Open Access ORIGINAL ARTICLE

Clinical Presentation and Outcome of Covid-19 Infection in Patients Undergoing Maintenance Hemodialysis

Muhammad Ali[1], Shafique Ahmed[2], Abdul Manan Junejo[3], Ayesha Ejaz[4], Hina Iram[5], Heer Gul[6]

[1]Assistant Professor, Department of Nephrology, Fazaia Ruth Pfau Medical College, Karachi, Pakistan.
[2,5,6]Registrar, Department of Nephrology, Jinnah Postgraduate Medical Center, Karachi, Pakistan.
[3]Professor, Department of Nephrology, Jinnah Postgraduate Medical Center, Karachi, Pakistan.
[4]Assistant Professor, Department of Nephrology, Jinnah Postgraduate Medical Center, Karachi, Pakistan.

ABSTRACT

Background: WHO declared Covid-19 a pandemic disease; although 80% of patients with CoV-2 infection have no or mild symptoms, the remaining 20% of patients develop complications. In patients undergoing dialysis, mortality could be higher than that in the general population. This study was conducted to assess the frequency, clinical presentation, and outcome of COVID-19 infection in patients of end-stage renal disease (ESRD) on maintenance hemodialysis.

Methodology: This Cross-sectional study was conducted at Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi, from April to September 2020. This study included 130 patients of either gender of End-Stage Renal Disease on maintenance hemodialysis for at least 3 months. Two Samples for COVID-19 PCR were taken through nasal swab. Blood samples were collected for hemoglobin level, total and differential leucocyte count, platelet count, intact Parathyroid hormone, vitamin D level, Urea, Creatinine, ferritin, transferrin saturation, procalcitonin, D-Dimer, C-reactive proteins, and lactate dehydrogenase. Radiological assessment was done by X-ray Chest. Urea reduction ratio and single pool Kt/V was used for assessment of adequacy of hemodialysis.

Results: Out of 130 patients on hemodialysis, COVID-19 was detected in 52 patients, of which males were 69.2% and females were 30.8%. The most common presentation was shortness of breath (28.8%), followed by cough (19.2%). Home isolation was advised to 38.5% while noninvasive ventilation was given to 34.6%. Mechanically ventilated patients were 26.9%. There were 63.5% patients who recovered and were discharged from the hospital or home-isolated, while 19 patients died (36.5%).

Conclusion: COVID-19 pandemic has high chances of infection with increased mortality in people with chronic diseases, especially those having ESRD on hemodialysis. This spread of infection can be hampered with standard measures of disinfection in centers, social distancing in patients, and the use of a face mask.

Keywords: Covid-19, Cough, Hemodialysis, Home isolation, Ventilation

Authors' Contribution:
[1]Conception; Literature research; manuscript design and drafting; [2,3]Critical analysis and manuscript review; [4,5]Data analysis; Manuscript Editing.

Correspondence:
Muuhammad Ali
Email: maunar2002@gmail.com

Article info:
Received: March 15, 2021
Accepted: May 13, 2022

***Cite this article**. Ali M, Ahmed S, Junejo A M, Ejaz A, Iram H, Gul H. Clinical Presentation and Outcome of Covid-19 Infection in Patients Undergoing Maintenance Hemodialysis. J Islamabad Med Dental Coll. 2022; 11(2):89-95. DOI: https://doi.org/10.35787/jimdc.v11i2.694.*

***Funding Source:** Nil*
***Conflict of Interest:** Nil*

Introduction

In December 2019, a new viral infection emerged from the Wuhan city of China by causing Severe Acute Respiratory Syndrome (SARS). Novel Coronavirus (COVID-19) is a new strand of the coronavirus family (SARS-CoV-2) that came out as a new challenge for humanity. It was declared as a pandemic by the World Health Organization on 11th March 2020. Up till now, millions of people have been affected by the pandemic directly and as of now (22nd January 2021), around 96 million people have been diagnosed with COVID-19 worldwide. Out of them, two million deaths have been reported. In Pakistan, this counts to 52,9000 cases, with around 11,000 deaths.[1,2]

COVID-19, is usually asymptomatic (60-80%), but may present with pneumonia (15%), or respiratory distress leading to intensive care admission (3-5%).[3] Some documented symptoms include fever, sore throat, body aches, cough, shortness of breath, pulmonary hemorrhages, and multi-organ failure.

