Original Article

Single-center Haemodialysis Experience in India During COVID-19

Abstract

Introduction: Since COVID-19 has been announced as a pandemic, outcome of dialysis patients in terms of morbidity and mortality from India is lacking. We studied the clinical, epidemiological features of COVID-19 along with outcome in terms of mortality in our dialysis cohort. **Methods:** Data of End-Stage Kidney Disease (ESKD) patients who were admitted in COVID-19 designated hospital block as positive and suspected patients from 1st April 2020 to 31st July 2020 was retrieved. Data about epidemiological characteristics, clinical features, mortality outcomes of COVID-19 positive and negative patients were analyzed. **Results:** A total of 97 ESKD patients were admitted during the study period, of which 44 (45.4%) and 53 (54.6%) patients were found to be COVID-19 positive and negative respectively. The mean age of COVID positive patients was 46 years with 54.5% being female. Only three patients (6.8%) remained asymptomatic throughout the course of illness. Amongst COVID-19 positive, 20 (45.45%) were severely ill while 18 (40.9%) were having mild illnesses. Breathlessness (65.9%) and fever (61.4%) were common symptoms. The death occurred in 17 (38.6%) and 25 (47.1%) COVID-19 positive and negative ESKD patients respectively. 14 (82.3%) patients who expired amongst COVID-19 positive were having severe illness and significantly more were associated with negligible residual renal function. **Conclusions:** Breathlessness and fever were common symptoms amongst COVID-19 ESKD patients. Very few patients remained asymptomatic in our cohort and significantly more mortality is observed in severely ill patients and those with negligible residual renal function.

Keywords: *COVID-19, end-stage kidney disease (ESKD), health care workers (HCW), India*

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Introduction

Subsequent to World Health Organization (WHO) declaration of novel Corona Virus Disease -19 (COVID-19) as a pandemic**,** as of July 2020, nearly 19.4 million individuals were infected and was responsible for 722K casualties worldwide.[1] India acquired its first case on 30th January 2020. Increased morbidity and mortality are observed in older individuals especially those with hypertension, diabetes, cardiac ailments, hence making End-stage kidney patients (ESKD) patients as most vulnerable.[2]

Rapid spread of Severe Acute Respiratory Syndrome – Coronavirus 2 (SARS-CoV-2), sudden unprecedented, national wide prolonged complete lockdown, widespread fear among patients and health care workers (HCW) have seriously affected care of hemodialysis patients. Health systems have to struggle together with rapidly changing policies due to new information and assumption-based models of disease transmission. Dialysis patients inevitably need to visit healthcare facilities. Hence, travel and accompaniment make isolation difficult, making them more susceptible populations for infection.

Detailed literature about epidemiological, clinical features along with outcome of COVID-19 in ESKD and maintenance hemodialysis (MHD) patients from South East Asia is lacking. Limited data is available on 23 patients from Spain[3] and 131 patients from Zhongnam hospital, China.[4] Clinical profile and outcome of non-COVID ESKD patients admitted during the COVID pandemic is also lacking. Further, data on HCW transmission is also lacking.

Here, we report our early experience on clinical profile and patient outcomes in COVID-19 infected and noninfected ESKD patients admitted in isolated hospital block.

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Materials and Methods

Study design

This is a case series from tertiary, public sector teaching hospitals in India. Data of patients admitted from April 1, to July 31, 2020 were retrieved and analyzed. Institutional ethics committee approval was taken (Letter no. 431 (80/2020)/IEC/ABVIMS/RMLH). Only patients with ESKD who were advised renal replacement therapy and patients on maintenance hemodialysis (MHD) were included in the study. Patients with acute kidney injury (AKI), acute on chronic kidney disease (AOCKD), and CKD stage 3 and 4 were excluded.

Definitions

Severe Acute Respiratory Illness (SARI): History of fever or measured fever of ≥38° C and cough with onset within the last 10 days and requires hospitalization.[5]

COVID Positive: A person with laboratory confirmation of COVID-19 infection, irrespective of clinical signs and symptoms.

COVID Suspect: Presenting with SARI symptoms requiring admission without any report of COVID-19.

COVID negative: All patients with 10 days after symptom onset, plus at least 3 days without symptoms (without fever and respiratory symptoms) and COVID RT-PCR negative.

