about symptoms related to COVID-19. Those suspected of having COVID-19 were then dialysed in a separate area at different times from the usual shift to minimise interaction with other patients. These suspected or confirmed had to have two negative PCR negative tests before returning to dialysis on their original days and times. All confirmed COVID-19 patients were dialysed in a separate area and on different days. Even after all these measures, preventing cross-contamination remained highly challenging during the second wave which indicated that optimal screening and managing approach for HD patients was still lacking, and there was need for more restrictive screening criteria to combat this problem.

Table-4: Univariate analysis of study variables with disease severity and outcome.

Variables	Disease Severity			Outcome		
	Univariate regression analysis			Univariate regression analysis		
	Odds ratio	CI (lower-upper)	*p*-value	Odds ratio	CI (lower-upper)	*p*-value
Age (years)						
< 60 .		1			1	
>& = 60 yrs.	6.8	1.3 – 35.4	0.023	6.8	1.1 – 30.6	0.036
Gender						
Female	1	1				
Male	1.1	0.8 – 4	0.908	1.1	0.29 – 4.1	0.894
Diabetes	3.2	0.8 – 12.4	0.091	4.5	1.1 – 19.5	0.043
CAD	4.5	0.97 – 16.8	0.054	4.8	1.1 – 20.4	0.034
Obesity (BMI > 30)	0.97	0.21 – 4.5	0.973	1.1	0.24 – 5.2	0.89
HD Vintage						
< 5 years		1			1	
>& = 5 years	1.9	0.53 – 6.8	0.321	1.5	0.41 – 5.5	0.541
Dialyzer use						
Single-use		1			1	
Re-use	0.58	0.16 – 2.1	0.405	0.71	0.2 – 2.6	0.609
Vaccination						
Flu vaccine	2.2	0.51 – 9.5	0.291	1.9	0.44 – 8.3	0.391
BCG vaccine	0.52	0.1 – 2.7	0.443	0.46	0.09 – 2.4	0.359
Clinical parameter						
Anaemia	1	0.25 – 4.1	0.975	1.2	0.3 – 4.8	0.813
Lymphocytopenia	2.9	0.67 – 12.2	0.158	2.5	0.57 – 10.6	0.229
Thrombocytopenia	11.3	1.9 – 66.7	0.008	6.3	1.2 – 31.9	0.028
SPO_2	19.8	4 – 97.5	<0.001	30.8	5.2 - 183	<0.001
C-reactive protein	0.39	0.1 – 1.4	0.154	0.49	0.13 – 1.8	0.282
Ferritin	0.68	0.14 – 3.3	0.634	0.6	0.12 - 3	0.526
Serum albumin	0.96	0.25 – 3.4	0.908	0.7	0.19 – 2.7	0.586

CI: Confidence interval, CAD: Coronary artery disease, BMI: Body mass index, HD: Haemodialysis, BCG: Bacille Calmette-Guerin, SPO_2: Oxygen saturation; Disease Severity: severe vs non-severe; Outcome: Recovery vs death.

Table-5: Multivariate analysis of study variables with disease severity and outcome.

Variables	Disease Severity			Outcome		
	Multivariate regression analysis			Multivariate regression analysis		
	Odds ratio	CI (lower-upper)	*p*-value	Odds ratio	CI (lower-upper)	*p*-value
Age (years)						
< 60		1			1	
>& = 60	133.5	0.96 – 18499	0.052	26.6	0.62 – 1152	0.088
Diabetes (Yes vsNo)	9.8	0.2 – 427.9	0.234	8.3	0.3 – 221.5	0.209
CAD	6.2	0.27 - 143	0.256	9.1	0.445 - 186	0.151
Clinical parameter						
Lymphocytopenia	1.7	0.1 – 26.7	0.722	0.92	0.06 – 13.1	0.948
Thrombocytopenia	123.9	1.2 - 13066	0.043	19.4	0.47 – 798.7	0.118
SPO_2	55.6	2.4 – 1268	0.012	60.1	3.1 – 1190.8	0.007
C-reactive protein	0.07	0.003 – 1.9	0.115	0.2	0.01 – 2.9	0.235

CI: Confidence interval, CAD: Coronary artery disease, SPO_2: Oxygen saturation;
Confounders: Age, Diabetes mellitus, Coronary heart disease.