When severe, it leads to sepsis, SARS, and cytokine release syndrome (a fatal condition that leads to death with a mortality rate of around 1.4-8%).[4] Currently, the gold standard test for diagnosis is Real-time PCR (Reverse Transcription Polymerase Chain Reaction) that detects viral RNA, by taking upper respiratory tract swabs. However, multiple laboratory tests (like C-reactive protein, D-Dimer, Procalcitonin, Ferritin, Lactate Dehydrogenase) and radiological investigations (like X-ray, Ultrasonography, and High-resolution computerized tomography) are carried out to assess the disease severity and outcomes.[5]

The old-age population, especially those with comorbid conditions (like Diabetes mellitus, chronic kidney disease, ischemic heart diseases, chronic lung diseases, obesity, and hypertension) are at a higher risk of being infected, and that too with poor prognosis.[6,7] Further, patients undergoing maintenance hemodialysis are at a greater risk of infection as compared to general population due to in-center dialysis or frequently traveling to hemodialysis centers, and lack of social distancing.[8,9] Moreover, patients with end-stage renal disease (ESRD) are immunocompromised and their comorbidities (like Diabetes mellitus, Hypertension, ischemic heart diseases, renal stone diseases, or multiple myeloma), put them at higher risk.[10]

The largest data from Wuhan by Xiong F *et al*. included 7154 patients undergoing hemodialysis, of which 154 had laboratory-confirmed COVID-19. Cardiovascular disease and hypertension were the most common comorbid conditions (68.7%) among those patients. Only 51.9% of patients manifested with fever, while 21.4% remained asymptomatic.[11]Another study from China by Wun J *et al*. stated that fatigue was the most common symptom (59%) in hemodialysis patients with COVID-19, followed by dry cough (49%) and fever (47%) respectively.[12]

COVID-19 in-patients with ESRD undergoing hemodialysis have a variable presentation and mortality. In Europe, reported mortality is around 15 to 20%, highest in Italy 23.6%, while in Spain mortality rate is 12.8%[13] and 28% mortality reported in the United States of America.[14]

This study will give the baseline information about the frequency, clinical presentation, and outcome of COVID-19 infection in patients of end-stage renal disease (ESRD) on maintenance hemodialysis in our setting. Further, the findings will help to evaluate the preventive measures for Covid-19 taken among high-risk patients and help the policy makers in devicing strategies.

Methodology

This cross- sectional study was conducted at the Department of Nephrology, Jinnah Postgraduate Medical Centre, Karachi, Pakistan from April to September 2020. Ethical approval was taken from the institutional ethical review board and patients

were enrolled in this study from the Dialysis unit of the department after taking informed written consent. All the male and female patients with ESRD on regular hemodialysis, at least once a week for at least three months and aged between 14 years to 70 years were included. Patients of acute kidney injury were excluded from the study. The calculated sample size was 130 by Open Epi version 3 at 95% confidence level and anticipated frequency 50%. The patients' information regarding primary cause of renal failure and comorbid conditions was noted. Clinical signs and symptoms like fever, cough, sore throat, body aches, and shortness of breath were assessed and marked on a pre-designed Performa.

Blood samples were collected for Hemoglobin level, intact Parathyroid hormone, Vitamin D, Urea and Creatinine, Ferritin, Transferrin saturation, Procalcitonin, D-Dimer, C-reactive protein, and Lactate dehydrogenase. Radiological imaging was done with an X-ray chest AP view only due to the limitation of access for computed tomography (CT).

Adequacy of hemodialysis was calculated as urea reduction ratio (URR) and single pool (Sp) Kt/V (where Kt/V shows dialysis adequacy by incorporating dialyzer clearance of urea-K, dialysis time-t, and volume of distribution of urea-V). Dialysis weekly schedule, duration, and the access used were also noted.