The illness in COVID positive ESRD patients was classified into mild, moderate, and severe according to WHO staging.[6]

Mild Disease: Patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

Moderate disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including SpO2 ≥90% on room air

Severe disease: Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress or SpO2 <90% on room air.

COVID patient flow

All patients with flu-like symptoms were reported to Flu corner zone for screening. Patients with symptoms suggestive of SARI were isolated. Those who were presenting with COVID-19 positive report were admitted in COVID-19 block and those admitted with SARI complaints suspicious of COVID-19 were admitted as "COVID suspect" in Isolation block. COVID suspect patients were labeled as COVID – Negative if the RT PCR turned out to be negative [Figure 1].

Data collection

The records of all the patients seen by the Nephrology team were reviewed and data of patients admitted in both COVID block and isolation wards was retrieved. Demographic and clinical parameters were obtained including age, gender, diabetes mellitus, hypertension, coronary heart disease, and medication history including immunosuppressive drugs, anti-hypertensive medications. The blood investigations including complete blood count, renal function tests, serum electrolytes, Liver Function tests, serology for Hepatitis B, Hepatitis C, Human Immunodeficiency Virus, urine routine and microscopy and maging whichever available were noted. All other available investigations, treatment details including residual urine output, drugs, dialysis sessions, duration of stay, and outcome of patient were recorded.

All hemodialysis sessions of COVID positive and suspect patients were performed in isolation block till they have COVID RT-PCR negative reports and asymptomatic for 3 days. The main dialysis unit was continued to be operated for non-COVID patients. Appropriate measures were taken for safe discard of dialysate by using plastic pipes connecting to proper drain system. COVID-19 RT-PCR was performed weekly till report is negative.

HCWs from Nephrology department such as dialysis technicians, resident doctors and faculty posted in COVID-19 duty were in rotation every 15 days. The patients were ensured to wear any form of mask either surgical or cloth mask. In COVID positive and suspect block, full PPE with N95 mask, full gown, goggle, and face shield were given for technical staff to carry out dialysis.

Outcomes parameters as death or discharge was noted till 31st July 2020.

Statistical analysis

The collected data was transformed into variables, coded, and entered in Microsoft Excel, and data were analyzed using SSPS software. version 24 (Inc., Chicago, Illinois, USA). Categorical variables were shown as percentages and frequencies. Continuous variables were presented as the mean ± standard deviation. For quantitative data, an independent-samples *T* test was used. Chi-square test was used for qualitative data. Difference in variables was expressed by *P* value. A value of *P* value less than 0.05 was considered statistically significant.

Results

Of the total of 218 patients, AKI, AOCKD, and non-dialysis requiring CKD stage 3 and 4 were excluded. During the study period, 97 ESKD patients on MHD were admitted in the hospital, of which 44 and 53 were COVID positive and negative patients. The death occurred in 17 and 25 COVID positive and negative patients [Table 1].

Table 1: Baseline Characteristics of COVID-19 positive and COVID-19 negative ESKD patients

Clinical Parameters	COVID-19 Positive ESKD (*n*=44) *n* (%)	COVID-19 Negative ESKD (*n*=53) *n* (%)	*P*
Age in years	46±14.2	42.1+13.6	0.17
Male	20 (45.45)	27 (50.9)	0.59
Symptomatology			
Fever	27 (61.7)	30 (56.6)	0.64
Cough	17 (38.7)	11 (20.7)	0.054
Breathlessness	29 (65.9)	26 (49.1)	0.097
Loose motions	12 (27.3)	5 (9.43)	0.096
Hemoptysis	8 (18.2)	4 (7.5)	0.285
Anosmia	1 (2.3)	0	0.36
Sore throat	3 (6.8)	0	0.11
Co-morbidities			
Diabetes Mellitus	10 (22.7)	9 (16.9)	0.82
Hypertension	37 (84.1)	45 (84.9)	0.67
Coronary Artery Disease	7 (15.9)	3 (5.6)	0.09
Hepatitis B positivity	0	1 (1.9)	0.36
Hepatitis C positivity	1 (2.3)	0	0.27
Contact History	12 (27.3)	4 (7.5)	0.009
Immunosuppressant	3 (6.8)	1 (1.9)	0.015
ACEi/ARB	1 (2.3)	1 (1.9)	0.89
Dialysis Vintage (IQR in months)	5.5 (3-8)	4 (0-12)	0.82
Death	17 (38.6)	25 (47.2)	0.40
Vascular Access			
AVF	25	23	
JTC	6	3	
JNTC	9	6	
FNTNC	4	9	