Similar to the first wave[7,9] the majority of HD patients who contracted COVID-19 in the second wave in the current study were older (median age 61.5 years) that was significantly higher than the general population (43.2±5.7 years|) data both during the first[23] and the second wave.[24] The current study also showed that the patients aged 60 years or more had 6.8 times more severe disease and 5.8 times more deaths than patients with age less than 60 years This correlates with the findings in general both during the first[25] and the second wave.[26]

According to the literature, COVID-19 patients with underlying conditions, such as DM, HTN, cardiovascular disease (CVD), obesity or old age, are highly susceptible and often have more serious disease.[27] However, the current study found no significant relationship between co-morbidities, such as DM, HTN, CAD and obesity, and disease severity.

The symptoms and complications noted in the current study were similar to the most frequent signs and symptoms in both waves.[26] CXR finding was ground-glass opacity which correlated with finding during the first wave.[7,9] Financial constrains in resource-limited countries, like Pakistan, limited the accessibility of computed tomography (CT) of chest in these patients, but correct diagnosis of COVID-19 with CXR

ranged from 57% to 89% which is compatible with chest CT that correctly diagnosed COVID-19 in 89.9%.[28]

The current study showed that significant number of patients developed severe to critical disease and required HDU or ICU admission and mechanical ventilation. A study in Spain[26] done in the general population observed that the second wave caused significantly fewer number of admissions to Internal Medicine department and ICUs, with shorter duration of hospitalisation. Another study[26] further noticed that patients in the second wave were treated more often with non-invasive mechanical ventilation and corticoids, which was also the case in the current study, and less often with invasive mechanical ventilation, conventional oxygen therapy and anticoagulants. Another study done in Spain[24] found that in general population, the proportion of patients with mild or severe symptoms compared with those without symptoms or with minor symptoms, was significantly higher during the first wave compared to the second wave.

A high rate of death (28.3%) was found in HD patients during the second COVID-19 wave in the current study. This was similar to the findings related to the first wave,[8,20] but was significantly higher than that observed in the general population in Pakistan.[28] The current study compared the number of deaths in the preceding year during the same period at the dialysis centre (i.e. from November 2019 to February 2020) with the number of deaths during the second wave (i.e. from November 2020 to February 2021), and studied the impact of COVID-19 on mortality in HD patients. Overall deaths during the second wave in HD patients were 1.54 times higher than the same period before the COVID-19 pandemic, of which deaths due to COVID-19 were 38.2%.

The current study has certain limitations, like a small sample size and non-availability of CT chest. Despite the limitations, the current study is the first from Pakistan or any developing country providing information about epidemiological and clinical characteristics as well as outcomes of patients undergoing maintenance HD during the second COVID-19 wave. Some of the findings will help in understanding the behaviour of the second COVID-19 wave and to make policies for controlling cross-infection and overall management of HD patients.

Conclusion

There was a high susceptibility of HD patients in the second wave COVID-19 compared to the general population with asymptomatic patients, and patients in the incubation period may be the primary source of COVID-19 spread within the HD centre. Disease symptoms, radiological findings and laboratory tests were similar to those in general and during the first wave. Patients aged >60 years and those who presented with thrombocytopenia and decreased SPO_2 had high mortality rate. Mortality in HD patients was higher than the general population, especially with critical disease. Death associated with COVID-19 in HD patients was 1.54 times higher. A high susceptibility and poor outcome suggested that the country wsa still not fully prepared during the second COVID-19 wave, and needed more experience and better management policies for HD patients.

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