After the diagnosis of COVID-19 infection, in the first patient, at our hemodialysis center, with persistent shortness of breath, a strict screening and triage system was implemented. Patients were screened for symptoms of COVID-19 before initiating hemodialysis. A mandatory checking of body temperature was also done before shifting the patient for hemodialysis in unit. Overall, screening by nasopharyngeal swab was carried out after the diagnosis of two other patients. A total of 130 patients of ESRD on hemodialysis were assessed for clinical features of COVID-19. Two samples were taken as swabs from the nasopharynx for RT-PCR and COVID-19 was diagnosed as per results.

Management details were listed as home isolation, hospitalization, and mechanical ventilation according to the severity of clinical features. During the home isolation, no specific treatment was given but family was counselled for close observation of any worsening of symptom. While, outcome parameters were noted as discharge from the hospital (according to the hospital's discharge protocol and asymptomatic) and death.

Data was analyzed with IBM SPSS Version 21. Continuous variables like laboratory parameters and dialysis parameters were recorded as mean with standard deviation, while categorical variables like causes, co morbidity, clinical features, radiological findings, weekly schedules, dialysis access, management plans, and outcomes were recorded in frequency and percentages. Cross-tabulation was done to find the outcome according to the different variables. Chi square test was applied to find significant association between categorical variables while student t-test was used to compare means of different continuous variables. Statistical significance was set at a p-value less than 0.05.

Results

In total of 130, COVID-19 was confirmed in 40% (n=52) patients, out of them males were 69.2% (n=36) and females were 30.8% (n=16) with a mean age of 45.90 ±14.33 years. Diabetes Mellitus (DM) was found to be the most common cause of ESRD (40.4%), followed by hypertension (19.2%). Shortness of breath was the most common active complaint in these patients (28.8%), followed by cough (19.2%) and sore throat (17.3%). X-ray chest revealed bilateral ground-glass opacification in 28.8%, local patchy shadow in 28.8% and bilateral patchy shadow in 25% patients, while X-rays were normal in 17.3% (Table 1).

Table I: Causes of the end-stage renal disease and clinical features of covid-19 (n=52)		
	Frequency	**Percentage**
Primary Cause Of ESRD		
Diabetes mellitus	21	40.4%
Hypertension	10	19.2%
Chronic glomerulonephritis	8	15.4%
Bilateral small size kidneys	7	13.5%
Renal stone	4	7.7%
Multiple Myeloma	1	1.9%
Contrast induced Nephropathy	1	1.9%
Symptoms		
Shortness of breath	15	28.8%
Fever	11	21.2%
Cough	10	19.2%
Sore throat	9	17.3%
None (asymptomatic)	6	11.5%
Diarrhea	1	1.9%
Radiological findings (X-ray)		
Bilateral ground-glass opacification	15	28.8%
Local patchy shadow	15	28.8%
Bilateral patchy shadow	13	25%
Normal	9	17.3%

Patients' hemodialysis characteristics are given in Table 2, while the laboratory investigations are listed in table 3.

Table II: Patient hemodialysis characteristics (n=52)		
	Frequency	**Percentage**
Session-week		
Thrice per week	29	55.8%
Twice per week	20	38.5%
Once per week	3	5.8%
Access for Hemodialysis		
Arteriovenous fistula	35	67.3%
Tunnel catheter	7	13.5%
Non Tunnel catheter	6	11.5%
AV Graft	4	7.7%
	Mean	**Standard Deviation**
Hemodialysis Adequacy parameters		
Duration (years)	3.75	1.466
Urea reduction ratio (%)	66.345	4.057
Sp Kt/V	1.155	0.125

Abbreviations: Sp Kt/V: Single pool Kt/V where Kt/V shows dialysis adequacy by incorporating dialyzer clearance of urea (K), dialysis time (t), and volume of distribution of urea (V)