Values are presented as *n* (%) for categorical variables and as mean±standard deviation or median (IQR) for continuous variables. ACE I - Angiotensin Converting Enzyme Inhibitors, ARB - Angiotensin receptor blockers. AVF - Arteriovenous Fistula; JTC - Jugular Tunneled Catheter; JNTC - Jugular Non Tunneled Catheter; FNTC -Femoral Non Tunneled Catheter

Median duration of hospital stay was 14 (IQR 6-28) days. Only three patients amongst 44 (6.8%) who were detected positive during contact tracing remained asymptomatic throughout course of clinical illness. Ten patients remained COVID-19 RT-PCR positive for more than three weeks. History of exposure to COVID positive patient was noted in 12 (27.27%) patients. Associated comorbidities are shown in Table 1.

As per WHO classification of severity for COVID-19, 18 (40.9%), 6 (13.6%) and 20 (45.45%) patients were having mild, moderate and severe illness. In patients with mild illness, 3 patients developed sudden cardiac death during the hospital stay and the others recovered. In patients with severe illness, 14 (82.3%) of patients died, of which 12 patients were intubated during the early course of illness. All patients in moderate illness recovered and were discharged and therefore, mortality was seen in 17 (38.6%) patients. All treatment decisions were taken by physician and intensivists except the dialysis decision which was taken by Nephrology team.

Steroids were given to 6 severely ill patients (13.63%), out of which only one patient survived. Twelve patients (27.27%) admitted in initial months of COVID pandemic received Hydroxychloroquine (HCQ), while one severely ill patient received Tocilizumab but succumbed to the illness. Oseltamivir and Ivermectin was given to 15 and 3 patients respectively. Antibacterial agents were selected/changed as per the clinician's judgment. Urine output less than 200 ml/day was seen in 12 (70.58%) amongst 17 patients who expired and only in 2 patients (7.4%) of 27 patients who are alive. Table 2 shows a comparison of clinical features, biochemical and treatment parameters between alive and expired COVID positive ESKD patients.

During study period, total of 28 health care workers from the department of Nephrology were actively involved in care of COVID positive and suspect patients. Rotational duty for 15 days with 2 dialysis technicians, 2 senior resident doctors and 1 faculty were posted. None of them have developed COVID.

Discussion

In this retrospective case series, we report early experience of managing COVID-19 positive ESKD patients in tertiary public care hospital in India. There are very few studies

Table 2: Comparison of Lab parameters, Management between alive and expired patients

	Alive patients (27)	Expired patients (17)	*P*
Age (Years)	47 (32-58)	46 (36.5-55.5)	0.98
Duration of hospital stay (days)	21 (14-30)	5 (3-10.5)	0.001
Dialysis Vintage (Months)	6 (3-8)	5 (2.5-9)	0.88
Vascular access			0.76
Catheter	11	8	
Fistula	16	9	
Co-morbidities			
Diabetes	4	6	0.15
Coronary artery disease	3	4	0.40
Hypertension	23	14	1
Number of patients with Residual urine output <200 ml/day	2	12	0.001
Symptoms			
Fever	17	10	1
Cough	10	7	1
Breathlessness	15	14	0.10
Loose motions	6	6	0.49
Hemoptysis	3	5	0.23
Investigations:			
Hemoglobin gm/dl	8.63±1.69	7.83±1.55	0.13
Leucocyte count per µL (IQR)	8800 (4500-12000)	11000 (6250-14150)	0.27
Platelet count lac/µL	1.6 (1.5-2)	1.76 (1.54-2.25)	0.51

Values are presented as absolute numbers (*n*) for categorical variables and as mean±SD or median (Interquartile range) continuous variables. Data was compared with unpaired *t* test or Fischer's exact test