Table III: Laboratory tests (n=52)	
	Mean ± Standard deviation
Lactate dehydrogenase (U/L)	596.269 ± 273.091
C-reactive protein (mg/L)	106.794 ± 50.833
Procalcitonin (ng/mL)	2.991± 2.458
D-Dimer (µg/ml)	2.5173± 1.905
Creatinine (mg/dL)	7.35 ± 1.833
Albumin (mg/dL)	2.898 ±0.238
Intact parathyroid hormone (pg/dL)	692.63 ± 559.98
Vitamin D (ng/dL)	17.041 ± 6.643
Ferritin (ng/ml)	665.26 ± 468.433
Hemoglobin (g/dL)	10.1758 ± 1.480
WBC ($x10^9$/L)	14.53 ± 5.42
Platelets ($x10^9$/L)	211.53 ± 83.13
Lymphocytes ($x10^9$/L)	1.38 ± 0.692
Aspartate aminotransferase (U/L)	36.50 ± 10.85
Alanine transaminase (U/L)	39.21 ± 11.569

Table IV: Association of outcome according to various factors and action taken (n=52)				
	Outcome		Total	p-Value
	Discharge (n=33)	Expired (n=19)		
Gender				
Male	21	15	36	0.249
Female	12	4	16	
Primary Cause of ESRD				
Diabetes mellitus	10	11	21	0.06
Hypertension	9	1	10	
Chronic glomerulonephritis	6	2	8	
Bilateral small size kidneys	6	1	7	
Renal stone	1	3	4	
Multiple Myeloma	1	0	1	
Contrast induced Nephropathy	0	1	1	

There was significant association between gender and outcome with more females being discharged and males expired. There was significant association between primary cause of ESRD and outcome of the patient with more deaths reported among those having contrast induced Nephropathy and renal stone being primary cause of ESRD.

Home isolation was advised to 20 (38.5%) patients, while noninvasive ventilation was given to 18 (34.6%). Mechanically ventilated patients were 14 (26.9%). Out of them, 33 (63.5%) patients recovered. While nineteen patients expired (36.5%), All those patients who were mechanically ventilated (n=14) expired, and there was significant association between action taken and outcome of the patient. More deaths reported among those who were mechanically ventilated as compared to non-invasive ventilation and home isolation.(p=0.001)

Discussion

Although the Coronavirus family, i.e. SARS-CoV-2, SARS-CoV, and MERS-CoV, have caused major health issues in this century, COVID-19 (SARS-CoV-2) proved most serious of all.[15] Hemodialysis patients are at an increased risk of infection. However, data about these patients is limited. In our study, among 130 patients on maintenance hemodialysis,40% were found to have COVID-19 infection, out of which 36.5% expired.

In our study, diabetes mellitus was the most common primary cause of end stage renal disease and possibly a risk factor for COVID-19 (40.4%), followed by hypertension (19.2%), while chronic glomerulonephritis was found in 13.4%. In comparison, a multicenter study from China reported unknown etiology in 29.4%, chronic glomerulonephritis in 21.6%, and hypertension in 21.6%.[16] Moreover, the Chinese Centers of Disease Control and Prevention estimated the mortality rate of COVID-19 patients with cardiovascular disorders, diabetes, chronic respiratory disease, and hypertension as 10.5%, 7.3%, 6.3%, and 6.0% respectively.[17]

Shortness of breath was the main clinical presentation in our study population (28.8%), this may be due to COVID-19 pneumonia superimposed on damaged or lungs with recurrent volume overload. It was also reported as the most common symptom from Spain by Goicoechea M *et al*.[3] Other clinical symptoms in our study like cough and sore throat were found in 22.2% each, while fever was found in 18.6%. A multicenter study from Italy by Alberici F *et al*. reported fever (68%) as most common symptom, followed by shortness of breath in 25%, and cough in 23%.[18]