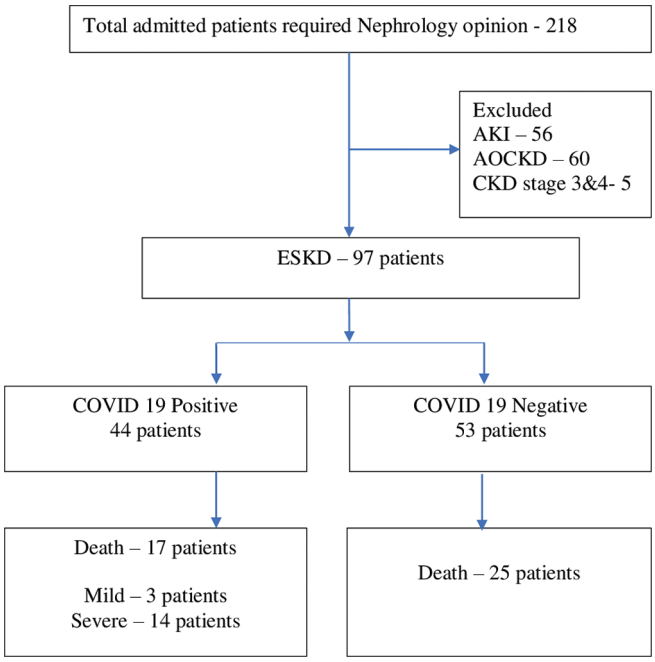

Figure 1: Patient flow and outcome of ESRD patients with and without COVID 19. (AKI – Acute Kidney Injury, AOCKD – Acute on CKD, CKD – Chronic Kidney Disease, ESKD – End Stage Kidney Disease)

from India documenting the experience of performing dialysis for COVID-positive patients. Ours was one of the COVID designated hospital. All COVID positive and suspected patients were dialyzed bedside in an isolation block to prevent spread of infection in hospital premises during the transfer as recommended by Indian Society of Nephrology guidelines endorsed by MOHFW.[7]

During this pandemic, our data shows the majority of the ESKD patients admitted were of non-COVID, reflecting that the nonspecific SARI symptoms mainly fever and breathlessness were commonly present in these patients probably because of other community-acquired or catheter-related infections and overall volume overload state. Many patients who presented with breathlessness amongst COVID negative group improved with dialysis. This may be due to missing hemodialysis sessions as some of the dialysis centers were not accepting any symptomatic patients leading to delayed referral to our center.The unprecedented lockdown, closure of day care dialysis units, higher fear and suspicion of COVID with SARI symptoms causes referral and delayed presentation, which accounted for much higher mortality seen in non COVID than COVID-19 positive patients. Re-allocation of health care to COVID-19 related illness, management of patient by SARI physicians than Nephrologist and the delay in dialysis initiation might also be responsible for higher mortality in non COVID patients apart from the higher incidence of sepsis and cardiac death in ESKD patients. This study highlights importance of reinforcement of care to non-COVID ESKD patients when the whole health system was allocated to COVID-19 related admissions.

COVID-19 positives in our center were younger (46 ± 16 years) when compared with similar group of 131 patients reported from Wuhan (63.2 ± 13.1 years)[4] and 25 patients from Spain (66 ± 15 years).[3] The co-morbid illness including diabetes (22.72%) and coronary artery disease (15.9%) was less when compared with series from Spain (48% and 32% respectively). This may be due to much younger patients in our series. In the initial report from Zhongnan Hospital of Wuhan University, China,[8] most common symptoms were fever (98.6%), fatigue (69.6%) and dry cough (59.4%) while lymphopenia was seen in 70.3% of patients. In our cohort of mainly CKD MHD patients, the most common symptoms were breathlessness (65.90%) followed by fever (61.36%) and cough (38.63%). Fever as presenting symptoms was much less common when compared with non- CKD COVID positive patients. In a series of 5 CKD-MHD patients from China, most common symptom was diarrhea (80%). This is in contrast with our observation twelve patient (27.27%) on presentation had complaints of loose motion.[9] Common presentation of breathlessness can be attributed to closure of the outpatient dialysis centers leading to delayed presentation with fluid overload. In our cohort, presentation with leukopenia was not commonly observed even in severely ill patients.

In a case series of 37 patients from Mumbai, India, mortality was observed in 37.8% of patients which is similar to seen in our study.[10] Similar high mortality of 30.5% is also observed in series of 36 maintenance hemodialysis patients from Spain.[11] In our series, 14 patients (88.23%) amongst 17 expired patients were severely ill at the time of presentation. They were associated with decreased hospital stay due to high rate mortality and delayed presentation to health care facilities. Another factor associated with increased mortality was absence of residual renal function, making them more prone to develop volume overload state. These patients as such could not tolerate the delay in dialysis and seeking healthcare facility early becomes difficult due to travel restrictions and vehicle availability.[12] Investigations such procalcitonin, serum Ferritin, D-dimer and Interleukin-6 were not available in-house, hence majority of decisions were guided by clinical features. Significant mortality observed in patients admitted in COVID suspect ward and later turning COVID negative is an important finding, reported here for the first time. Lack of adequate care and delayed presentation in this group can be attributed for the same. In addition it is worth to check COVID antibodies amongst survivors in COVID-19 negative group who may have been missed by conventional diagnostic strategy.

Though MOHFW guidelines suggest not reducing dialysis frequency, dialysis sessions were delayed under observation to cater to maximum number of patients with available resources. As per EUDIAL working group of ERA EDTA,[13] all symptomatic patients should wear a proper surgical or N95 mask. In our setting due to lack availability of N95 masks, it was ensured that all patients used cloth or triple layer surgical masks. Since hardness of raw water was more than 1000 ppm, portable Reverse Osmosis (RO) unit could not be utilized. In this unexpected pandemic situation, the crisis was effectively managed with portable RO tank which became the able solution to provide bedside dialysis. Although water quality, infection and disinfection of tank were major concerns, but we found no significant adverse events with the use of portable RO tank. In the absence of much data on the use of portable tank, we document this as a solution for water transport till the much better solutions for water quality is available. DIASAFE© plus or CF – 609 Endotoxin retention filter© was used in all dialysis.

Although dialyzer reprocessing and reuse is being done in routine dialysis unit, it was avoided in isolation dialysis due to uncertain risk of infection. In our setup, investigation work up of COVID-19 suspect and positive patients were restricted only to essential studies. Hence as per hospital policy, use of imaging studies was restricted and was done only when definitely indicated for patient management. American College of Radiology recommends against use of routine CT for screening for COVID-19 infection.[14]

Prolonged shedding of virus is hemodialysis patients has been reported from Japan.[15] In our series, 10 patients had SARS COVID-19 RT-PCR positivity for more than 21 days. Maximum positivity was noted up-to 9 weeks after 1st report. All our patients were discharged in the initial months after 2 consecutive COVID negative reports but with more evidence available, from the month of June, patients were discharged after 3 days of asymptomatic period with a single COVID-19 negative RT PCR report. With the availability of adequate scientific data, about lack of infectivity amongst prolonged virus shedders, repeat COVID testing can be omitted. This needs to be accompanied by awareness amongst out-patient dialysis centres about the same as many patients may be denied for dialysis till documentation COVID-19 negative RT-PCR.

In our study, none of the HCW worker involved in dialysis care of these patients developed COVID-19 infection. This may be attributed to frequent hand washing and cough etiquette, appropriate PPE and repeated training of dialysis staffs about environmental disinfection after COVID exposure.[16]

Transfer of COVID positive or suspect patient to dialysis facility, making dedicated shifts for suspect patients in already limited slot availability, segregation of man power including technicians for COVID shifts and arrangement of space for donning and doffing in dialysis room are some of the primary challenges for converting unit into COVID compatible dialysis center. Decision about the same can be taken on need basis as the patient load increases. Till then bedside dialysis remains the viable option. Major limitation of dialyzing patient in isolation ward is increasing number presenting to our facility probably

related to closure of other tertiary care hospitals, hence more COVID designated dialysis units should be made operational and new units should be developed. Hence, pragmatic and realistic solutions to overcome existing problem of haemodialysis needs urgent attention and co-ordination amongst different stakeholders. Retrospective nature of study, unavailability of in-house investigations for C-Reactive Protein, d dimer, ferritin, Interleukin 6, incomplete data regarding the use of anticoagulation are the lacunae of the study. In the absence of outcome data in ESKD patients from India, this study highlights the clinical features, outcomes of COVID-19 infection and higher mortality seen in non-COVID patients.

Conclusion

There is significant mortality in severely ill COVID-19 positive and non-COVID ESKD patients. Breathlessness and fever were common symptoms. Very few patients remained asymptomatic throughout study period. Significantly more mortality is observed in patients without residual urine output.

Human and Animal Rights (with IRB Approval number)

This is retrospective case series. Ethics committee clearance received on 21st September 2020 letter no. 431 (80/2020)/IEC/ABVIMS/RMLH.

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Conflicts of interest

There are no conflicts of interest.

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