On radiological investigation with X-ray chest, we found bilateral ground-glass opacification as the most common finding (28.8%), followed by local patchy shadow (28.8%), while in 17.3% of patients, imaging was normal. Goicoechea M *et al*. from Italy

reported bilateral peripheral ground-glass opacification in 61%, unilateral lung involvement in 19%, and normal radiology in 19%. Similarly, Wu J *et al*. when assessed the COVID-19 patients on hemodialysis, quoted that on CT, there was bilateral ground-glass opacification in 82%, unilateral lung disease in 10%, and normal imaging in 8%.[12]

Most of the patients with mild disease were advised home isolation (38.5%). Intensive care unit admission with mechanical ventilation was given to 26.9%, while the remaining (34.6%) were hospitalized with noninvasive positive pressure ventilator support. In Wuhan, results showed that most patients (84%) were on simple oxygen therapy, 25% received noninvasive ventilation, while mechanical ventilation was given to 6%.[12]

As for an outcome of COVID-19 positive hemodialysis patients in our study, 63.5% were discharged after becoming asymptomatic and RT-PCR negative. The 36.5% patients expired, most of them were on mechanical ventilation in intensive care units. In results by La Milia V *et al*. from Lombardy Italy, 13 patients out of 25 expired (52%), while 28% were discharged and sent home asymptomatic.[12]

Similar results were given by jiaH Ng, who reported 31.7% in-hospital mortality of covid-19 hemodialysis population[19]. They also found that hypertension and medications for hypertension are associated with increased mortality.

We have found higher mortality in patients who required mechanical ventilation (p=0.000), while there was no significant association noted with other factors like CRP, lymphopenia, LDH or ferritin level as found in other studies from turkey[20] and by Anthony in Columbia university hospital.[21]

Our study is limited by small sample size, single-centeredness, and lack of HRCT chest facility. Large multicenter studies are required to find out the clinical and laboratory effects of COVID-19 in this specific population.

Conclusion

Population with end stage kidney disease is susceptible to Covid-19 infection with high rates of morbidity and mortality compared with general population.

Recommendations

Strict adherence to the preventive measures is necessary in order to halt the transmission of COVID-19 infection in end stage kidney disease patients, like use of personal protective gear for hemodialysis staff and patients, keeping one patient from other patient at a safe distance during hemodialysis, routine screening of the patients and medical staff, proper isolation and management of Covid-19 PCR positive patients and hemodialysis of COVID 19 ESRD patients in isolated and specific area reserved for these patients.

References

1. Rolling updates on Corona virus disease (COVID-19) [Internet]. World Health Organization. 2020 [cited2021 Jan 14]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen
2. COVID-19 Health Advisory Platform by Ministry of National Health Services Regulations and Coordination [Internet]. 2020 [Cited 2021 Jan 14]. Available from https://covid.gov.pk
3. Goicoechea M, Sánchez Cámara LA, Macías N, Muñoz de Morales A, Rojas Á G, Bascuñana A, et al. COVID-19: clinical course and outcomes of 36 hemodialysis patients in Spain. Kidney Int. 2020;98(1):27-34. **DOI: 10.1016/j.kint.2020.04.031**
4. Madjid M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronaviruses on the Cardiovascular System: A Review. JAMA cardiology. 2020;5(7):831-40. **doi: 10.1001/jamacardio.2020.1286.**
5. Konrad R, Eberle U, Dangel A, Treis B, Berger A, Bengs K, et al. Rapid establishment of laboratory diagnostics for the novel coronavirus SARS-CoV-2 in Bavaria, Germany, February 2020. Euro Surveill. 2020;25(9) **doi: 10.2807/1560-7917.ES.2020.25.9.2000173**

6. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med. 2020;382(8):727-33 **DOI: 10.1056/NEJMoa2001017**
7. Wynants L, Van Calster B, Collins GS, Riley RD, Heinze G, Schuit E, et al. Prediction models for diagnosis and prognosis of covid-19 infection: systematic review and critical appraisal. Bmj. 2020;369:m1328. **doi: https://doi.org/10.1136/bmj.m1328**
8. Corbett RW, Blakey S, Nitsch D, Loucaidou M, McLean A, Duncan N, et al. Epidemiology of COVID-19 in an Urban Dialysis Center. JASN. 2020;31(8):1815-23. **Doi 10.1681/ASN.2020040534**
9. Li J, Xu G. Lessons from the Experience in Wuhan to Reduce Risk of COVID-19 Infection in Patients Undergoing Long-Term Hemodialysis. CJASN. 2020;15(5):717-9. **DOI: https://doi.org/10.2215/CJN.03420320**
10. Ajaimy M, Melamed ML. COVID-19 in Patients with Kidney Disease. CJASN. 2020;15(8):1087-9. **DOI: 10.2215/CJN.09730620**
11. Xiong F, Tang H, Liu L, Tu C, Tian JB, Lei CT, et al. Clinical Characteristics of and Medical Interventions for COVID-19 in Hemodialysis Patients in Wuhan, China. JASN. 2020;31(7):1387-97. **doi: 10.1681/ASN.2020030354.**
12. Wu J, Li J, Zhu G, Zhang Y, Bi Z, Yu Y, et al. Clinical Features of Maintenance Hemodialysis Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. CJASN. 2020;15(8):1139-45. **DOI: 10.2215/CJN.04160320**
13. La Milia V, Bacchini G, Bigi MC, Casartelli D, Cavalli A, Corti M, et al. COVID-19 Outbreak in a Large Hemodialysis Center in Lombardy, Italy. Kidney Int Rep. 2020;5(7):1095-9. **doi: 10.1016/j.ekir.2020.05.019**
14. Fisher M, Yunes M, Mokrzycki MH, Golestaneh L, Alahiri E, Coco M. Chronic Hemodialysis Patients Hospitalized with COVID-19: Short-term Outcomes in the Bronx, New York. Kidney360. 2020;1(8):755 **doi: 10.34067/KID.0003672020**
15. Rabaan AA, Al-Ahmed SH, Haque S, Sah R, Tiwari R, Malik YS, et al. SARS-CoV-2, SARS-CoV, and MERS-COV: A comparative overview. Le infezioni in medicina. 2020;28(2):174-84. **DOI https://doi.org/10.1186/s12941-020-00414-7**
16. Xu X, Nie S, Sun J, Kong Y, Liang M, Li D, et al. The Cumulative Rate of SARS-CoV-2 Infection in Chinese Hemodialysis Patients. Kidney Int Rep. 2020;5(9):1416-21. **DOI: 10.1016/j.ekir.2020.07.010**
17. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China]. Zhonghua liu xing bing xue za zhi = Zhonghua liuxingbingxue zazhi. 2020;41(2):145-51. **DOI: 10.3760/cma.j.issn.0254-6450.2020.02.003**
18. Alberici F, Delbarba E, Manenti C, Econimo L, Valerio F, Pola A, et al. A report from the Brescia Renal COVID Task Force on the clinical characteristics and short-term outcome of hemodialysis patients with SARS-CoV-2 infection. Kidney Int. 2020;98(1):20-6. **doi: 10.1016/j.kint.2020.04.030**
19. Ng JH, Hirsch JS, Wanchoo R, Sachdeva M, Sakhiya V, Hong S, et al.Northwell COVID-19 Research Consortium and the Northwell Nephrology COVID-19 Research Consortium. Outcomes of patients with end-stage kidney disease hospitalized with COVID-19. Kidney Int. 2020 Dec;98(6):1530-1539. **doi: 10.1016/j.kint.2020.07.030.**
20. Aydin Bahat K, Parmaksiz E, Sert S. The clinical characteristics and course of COVID-19 in hemodialysis patients. Hemodial Int. 2020 Oct;24(4):534-540. **doi: 10.1111/hdi.12861.**
21. Valeri AM, Robbins-Juarez SY, Stevens JS, Ahn W, Rao MK, Radhakrishnan J, et al.Presentation and Outcomes of Patients with ESKD and COVID-19. J Am Soc Nephrol. 2020 Jul;31(7):1409-1415. **doi: 10.1681/ASN.2020040470.**